IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

• EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

WARNINGS AND PRECAUTIONS

• Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.

• Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.

• There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

This material is intended for use by payers, formulary committees, or other similar entities for purposes of population-based drug selection, coverage, and/or reimbursement decision making, pursuant to FD&C Act Section 502(a).

EYLEA is a registered trademark of Regeneron Pharmaceuticals, Inc.

© 2021, Regeneron Pharmaceuticals, Inc. All rights reserved.

777 Old Saw Mill River Road, Tarrytown, NY 10591
ADVERSE REACTIONS

• Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.
• The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.
• Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

INDICATIONS

EYLEA® (aflibercept) Injection 2 mg (0.05 mL) is indicated for the treatment of patients with Neovascular (Wet) Age-related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).

References:

07/2021
EYL.21.070030

Please see Brief Summary of full Prescribing Information on the following page.
Adverse Reactions

| Table 1 | Most Common Adverse Reactions (≥ 3%) in Wet AMD Studies | Table 2 | Most Common Adverse Reactions (≥ 3%) in RVO Studies |

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Baseline to Week S2</th>
<th>Baseline to Week 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline to Week 52</td>
<td>Baseline to Week 96</td>
<td>EYLEA (N=152)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EYLEA (N=578)</td>
</tr>
<tr>
<td>Conjunctival hemorrhage</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>Nausea</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Eye pain</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>Thromboembolic events</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Conjunctival hemorrhage</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Nausea</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Eye pain</td>
<td>7%</td>
<td>7%</td>
</tr>
</tbody>
</table>

Less common adverse reactions reported in ≤ 3% of patients treated with EYLEA were hyperpigmentation, retinal detachment, and visual field defects.

Macular Edema Following Retinal Vein Occlusion (RVO): The data described below reflect exposure to EYLEA in 1824 patients treated with the 2 mg dose in 2 double-masked, controlled clinical studies (VIVID and VISTA) from baseline to week 52 and from baseline to week 100.

Adverse Reactions

<table>
<thead>
<tr>
<th>Baseline to Week S2</th>
<th>Baseline to Week 100</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Conjunctival hemorrhage</td>
<td>9%</td>
</tr>
<tr>
<td>Nausea</td>
<td>4%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4%</td>
</tr>
<tr>
<td>Eye pain</td>
<td>9%</td>
</tr>
<tr>
<td>Thromboembolic events</td>
<td>2%</td>
</tr>
<tr>
<td>Conjunctival hemorrhage</td>
<td>3%</td>
</tr>
<tr>
<td>Nausea</td>
<td>2%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2%</td>
</tr>
<tr>
<td>Eye pain</td>
<td>7%</td>
</tr>
</tbody>
</table>

Less common adverse reactions reported in ≤ 3% of patients treated with EYLEA were hyperpigmentation, retinal detachment, and visual field defects.

EYLEA is a vascular endothelial growth factor (VEGF) inhibitor indicated for the treatment of patients with Neovascular (Wet) Age-Related Macular Degeneration (AMD), Macular Edema Following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).
Chairman’s Letter

Our emerging health leaders cover story has become a high point in our editorial calendar. This year we increased the roster of up-and-comers to a baker's dozen. It just became too difficult to boil down the list to the usual 10. As always, the range of backgrounds, talents, training and experiences is inspiring. The inventiveness and vibrancy of American healthcare shines through even with the COVID-19 pandemic still casting an unpredictable shadow over the country.

Some of the leaders we feature in this issue are climbing ladders at the most recognizable boldface names and acronyms of American healthcare: Optum, Express Scripts, Horizon Blue Cross Blue Shield of New Jersey, ICER and UPMC. Others are in the exciting world of startups, innovating and possibly disrupting the status quo. For all its problems and expense, healthcare is one of the most dynamic parts of the American economy. We have its entrepreneurs to thank for that.

We are also proudly featuring the 2021 Pharmacy Benefit Management Institute® Annual National Conference in this issue. Managed Healthcare Executive® is the official publication of PBMI®, and MJH Life Sciences™ welcomed the institute into its portfolio last year. The format for this three-day conference was a hybrid model, with some in-person attendees in Orlando, Florida, and others participating remotely. But almost every speaker mentioned how good it felt to be “unZoomed” and back at an in-person event. The presentations covered everything from digital therapeutics to utilization management to interoperability. Scott Gottlieb, M.D., the former FDA commissioner and the keynote speaker, was sanguine about the near-term future of the pandemic — he is not overly concerned about variants, for example — and also about a forever-changed healthcare system that will be delivering more and more care at home because of telehealth and at-home testing.

So we hope you leave this issue with a sense of optimism. The future of the PBMI conference is bright. And we have emerging health leaders guiding us and American healthcare on a promising path forward.

Mike Hennessy Sr.
Chairman and Founder of MJH Life Sciences™
2021 PBMI® ANNUAL NATIONAL CONFERENCE

44 Scott Gottlieb, M.D., former FDA commissioner
46 Kerri Tanner, Optum
48 Kim Diehl-Boyd, CoverMyMeds
50 Javier Gonzalez, Abarca
52 David Skomo and Nick Page, WellDyne
52 Thatcher Sloan, Confidio

13 EMERGING HEALTH LEADERS

12 As healthcare sees a shiny future with AI, some see some glare
32 Drugmakers look to quell COVID-19 cytokine storms
42 Network adequacy rules for cancer care are often inadequate

TECHNOLOGY

DRUGS IN THE PIPELINE

ONCOLOGY

DEPARTMENTS

10 Editorial Advisory Board

Managed Healthcare Executive® ISSN 1533-9300, Digital ISSN 2150-7120 is published monthly by MJH Life Sciences™, 2 Clarke Drive, Suite 100 Cranbury, NJ 08512. Subscription rates: 1 year $99.00, 2 years $145.00 in the United States & Possessions; 1 year $122.00, 2 years $173.25 in Canada and Mexico; 1 year $192.00, 2 years $295.00 in all other countries. For air-expedited service, include an additional $87.00 per order annually. Single copies (prepaid only): $9.00 in the United States, $22.00 all other countries. Back issues, if available: $15.00 in the U.S.; $17.00 all other countries. Include $6.85 per order plus $2 per additional copy for U.S. postage and handling. If shipping outside the U.S., include an additional $10 per order plus $3 per additional copy.

Managed Healthcare Executive does not verify any claims or other information appearing in any of the advertisements contained in the publication and cannot take responsibility for any losses or other damages incurred by readers in reliance of such content.

Managed Healthcare Executive® welcomes unsolicited articles, manuscripts, photographs, illustrations and other materials but cannot be held responsible for their safekeeping or return.

Library Access: Libraries offer online access to current and back issues of Managed Healthcare Executive® through the EBSCOhost databases.

To subscribe, call toll-free 888-527-7006. Outside the U.S. call 218-760-6477.

Managed Healthcare Executive® does not verify any claims or other information appearing in any of the advertisements contained in the publication and cannot take responsibility for any losses or other damages incurred by readers in reliance of such content.

Managed Healthcare Executive® welcomes unsolicited articles, manuscripts, photographs, illustrations and other materials but cannot be held responsible for their safekeeping or return.

Library Access: Libraries offer online access to current and back issues of Managed Healthcare Executive® through the EBSCOhost databases.

To subscribe, call toll-free 888-527-7006. Outside the U.S. call 218-760-6477.
For your appropriate members with uncontrolled moderate-to-severe atopic dermatitis (AD)

**INDICATION**

DUPIXENT is indicated for the treatment of patients aged 6 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. DUPIXENT can be used with or without topical corticosteroids.

**IMPORTANT SAFETY INFORMATION**

**CONTRAINDICATION:** DUPIXENT is contraindicated in patients with known hypersensitivity to dupilumab or any of its excipients.

**WARNINGS AND PRECAUTIONS**

**Hypersensitivity:** Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum, anaphylaxis and serum sickness or serum sickness-like reactions, were reported in <1% of subjects who received DUPIXENT in clinical trials. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT.

**Conjunctivitis and Keratitis:** Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received DUPIXENT. Conjunctivitis was the most frequently reported eye disorder. Most subjects with conjunctivitis or keratitis recovered or were recovering during the treatment period. Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information on the following pages.

IL, interleukin.

**APPROVED FOR A BROAD AGE RANGE**

6+ YEARS OF AGE

Real adult and adolescent patients treated with DUPIXENT. Individual results may vary. Child is not an actual patient.

**RAPID AND SUSTAINED RESULTS**

in adults

**DEMONSTRATED LONG-TERM SAFETY PROFILE**

in adults

• **DUPIXENT IS A DUAL INHIBITOR OF IL-4 AND IL-13 SIGNALING**

• **DUPIXENT AVOIDS BROAD IMMUNOSUPPRESSION**
  – It is unknown if DUPIXENT will influence the immune response against helminth infections

**INDICATION**

DUPIXENT is indicated for the treatment of patients aged 6 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. DUPIXENT can be used with or without topical corticosteroids.

**IMPORTANT SAFETY INFORMATION**

**CONTRAINDICATION:** DUPIXENT is contraindicated in patients with known hypersensitivity to dupilumab or any of its excipients.

**WARNINGS AND PRECAUTIONS**

**Hypersensitivity:** Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum, anaphylaxis and serum sickness or serum sickness-like reactions, were reported in <1% of subjects who received DUPIXENT in clinical trials. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT.

**Conjunctivitis and Keratitis:** Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received DUPIXENT. Conjunctivitis was the most frequently reported eye disorder. Most subjects with conjunctivitis or keratitis recovered or were recovering during the treatment period. Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

Please see additional Important Safety Information and Brief Summary of full Prescribing Information on the following pages.

IL, interleukin.
IN A CHRONIC SYSTEMIC DISEASE...

Review the data and important considerations for this long-term treatment

**Itch relief after the first dose (as measured at Week 2) and skin clearance sustained at 1 year in adults taking DUPIXENT + TCS**

**Adult safety profile across 52 weeks generally consistent with Week 16**

Most common adverse reactions (incidence ≥1% at Week 16) in adult patients with atopic dermatitis are injection site reactions, conjunctivitis, blepharitis, oral herpes, keratitis, eye pruritus, other herpes simplex virus infection, and dry eye.

The safety profile in children and adolescents through Week 16 was similar to that of adults with atopic dermatitis.

**TRIAL RESULTS:** The primary endpoint in Trials 3 and 6 was change from baseline in the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and ≥2-point improvement at Week 16 (39% of adults treated with DUPIXENT + TCS vs 12% with placebo + TCS in Trial 3, \(P<0.0001\); and 24% of adolescents treated with DUPIXENT vs 2% with placebo in Trial 6, \(P<0.001\)). In Trial 8, the primary endpoint was change from baseline in the proportion of subjects with an IGA 0 or 1 at Week 16 (39% of children ≥30 kg treated with DUPIXENT + TCS vs 10% with placebo + TCS, and 30% of children <30 kg treated with DUPIXENT + TCS vs 13% with placebo + TCS). Other endpoints included change from baseline in the proportion of subjects with EASI72 at Week 16 (improvement of ≥75%; 69% of adults treated with DUPIXENT + TCS vs 23% with placebo + TCS in Trial 3, \(P<0.0001\); 42% of adolescents treated with DUPIXENT vs 8% with placebo in Trial 6, \(P<0.001\); 75% of children ≥30 kg treated with DUPIXENT + TCS vs 26% with placebo + TCS, and 75% of children <30 kg treated with DUPIXENT + TCS vs 28% with placebo + TCS in Trial 8); and itch reduction defined by ≥4-point improvement in the Peak Pruritus NRS at Week 16 (59% of adults treated with DUPIXENT + TCS vs 20% with placebo + TCS in Trial 3, \(P<0.0001\); 37% of adolescents treated with DUPIXENT vs 5% with placebo in Trial 6, \(P<0.001\); 61% of children ≥30 kg treated with DUPIXENT + TCS vs 13% with placebo + TCS, and 50% of children <30 kg treated with DUPIXENT + TCS vs 12% with placebo + TCS in Trial 8). Trial 3 also assessed endpoints at Week 52. IGA: 36% of adults treated with DUPIXENT + TCS vs 13% with placebo + TCS; EASI-75: 65% of adults treated with DUPIXENT + TCS vs 22% with placebo + TCS; Peak Pruritus NRS: 51% of adults treated with DUPIXENT + TCS vs 13% with placebo + TCS; \(P<0.0001\). In Trial 3, improvement was seen as early as at Week 2, with EASI-75 achieved by ≥20% of adults treated with DUPIXENT + TCS vs ≥9% with placebo + TCS (post-hoc analysis), and itch reduction (≥4-point improvement in the Peak Pruritus NRS) achieved by ≥18% of adults treated with DUPIXENT + TCS vs 8% with placebo + TCS (\(P<0.0002\)).

**IMPORTANT SAFETY INFORMATION (cont’d)**

**WARNINGS AND PRECAUTIONS (cont’d)**

**Reduction of Corticosteroid Dosage:** Do not discontinue systemic, topical or inhaled corticosteroids abruptly upon initiation with DUPIXENT. Reductions in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

**Atopic Dermatitis Patients with Comorbid Asthma:** Advise patients not to adjust or stop their asthma treatments without consultation with their physicians.

**Parasitic (Helminth) Infections:** It is unknown if DUPIXENT will influence the immune response against helminth infections. Treat patients with pre-existing helminth infections before initiating therapy with DUPIXENT. If patients become infected while receiving treatment with DUPIXENT and do not respond to anti-helminth treatment, discontinue treatment with DUPIXENT until the infection resolves.

**BSA, body surface area; Q2W, once every 2 weeks; Q4W, once every 4 weeks.**

**SANOFI GENZYME**

**REGENERON**

© 2021 Sanofi and Regeneron Pharmaceuticals, Inc. All Rights Reserved.

**DUPXENT®** is a registered trademark of Sanofi Biotechnology.
SELECT IMPORTANT SAFETY INFORMATION

WARRIORS AND PRECAUTIONS

Hypersensitivity: Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum, anaphylaxis and serum sickness or serum sickness-like reactions, were reported in <1% of subjects who received DUPIXENT in clinical trials. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT.

Please see additional Important Safety Information below.

TRIAL DESIGNS: A total of 251 adolescents in Trial 6, 367 children (6-11 years of age) in Trial 8 (16 weeks each), and 421 adults in Trial 3 (52 weeks) with moderate-to-severe atopic dermatitis inadequately controlled with topical prescription therapies were randomized to DUPIXENT or placebo. All patients in Trials 3 and 8 received concomitant TCS. All DUPIXENT-treated adults and adolescents ≥60 kg received 300 mg Q2W after a 600 mg loading dose. Adolescents <60 kg and children ≥30 kg but <60 kg received 200 mg Q2W after a 400 mg loading dose. Children 15 kg but <30 kg received 300 mg Q4W after a 600 mg loading dose. In Trials 3 and 6, patients had moderate-to-severe disease, with an IGA score ≥3 (overall lesion severity scale of 0 to 4), an EASI score ≥16 on a scale of 0 to 72, and BSA involvement ≥10%. In Trial 8, patients had an IGA score of 4 (severe), an EASI score ≥21, and BSA involvement ≥30%. At baseline, ≥50% of adults and ≥40% of adolescents had an IGA score of 3 (moderate), 50% of adults and 35% of adolescents had an IGA of 4 (severe) mean EASI score was 31 for adults, 36 for adolescents, and 37.9 for children; weekly averaged Peak Pruritus NRS was 7.7 for adults, 8 for adolescents, and 7.8 for children, on a scale of 0 to 10.15

IMPORTANT SAFETY INFORMATION (cont’d)

ADVERSE REACTIONS: The most common adverse reactions (incidence ≥1% at Week 16) in adult patients with atopic dermatitis are injection site reactions, conjunctivitis, blepharitis, oral herpes, keratitis, eye pruritus, other herpes simplex virus infection, and dry eye. The safety profile in children and adolescents through Week 16 was similar to that of adults with atopic dermatitis. In an open-label extension study, the long-term safety profile of DUPIXENT in adolescents and children observed through Week 52 was consistent with that seen in adults with atopic dermatitis.

DRUG INTERACTIONS: Avoid use of live vaccines in patients treated with DUPIXENT.

USE IN SPECIFIC POPULATIONS

• Pregnancy: There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to DUPIXENT during pregnancy. Healthcare providers and patients may call 1-877-511-8972 or go to https://mothertobaby.org/ongoing-study/dupixent/ to enroll in or obtain information about the registry. Available data from case reports and case series with DUPIXENT use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, DUPIXENT may be transmitted from the mother to the developing fetus.

• Lactation: There are no data on the presence of DUPIXENT in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for DUPIXENT and any potential adverse effects on the breastfed child from DUPIXENT or from the underlying maternal condition.

BSA, body surface area; Q2W, once every 2 weeks; Q4W, once every 4 weeks.

Please see Brief Summary of full Prescribing Information on the following pages.
DUPIXENT® (dupilumab) injection, for subcutaneous use Rx only

Brief Summary of Prescribing Information

1 INDICATIONS AND USAGE

1.1 Atopic Dermatitis

DUPIXENT® is indicated for the treatment of patients aged 6 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. DUPIXENT can be used with or without topical corticosteroids.

2 CONTRAINDICATIONS

DUPIXENT is contraindicated in patients who have known hypersensitivity to dupilumab or any of its excipients [see Warnings and Precautions (5.1)].

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum and serum sickness or serum sickness-like reactions, were reported in less than 1% of subjects who received DUPIXENT in clinical trials. Two subjects in the atopic dermatitis development program experienced serum sickness or serum sickness-like reactions that were associated with high titers of antibodies to dupilumab. If a clinically significant hypersensitivity reaction occurs, institute appropriate therapy and discontinue DUPIXENT [see Adverse Reactions (6.1, 6.2)].

5.2 Conjunctivitis and Keratitis

Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received DUPIXENT. Conjunctivitis was the most frequently reported eye disorder. Most subjects with conjunctivitis or keratitis recovered or were recovering during the treatment period [see Adverse Reactions (6.1)].

Advise patients to report new onset or worsening eye symptoms to their healthcare provider.

5.5 Reduction of Corticosteroid Dosage

Do not discontinue systemic, topical, or inhaled corticosteroids abruptly upon initiation of therapy with DUPIXENT. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in inhaled corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.

5.6 Patients with Comorbid Asthma

Advise patients with atopic dermatitis who have co-morbid asthma not to adjust or stop their asthma treatments without consultation with their physicians.

5.7 Parasitic (Helminth) Infections

Patients with known helminth infections were excluded from participation in clinical studies. It is unknown if DUPIXENT will influence the immune response against helminth infections.

Treat patients with pre-existing helminth infections before initiating therapy with DUPIXENT. If patients become infected while receiving treatment with DUPIXENT and do not respond to antihelminthic treatment, discontinue treatment with DUPIXENT until the infection resolves.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail elsewhere in the labeling:

• Hypersensitivity [see Warnings and Precautions (5.1)]
• Conjunctivitis and Keratitis [see Warnings and Precautions (5.2)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adults with Atopic Dermatitis

Three randomized, double-blind, placebo-controlled, multicenter trials (Trials 1, 2, and 3) and one dose-ranging trial (Trial 4) evaluated the safety of DUPIXENT in subjects with moderate-to-severe atopic dermatitis. The safety population had a mean age of 38 years; 41% of subjects were female, 67% were white, 24% were Asian, and 6% were black, in terms of comorbid conditions, 48% of the subjects had asthma, 49% had allergic rhinitis, 37% had food allergy, and 27% had allergic conjunctivitis. In these 4 trials, 1472 subjects were treated with subcutaneous injections of DUPIXENT, with or without concomitant topical corticosteroids (TCS).

A total of 739 subjects were treated with DUPIXENT for at least 1 year in the development program for moderate-to-severe atopic dermatitis. Trials 1, 2, and 3 are 48-week (Trials 1 and 2; and 16 weeks (Trial 3)) studies to evaluate the safety of DUPIXENT therapy to placebo through Week 16. Trial 3 compared the safety of DUPIXENT + TCS to placebo + TCS through Week 52. Trials 0 to 16 (Trials 1, 2, and 4) through Week 16. Trials 1 and 2 compared the adverse reactions that occurred at a rate of at least 1% in the DUPIXENT 300 mg Q2W and placebo groups.

Table 2 summarizes the adverse reactions that occurred at a rate of at least 1% in the DUPIXENT 300 mg Q2W and placebo groups. DUPIXENT + TCS group, all at a higher rate than in their respective comparator groups during the first 16 weeks of treatment.

| Table 2: Adverse Reactions Occurring in ≥1% of the DUPIXENT Monotherapy Group or the DUPIXENT + TCS Group in the Atopic Dermatitis Trials through Week 16 |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| **Adverse Reaction**        | **DUPIXENT Monotherapy**    | **DUPIXENT + TCS**          |
| Injection site reactions    |                51 (10) | 28 (5) | 11 (10) | 18 (6) |                51 (10) | 12 (2) | 10 (9) | 15 (5) |                |
| Blepharitis                  | 2 (<1) | 1 (<1) | 5 (5) | 2 (1) | 2 (<1) | 1 (<1) | 4 (4) | 0 (0) | 2 (2) | 1 (<1) |
| Oral herpes                  | 20 (4) | 8 (2) | 3 (3) | 5 (2) | 10 (2) | 6 (1) | 1 (1) | 1 (<1) | 10 (2) | 6 (1) | 1 (1) | 1 (<1) |
| Keratitis                    | 1 (<1) | 0 (0) | 4 (4) | 0 (0) | 1 (<1) | 0 (0) | 2 (2) | 1 (1) | 1 (<1) | 0 (0) | 2 (2) | 1 (1) |
| Eye pruritus                 | 3 (1) | 1 (<1) | 2 (2) | 1 (1) | 1 (<1) | 0 (0) | 2 (2) | 1 (1) | 1 (<1) | 0 (0) | 2 (2) | 1 (1) |
| Other herpes simplex virus infection | 10 (2) | 6 (1) | 1 (1) | 1 (<1) | 10 (2) | 6 (1) | 1 (1) | 1 (<1) | 10 (2) | 6 (1) | 1 (1) | 1 (<1) |
| Dry eye                     | 1 (<1) | 0 (0) | 2 (2) | 1 (1) | 1 (<1) | 0 (0) | 2 (2) | 1 (1) | 1 (<1) | 0 (0) | 2 (2) | 1 (1) |

*Pooled analysis of Trials 1, 2, and 4.

8 USE IN SPECIFIC POPULATIONS

8.5 Geriatric Use

Use of DUPIXENT in this age group is supported by Trial 6 which included patients 6 years of age and older with moderate-to-severe atopic dermatitis. The safety of DUPIXENT in these subjects through Week 16 was similar to the safety profile from studies in adults with atopic dermatitis.

The long-term safety of DUPIXENT was assessed in an open-label extension study in subjects 12 to 17 years of age with moderate-to-severe atopic dermatitis (Trial 7). The safety profile of DUPIXENT in subjects followed through Week 52 was similar to the safety profile observed at Week 16 in Trial 6. The long-term safety profile of DUPIXENT observed in adolescents was consistent with that seen in adults with atopic dermatitis.

Children with Atopic Dermatitis (6 to 11 Years of Age)

The safety of DUPIXENT was assessed in a trial of 250 subjects 12 to 17 years of age with moderate-to-severe atopic dermatitis (Trial 6). The safety profile of DUPIXENT in these subjects through Week 16 was similar to the safety profile from studies in adults with atopic dermatitis.

The long-term safety of DUPIXENT was assessed in an open-label extension study of 368 subjects 6 to 11 years of age with atopic dermatitis (Trial 7). Among subjects who entered this study, 19% had moderate and 72% (20%) had severe atopic dermatitis at the time of enrollment in Trial 7. The safety profile of DUPIXENT + TCS in subjects followed through Week 52 was similar to the safety profile observed through Week 16 in Trial 8. The long-term safety profile of DUPIXENT + TCS observed in pediatric subjects was consistent with that seen in adults and adolescents with atopic dermatitis [see Pediatric Use (8.4)].

Specific Adverse Reactions

Conjunctivitis and Keratitis

During the 52-week treatment period of concomitant therapy atopic dermatitis trial (Trial 3), conjunctivitis was reported in 1% of the DUPIXENT 300 mg Q2W + TCS group (20 per 100 subject-years) and in 9% of the placebo + TCS group (10 per 100 subject-years). In DUPIXENT atopic dermatitis monotherapy trials (Trials 1, 2, and 4) through Week 16, keratitis was reported in <1% of the DUPIXENT group (1 per 100 subject-years) and in 0% of the placebo group (0 per 100 subject-years). In the 52-week atopic dermatitis DUPIXENT + TCS trial (Trial 3), keratitis was reported in 4% of the DUPIXENT + TCS group (12 per 100 subject-years) and in 0% of the placebo + TCS group (0 per 100 subject-years). Most subjects with conjunctivitis or keratitis recovered or were recovering during the treatment period [see Warnings and Precautions (5.2)].

Eczema Herpeticum and Herpes Zoster

The rate of eczema herpeticum was similar in the placebo and DUPIXENT groups in the atopic dermatitis trials. Herpes zoster was reported in <0.1% of the DUPIXENT groups (<1 per 100 subject-years) and in <0.1% of the placebo group (1 per 100 subject-years) in the 16-week atopic dermatitis monotherapy trials. In the 52-week DUPIXENT + TCS atopic dermatitis trial, herpes zoster was reported in 1% of the DUPIXENT + TCS group (1 per 100 subject-years) and 2% of the placebo + TCS group (2 per 100 subject-years).
4 trials, 1472 subjects were treated with subcutaneous injections of DUPIXENT in subjects with moderate-to-severe atopic dermatitis. Because clinical trials are conducted under widely varying conditions, 6 ADVERSE REACTIONS with DUPIXENT and do not respond to antihelminth treatment, discontinue. Patients with known helminth infections were excluded from participation. Advise patients with atopic dermatitis who have comorbid asthma not to withdraw systemic corticosteroids.

5.1 Hypersensitivity

Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum, and anaphylaxis [see Warnings and Precautions (5.1)].

4 CONTRAINDICATIONS

DUPIXENT is contraindicated in patients who have known hypersensitivity to the other active components of the Adacel and a meningococcal polysaccharide vaccine (Adacel®) and a meningococcal polysaccharide vaccine (Menomune®). Antibody responses to tetanus toxoid and serogroup C meningococcal polysaccharide were assessed 4 weeks later. Antibody responses to both tetanus vaccine and meningococcal polysaccharide vaccine were similar in dupilumab-treated and placebo-treated subjects. Immune responses to the other active components of the Adacel and Menomune vaccines were not assessed.

300 mg Q2Wc n (%)

10/1/21   11:01 AM

MHE1021_005-009_Dupixent.indd   9

Manufactured by: Regeneron Pharmaceuticals, Inc., Tarrytown, NY 10591 U.S. License # 1760; Marketed by sanofi-aventis U.S. LLC, (Bridgewater, NJ


Cynthia Hundorfean is president and CEO of Allegheny Health Network (AHN), an integrated healthcare delivery system that serves Western Pennsylvania. AHN is part of the Highmark Health family of companies.

Otis Brawley, M.D., is the Bloomberg Distinguished Professor of Oncology and Epidemiology at Johns Hopkins University and former chief medical and scientific officer of the American Cancer Society.

John Mathewson is chief operating officer for America’s Health Insurance Plans (AHIP), the national trade association that advocates for the health insurance community and the consumers they serve across the nation.

Ateev Mehrotra, M.D., M.P.H., is an associate professor of health care policy at Harvard Medical School and a hospitalist at Beth Israel Deaconess Medical Center in Boston.

John Mathewson is chief operating officer for America’s Health Insurance Plans (AHIP), the national trade association that advocates for the health insurance community and the consumers they serve across the nation.

Ateev Mehrotra, M.D., M.P.H., is an associate professor of health care policy at Harvard Medical School and a hospitalist at Beth Israel Deaconess Medical Center in Boston.

Margaret A. Murray, M.P.A., is the founding CEO of the Association for Community Affiliated Plans, which represents 54 non-profit safety net health plans in 26 states.

David Calabrese, RPh, M.H.P., is market president, Health Plans/PBMs at OptumRx, a pharmacy benefits firm that provides services for more than 65 million lives nationally.

Kevin Ronneberg, M.D., is vice president and associate medical director for health initiatives at HealthPartners, an integrated, non-profit provider and health insurance company located in Bloomington, Minnesota.

Marc Samuels, J.D., M.P.H., is the CEO of ADVI, a strategic advisory services life sciences firm in Washington, D.C.

Perry Cohen, Pharm.D., is CEO of The Pharmacy Group and the TPG family of companies, which provides services to associations, health plans, PBMs and pharmaceutical companies.

Rodrigo Cerdá, M.D., M.P.H., is vice president of clinical care transformation at Independence Blue Cross in Philadelphia.

Lili Brillstein is a nationally recognized thought leader in the advancement of Episodes of Care as a value-based approach for specialty care. She is the CEO of ECollaborative, which works with stakeholders across the healthcare continuum to successfully make the move from fee for service to value-based healthcare.

Don Hall, M.P.H., is principal of Dent Advisory Services, LLC, a management consulting practice focused on helping leadership improve organizational effectiveness and overall performance. He most recently served as president and CEO of a managed care organization.

Mission Managed Healthcare Executive* provides healthcare executives at health plans and provider organizations with analysis, insights and strategies to pursue value-driven solutions.

Attorney: David W. Weil, MD, J.D.; Austin, TX
Why LTACHs Are Often the Right Choice for Critically Ill Patients

By Sean R. Muldoon, M.D., M.P.H., FCCP, CMO; and Audra Early, SVP of Strategy and Network Development, Kindred Hospitals

Establishing the appropriate care delivery path for patients after a stay in the intensive care unit or medical surgery unit is essential to improving outcomes, readmissions and and managing total costs of care. Because of their clinical capabilities, long-term acute care hospitals (LTACHs) are often ideal treatment and recovery settings for medically complex patients and therefore valuable partners in healthcare networks.

Benefits to Payers Through a Specialized Patient Focus

Recent data shows that patients are being admitted to short-term acute care hospitals with increasingly complicated conditions, thereby amplifying the need for post–acute care partners who can help these patients fully recover.

Licensed as acute care hospitals, LTACHs are often the most appropriate next level of care for medically complex patients who need to see a physician every day. Physicians at LTACHs lead interdisciplinary teams made up of nurses, therapists and other clinicians who provide coordinated, patient-specific care. Additionally, these teams provide onsite 24/7 respiratory coverage for critical pulmonary patients, including those needing to be weaned off ventilators.

Despite increasing medical complexities, a recent ATI Advisory study reported that patients in LTACHs are almost half as likely to readmit to the hospital as SNF residents are.1 Additionally, Medicare Provider Analysis and Review (MEDPAR) claims analysis suggests that an LTACH’s per-patient-day costs are generally lower than those of a short-term acute care hospital. This makes them cost-effective settings for patients requiring continued acute care.2

LTACHs, therefore, are important partners within the healthcare ecosystem and provide efficient care for this niche patient population.

Comprehensive Rehabilitation for Lasting Recovery

Rehabilitation services at an LTACH are integrated with specialized acute care to help patients with medically complex conditions achieve the fastest and most complete recovery possible.

Early rehabilitation in an acute care setting, made possible through the expertise of LTACH physical therapists, occupational therapists, and speech language pathologists can have a considerable impact on care efficiency. One study found that improving access of patients on ventilators to early mobilization may reduce their length of stay by up to 45 days and shorten their time on ventilation by 2.3 days.3

As such, partnership with LTACHs can help certain patients fully recover more quickly and can positively affect length of stay and efficient care.

How Kindred Can Help

Kindred Hospitals specialize in the treatment of patients who require intensive care and rehabilitation in an acute hospital setting. The clinical capabilities at Kindred Hospitals allow them to improve outcomes. And their focus on transparency, patient access and collaboration makes them valuable care partners.

Kindred health plan partnerships are customized by product and can be built on diagnosis-related group rates, negotiated per diem rates or value-based agreements.

Visit kindredmanagedcare.com to request a conversation about how Kindred Hospitals’ level of service can help manage your critically complex patients.

REFERENCES

2. Kindred Healthcare calculations using data from CMS MEDPAR, 2019

Sean R. Muldoon, M.D., M.P.H., FCCP
Dr. Sean R. Muldoon serves as senior vice president and chief medical officer for Kindred Healthcare’s hospital division. As a member of the Division Executive Committee, he is involved with government programs, clinical care oversight, medical staff affairs and strategic relationships. He has been an adviser and representative for post-acute care patients and providers at CMS, the AHA and the National Quality Forum.

Audra Early
Audra Early serves as Kindred Healthcare’s senior vice president of strategy and network development for the hospital division. Early’s responsibilities include working to improve network strategies in all of the Kindred hospitals across the country, managed care and provider relations. She received her BS in registered nursing from Texas Woman’s University in Denton.
As healthcare sees a shiny future with AI, some see some glare

Artificial intelligence technology has reached the point where even early adopters are asking what its limits should be. by JARED KALTWASSER

Consider this: a patient feels a scratchiness in the back of her throat, so she calls her doctor’s office and speaks with a nurse. The nurse takes a wait-and-see approach, but the following day the patient spikes a fever and makes an appointment to see her primary care provider. A few questions and a positive strep test later, she is given a prescription and heads to her local pharmacy to have it filled.

Now imagine a different scenario. The patient’s throat feels a bit off, so she opens an artificial intelligence (AI)-based symptom checker on her smartphone. The symptom checker details a number of possibilities, but that list gets narrowed down the following day when she records a high fever. She opens her pharmacy’s app and orders an at-home strep test, which is delivered later that day. The test comes back positive, and within an hour the pharmacy is delivering her prescription after being automatically alerted to the positive test.

The first scenario is so routine it’s almost quaint. The second has the same outcome and treatment, yet it poses many fresh issues and possibly daunting challenges. In a highly regulated, change-averse industry, AI is forcing healthcare organizations and insurers to face major questions about which technologies to prioritize and how those technologies will affect future business models. Mahi Rayasam, Ph.D., MBA, a partner at management consulting firm McKinsey & Company who specializes in healthcare systems and analytics, says although fully automated healthcare would raise a lot of concerns, some aspects of it are definitely possible. “I could foresee a bot that will tell you, ‘OK, this seems like something that you should go to an urgent care for or you should schedule a (primary care provider) appointment,’” he says. The bot might then offer a list of nearby providers along with available appointment slots or up-to-date wait times, offering patients a one-click sign-up solution. “I mean, those kinds of applications will definitely happen,” Rayasam says.

Greg Johnsen, CEO of the healthcare chatbot firm Lifelink Systems, is one of the people working on exactly those types of products. Lifelink markets chatbots that automate workflows and provide patients with personalized information and services, using data from their electronic health records, among other sources. Johnsen noted that many workflows in healthcare require multiple conversations with multiple people, which precisely the kind of activity that AI can streamline. “These are multi-conversational flows, and almost all of them in healthcare are defined by — they have to be defined by — protocol,” he says. And if there is one thing machines can do reliably well, he says, it’s following protocols.

The limits of protocols

However, in the exam room and hospital wards, healthcare operations are largely guided by best practices and informed best guesses rather than strict protocols. AI can help there, too, but Rayasam says such technologies raise ethical and practical questions such as whether patients will act on recommendations made by bots and whether insurers will reimburse such care. More fundamentally, is it
safe to downplay the role of human providers in favor of machines? "I see a lot of patient safety concerns there," he says.

AI proponents sometimes paint a picture of super-efficient, super-smart AI taking over much of healthcare. But Rayasam says it is important to not remove human clinicians from healthcare decisions. As for insurers, he says, United States law prohibits companies using AI to overrule human decisions.

"Regulation prevents any denial of care based on (decisions made) without human intervention, i.e., without M.D. intervention," he says. "You cannot deny care without an M.D. going through that case thoroughly and then determining (whether) this particular care is not medically appropriate."

But what about cases in which an algorithm recommends a treatment based on an algorithmic analysis that is simply too complicated for a noncomputer scientist to understand?

"What you're hitting on is the topic of interpretability," says Saahil Jain, M.S., a computer scientist who has worked extensively on AI and machine learning in healthcare.

Jain says much of the debate around AI in healthcare has been focused on the interpretability of the results, meaning that physicians and other providers should be able to understand why a particular recommendation was made. However, the debate is not merely about how to make results interpretable; it’s also about whether interpretability is even that important. Although interpretability enables accountability, Jain notes that other areas of healthcare function just fine with mechanistic ambiguity.

"Honestly, there are a lot of drugs that we already use (for which) we don't really understand all the mechanisms by which they work," he says. "So it’s not new for us to use things that are not interpretable."

What’s more important, he says, is rigorous testing and randomized controlled trials that prove a technology works, as well as careful evaluation of the data used to come to conclusions.

**Eye on edge cases**

Even with rigorous trials, Johnsen's point about protocols will come into play. After all, some of the thorniest healthcare decisions relate to patients with rare conditions or rare characteristics. Insofar as AI and machine learning are reliant on big data, what happens if the available data are sparse?

"Solving for the edge cases is what really worries me," Rayasam says, adding that the problem is exacerbated by data silos — data locked away in proprietary databases that could be put to use if they were set free and mixed and matched with other data. Jain is excited about a concept called federated learning that aims to work around the problem.

"There are different ways of doing it, but one example might be that you have a model and everybody uses their data to train the model without sharing the data, without aggregating the data in one central place," he says.

Jain says some of the problems related to edge cases and data silos might be solved if federated learning became a widespread.

In the meantime, Johnsen says, a transformation of the healthcare industry can happen even without solving all of the ethical and technical problems associated with AI taking over clinical decisions. He says automating the parts of the system that need to run exactly the same way, every time, can lead to significant cost savings and efficiencies that lower the cost of healthcare. For instance, efforts to promote value-based care have centered on replacing the fee-for-service model with new models such as fixed-payment regimes where physicians are incentivized to lower the cost of care in order to earn higher profit margins. In theory, such models work by encouraging physicians to avoid unnecessary tests and procedures.

**Behind the scenes**

However, Johnsen says one of the easiest ways to improve healthcare and glean cost savings through AI would be to optimize operations in ways that improve the patient experience while reducing overhead. "You will see new models of physicians and physician groups, and entirely new models around primary care," he says. Although AI is sparking conversations about what the future of patient care will look like, Johnsen says much of the impact of AI at present is going on behind the scenes. "It's always the shiny bright object that gets focused on," he says, "but there's some real work to do and (some) real effective uses of AI in doing material things right now."

Jared Kaltwasser, a frequent contributor to Managed Healthcare Executive®, is a freelance writer in Iowa.

**“These are multiconversational flows, and almost all of them in healthcare are defined by — they have to be defined by — protocol.” — GREG JOHNSEN, CEO OF LIFELINK SYSTEMS**

"As healthcare sees a shiny future with AI, some see some glare"
This year we have selected a baker’s dozen of young healthcare executives and innovators who are shaping the future of American healthcare with their ideas, insights and leadership.

13 EMERGING HEALTH LEADERS

BY KAREN APPOLD AND PETER WEHRWEIN

FOLUSO AGBOOLA, MBBS, M.P.H.

Foluso Agboola, MBBS, M.P.H., vice president of research, Institute for Clinical and Economic Review (ICER) in Boston

Raised in Nigeria, I earned my medical degree from the University of Ilorin. My interest in evidence-based policy led me to pursue an M.P.H. in quantitative methods at Harvard. I’ve generated new evidence that’s influenced policy at both Harvard and Mass General Brigham. At ICER, I’ve risen from research scientist to my current role as VP of research, where I’ve played a key role in many ICER assessments, and I’ve had the privilege to mentor other researchers and health policy experts. As an immigrant, my path wasn’t always easy, but each step has helped me develop resiliency and equipped me with new skills to make me more effective.

Who has had the greatest influence on your life?
My mom. Although her formal education was minimal, her vision, hard work, commitment to excellence, and tenacity of purpose helped her build a successful fashion business and school in my Nigerian hometown. I’m forever grateful for the example she set, teaching me to never quit and to give my best to whatever my hands find to do.

Why did you decide to pursue a career

Managed Healthcare Executive.com
in healthcare?
At 13, I was diagnosed with adolescent idiopathic scoliosis, and I needed to wear a scoliosis brace for 23 hours each day for four years. My initial despondency gradually turned into a knowledge-seeking adventure that would forever shape the rest of my life. Relentlessly, I conducted extensive research on scoliosis seeking out all relevant material and questioning several physicians along the way. I learned more than just about scoliosis. I developed a keen interest in medical practice, and in how good evidence can improve lives.

Which career accomplishment has given you the greatest satisfaction?
I currently work with a diverse mix of brilliant, talented people who are passionate about improving the U.S. healthcare system. My path hasn’t always been easy, but several mentors have helped me along the way. I’m particularly excited about ICER’s new fellowship program to train new experts in health technology assessment.

What has your organization’s role been in the rollout of COVID-19 vaccines?
COVID-19 has increased public awareness around evidence, models, health equity, fair pricing, and fair access. I’m proud ICER played an important role in evaluating the evidence and price of emerging COVID-19 therapeutics and that we spurred a national conversation about drug pricing during a pandemic.

What would be the best way to reduce healthcare inequities in the U.S.?
I dream of a health system where everyone has sustainable access to high-value care. ICER helps realize this dream by pressuring drugmakers to price drugs in alignment with how well those drugs improve patients’ lives and pressuring U.S. payers to reward fair pricing with fair access. Further, my research often reveals how little information exists about the potential differences in a therapy’s safety and effectiveness across different patient populations. If the U.S. is going to reduce health inequities, clinical trial sponsors need to start recruiting far more diverse populations.

Name a book or article that everyone in healthcare should read.
Atul Gawande’s “Being Mortal” is a beautiful and thought-provoking book, reminding us that everyone will grow old and die someday, and that we can do a better job of taking care of the elderly.

Who has had the greatest influence on your life?
My mother. She modeled and instilled in me a guiding principle of grit and grace that shapes much of how I navigate the world, both professionally and personally.

Why did you pursue a career in healthcare?
My overarching goal is to be of service to people who are vulnerable. The instance of vulnerability I’m most drawn to is the vulnerability associated with threats to health and well-being. American culture is extremely hostile toward health, particularly for people of color. I’m interested in empowering
people and populations to fight back.

Which career accomplishment has given you the greatest satisfaction?
I successfully transitioned from academia, where I spent the initial years of my career, into a business environment. I’m grateful to work for an organization that values my academic training and love applying rigorous methods of inquiry to solve problems.

What has your organization’s role been in the rollout of COVID-19 vaccines?
UPMC Health Plan has worked closely with our healthcare delivery system to make COVID-19 vaccination broadly accessible within the communities we serve and has made a concerted effort to make vaccination readily available to vulnerable populations.

What would be the best way to reduce healthcare inequities in the U.S.?
Within the confines of the existing American healthcare system, the single best way to reduce healthcare inequities in the U.S. will be to dramatically increase the amount of community-based, digitally enabled care available, particularly in vulnerable communities.

Name a book or article that everyone in healthcare should read.
“Scarcity: Why Having Too Little Means So Much” by Sendhil Mullainathan and Eldar Shafir. The authors describe the negative and compounding consequences of scarcity of time, resources and support. Engaging with the American healthcare system requires large amounts of time and resources, often accompanied with little support. Since reading this book, I’ve continuously challenged myself and my teams to think about ways we might minimize the time and resources required for receipt of healthcare while maximizing the amount of support we provide.

“American culture is extremely hostile toward health, particularly for people of color.”
— Ellen Beckjord, Ph.D., M.P.H.

MATTHEW BENNETT

Matthew Bennett, president of Cigna Medical Group, a multispecialty group practice in Phoenix
I grew up in upstate New York and always dreamed of studying abroad. After working two jobs at age 16 to earn enough money to make this dream (come true), I attended high school in the Dominican Republic and the Netherlands. I went on to attend Duke University, where I studied public policy and economics.

I started my career as the special adviser of strategy and planning for Plowshares Institute, an international nonprofit organization nominated twice for the Nobel Peace Prize. A few years later, I co-created and led The Purpose Project, a nonprofit designed to address the growing generation gap in the social sector.

Taking my passion for leading organizations through change from the nonprofit world to healthcare, I joined Cigna Medical Group (CMG). Over the past 11 years, I’ve held various leadership roles across strategy, technology, operations, clinical and care delivery.

Who has had greatest influence on your life?
I can honestly say my parents. They instilled in me the importance of a strong sense of self, humility, generosity, an open mind, a sense of curiosity and an orientation to learn. Individually, my dad gave me the gift of an analytical and problem-solving orientation, and my mom’s gifts were empathy and emotional intelligence.

Why did you pursue a career in healthcare?
I was drawn to healthcare because of the sector’s transformative nature, and because of its unique ability to improve and save lives. Although there is much to appreciate about the American healthcare system — scientific innovation and research, skilled care and passionate professionals — we also have a need and opportunity to do better. As a nation, we spend a tremendous amount of money on healthcare, yet achieve subpar quality outcomes.

Which career accomplishment has given you the greatest satisfaction?
I’m extremely proud of CMG’s response through COVID-19. Our team of 1,200 clinicians, staff and leaders came together with a laser focus on driving rapid change and innovation to ensure patients had ongoing access to care and services. As a team, we consolidated locations to concentrate resources and staff into our 14 largest centers, ensured an ongoing supply of PPE, launched a telehealth solution in five weeks and introduced same-day medication delivery to patients’ front doors. We also provided community support through a COVID-19 hotline and testing including drive-thru locations and vaccine administration. We were one of the first nonhospital settings in the nation to offer monoclonal antibody infusion therapy.
What has your organization’s role been in the rollout of COVID-19 vaccines?
CMG has proactively partnered with local health departments to administer more than 16,000 vaccines at our centers and an additional 25,000 vaccines at a mass vaccination site we managed in partnership with the Arizona Department of Health Services, bringing the total provided by the Cigna Arizona team to more than 41,000.

What would be the best way to reduce healthcare inequities in the U.S.?
I believe one of the best ways is to improve access to affordable care for everyone, especially those in underserved communities. We can do this by closing the digital divide and making it simpler to access and use virtual and home-based solutions that provide individuals with high-quality care when, where and how they need it.

Name a book or article that everyone in healthcare should read.
“The Incentive Cure: The Real Relief for Health Care” by François de Brantes,* which sets forth a practical vision for the critical role that all stakeholders — individuals, healthcare providers and health insurers — have to play in improving healthcare.

*De Brantes is a member of the Managed Healthcare Executive® editorial advisory board.

MANIK BHAT

Manik Bhat, co-founder and CEO of Healthify, a health-tech company based in New York City

I grew up in Ohio and earned a B.S. in molecular and cellular biology from Johns Hopkins University. In 2013, I co-founded Healthify to help vulnerable people access nonclinical services such as food, transportation and housing, which play critical roles in health outcomes.

Shortly after I started Healthify, the company was accepted into Blueprint Health, a program that helps health start-ups meet business goals such as gaining customers, raising capital, building marketing and sales collateral, and refining investor pitches. After completing Blueprint Health’s program, my team and I successfully raised $500,000 to continue growing our technology platform and signed our first set of clients, which included Johns Hopkins HealthCare.

Who has had the greatest influence on your life?
My parents, who were both physicians. They sacriﬁced their careers and parts of their lives to move to the United States from Kashmir in 1995 to provide more opportunities for myself and my brother. They wanted to ensure that I had every opportunity to pursue my passions. This self-sacriﬁcing act signiﬁcantly inﬂuenced how I think about work and serving others.

Why did you pursue a career in healthcare?
During college and after graduation, I worked as a coordinator and volunteer at the Harriet Lane Clinic for Health Leads, a group associated with Johns Hopkins Hospital. I worked with families to understand their social needs and connect them to social services. From this experience, I decided to rescind my offer to attend medical school and was inspired to help create Healthify to address the socioeconomic barriers facing many Americans.

Which career accomplishment has given you the greatest satisfaction?
Healthify was recently acquired by WellSky, a health and community care technology company. Through this acquisition, Healthify and WellSky will help payers and providers across and within communities to better identify social needs, search for social services and coordinate care with an accountable network of community partners. Building a social enterprise, raising venture capital and then being acquired to produce a positive outcome for everyone involved was an amazing journey that I’m proud of.

What has your organization’s role been in the rollout of COVID-19 vaccines?
“Our team of 1,200 clinicians, staff and leaders came together with a laser focus ... to ensure patients had ongoing access to care and services.”
— Matthew Bennett, president of Cigna Medical Group

“Building a social enterprise, raising venture capital, and then being acquired to produce a positive outcome ... was an amazing journey that I’m proud of.” — Manik Bhat, co-founder and CEO of Healthify

Continued on page 21
For patients with Homozygous FH (HoFH) aged 12 years or older¹

**EVKEEZA® powerfully reduced LDL-C levels by an average of ~50% as an adjunct to current LLTs**¹*

**INDICATION**

EVKEEZA® is an ANGPTL3 (angiopoietin-like 3) inhibitor indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH).

**Limitations of Use:**

- The safety and effectiveness of EVKEEZA have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH).
- The effects of EVKEEZA on cardiovascular morbidity and mortality have not been determined.

**IMPORTANT SAFETY INFORMATION**

**Contraindication**

EVKEEZA is contraindicated in patients with a history of serious hypersensitivity reactions to evinacumab-dgnb or to any of the excipients in EVKEEZA. Serious hypersensitivity reactions, including anaphylaxis, have occurred.

**Warnings and Precautions**

**Serious Hypersensitivity Reactions:** Serious hypersensitivity reactions have occurred with EVKEEZA. If signs or symptoms of serious allergic reactions occur, discontinue EVKEEZA infusion, treat according to the standard-of-care, and monitor until signs and symptoms resolve.

Visit [EVKEEZAhcp.com](http://EVKEEZAhcp.com) to learn more about EVKEEZA

---

¹The LDL-C-lowering effect of EVKEEZA may be measured as early as 2 weeks. At week 24, the LS mean treatment difference between EVKEEZA and placebo in mean percent change in LDL-C from baseline was -40% (95% CI: -55% to -25%, P<0.0001). LS mean percent change in LDL-C from baseline with EVKEEZA was -47% and with placebo was +2%.

**LDL-C=low-density lipoprotein-cholesterol; LDLR=low-density lipoprotein receptor; LLTs=lipid-lowering therapies; LS=least squares.**
EVKEEZA® lowered LDL-C by ~50%, on average, at 24 weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>Placebo + LLTs</th>
<th>EVKEEZA + LLTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-20</td>
<td>-20</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>20</td>
</tr>
<tr>
<td>12</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>16</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>24</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

**Study design**

The efficacy and safety of EVKEEZA in the treatment of HoFH was demonstrated in a multicenter, double-blind, randomized, placebo-controlled study in patients with HoFH. The mean age of patients at baseline was 42 years (range: 12 to 75 years). Patients were on a background of LLTs, including maximally tolerated statins, ezetimibe, PCSK9 inhibitor antibodies, lomitapide, and lipoprotein apheresis. The mean LDL-C at baseline was 255 mg/dL in the double-blind treatment period, 43 patients were randomized to receive EVKEEZA 15 mg/kg IV every 4 weeks and 22 patients to receive placebo. In the open-label treatment period, 64 patients received EVKEEZA 15 mg/kg IV every 4 weeks.

The primary endpoint was percent change in LDL-C from baseline to week 24. At week 24, the LS mean treatment difference between EVKEEZA and placebo in mean percent change in LDL-C from baseline was -49% (95% CI: -65% to -33%; P<0.0001). LS mean percent change in LDL-C from baseline with EVKEEZA was -47% and with placebo was +2%.

A key secondary endpoint was the LS mean change in LDL-C from baseline to week 24. At week 24, the LS mean change in LDL-C from baseline for patients receiving EVKEEZA was -135 mg/dL compared with -3 mg/dL for patients receiving placebo (treatment difference -132 mg/dL; 95% CI: -175 to -89; P<0.001).2

At week 24, the LS mean difference between EVKEEZA and placebo for ApoB and non-HDL-C was -37% (95% CI: -49% to -25%; P<0.001) and -52% (95% CI: -65% to -39%; P<0.001), respectively.

Apob=apolipoprotein B; CI=confidence interval; DBTP=double-blind treatment period; IV=intravenous; non-HDL-C=non-high-density lipoprotein-cholesterol; PCSK9=proprotein convertase subtilisin kexin type 9; SE=standard error.

**IMPORTANT SAFETY INFORMATION (continued)**

**Embryo-Fetal Toxicity:** EVKEEZA may cause fetal harm when administered to pregnant patients. Advise patients who may become pregnant of the risk to a fetus. Consider obtaining a pregnancy test prior to initiating treatment with EVKEEZA. Advise patients who may become pregnant to use effective contraception during treatment and for at least 5 months following the last dose.

**Adverse Reactions**

Common adverse reactions (≥5%) were nasopharyngitis (16%), influenza-like illness (7%), dizziness (6%), rhinorrhea (5%), and nausea (5%).

**Use in Specific Populations**

**Pregnancy:** EVKEEZA may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. If a patient becomes pregnant while receiving EVKEEZA, healthcare providers should report EVKEEZA exposure by calling 1-833-385-3392.

**Lactation:** There are no data on the presence of evinacumab-dgnb in human milk or animal milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for EVKEEZA and any potential adverse effects on the breastfed infant from EVKEEZA or from the underlying maternal condition.

**Females and Males of Reproductive Potential:** Consider pregnancy testing in patients who may become pregnant prior to starting treatment with EVKEEZA. EVKEEZA may cause fetal harm when administered to a pregnant woman. Females of reproductive potential should use effective contraception during treatment with EVKEEZA and for at least 5 months following the last dose of EVKEEZA.

**Pediatrics:** The safety and efficacy of EVKEEZA have not been established in pediatric patients with HoFH who are younger than 12 years old.

Please see Brief Summary of full Prescribing Information on the next page.

EVKEEZA (evinacumab-dgnb) injection, for intravenous use

1 INDICATIONS AND USAGE

EVKEEZA is an ANGPTL3 (angiopoietin-like 3) inhibitor indicated as an adjunct to other LDL-C lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH).

2 WARNINGS AND PRECAUTIONS

2.1 Hypersensitivity Reactions

Serious hypereosinophilic syndromes have occurred in patients treated with EVKEEZA. In clinical trials, 1 (1%) EVKEEZA-treated patients has developed treatment-emergent antibodies to EVKEEZA. No patients developed treatment-emergent antibodies to EVKEEZA. For these reasons, comparison of the incidence of antibodies methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to EVKEEZA in the studies described below, with the incidence of antibodies in other studies or to other products may be misleading.

2.2 Infusion Reactions

Infusion reactions were reported in 6 (7%) patients treated with EVKEEZA and in 2 (3%) patients who received placebo. The following infusion reactions occurred in EVKEEZA-treated patients: infusion site pruritus, pyrexia, muscular weakness, nausea, and nasal congestion.

6.1 Clinical Trials Experience

Serious hypersensitivity reactions have occurred with EVKEEZA. In clinical trials, 1 (1%) EVKEEZA-treated patient experienced anaphylaxis versus 0 (0%) patients who received placebo. If signs or symptoms of serious hypersensitivity reactions occur during EVKEEZA infusion, treat according to the standard-of-care, and monitor until signs and symptoms resolve. EVKEEZA is contraindicated in patients with a history of serious hypersensitivity reaction to evinacumab-dgnb [see Contraindications (4)].

8.2 Lactation

The safety and effectiveness of EVKEEZA have not been established in pregnant patients. Administration of evinacumab to rabbits during organogenesis caused increased in fetal malformations at doses below the maternal dose. Administered subcutaneously at doses of 1, 5, 10 and 30 mg/kg every 3 days (Q3D) during the period of organogenesis resulted in fetal malformations (domed head, hydrocephalus, and cleft palate) and delayed ossification. In a combined fertility, embryofetal, and pre- and postnatal development study, female rats were administered evinacumab-dgnb via subcutaneous injection at doses of 30 and 100 mg/kg/Q3D beginning 2 weeks prior to mating and continuing to gestation day 21 or lactation day 21. Mean maternal systemic exposures were below the human exposure at the MRHD throughout the study. No maternal or developmental toxicity was observed.

8.3 Females and Males of Reproductive Potential

There are no data on the presence of evinacumab-dgnb in human milk. Studies in lactating rats indicate that EVKEEZA is transmitted from the mother to the developing fetus. Evinacumab-dgnb is a human IgG4 monoclonal antibody and may cause fetal harm when administered to pregnant patients. Administration of evinacumab to rabbits during organogenesis caused increased in fetal malformations at doses below the maternal dose. In an embryo-fetal development study in pregnant rabbits, evinacumab-dgnb was administered subcutaneously at doses of 1, 5, 10 and 30 mg/kg every 3 days (Q3D) during the period of organogenesis from gestation day 7 to day 19. Evinacumab-dgnb was teratogenic in rabbits, causing anophthalmia, dilation of the lateral and third ventricles of the brain, and fused fore/hind paws at maternal evinacumab-dgnb exposures below human exposure at the MRHD of 15 mg/kg every 4 weeks, based on AUC. Other fetal malformations, consisting of irregular and abnormal ossification of the skull, mandible, and metacarpal, and enlarged anterior and/or posterior fontanelles occurred and were consistent with significant maternal toxicity (including early deaths due to abortion and prematurity). Mean maternal systemic exposures were below the human exposure at the MRHD throughout the study. No maternal or developmental toxicity was observed.

9.3 Geriatric Use

Clinical studies of EVKEEZA did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.
Continued from page 17

Healthify has not had a direct role in the rollout of COVID-19 vaccines, but we recognize that racial disparities continue to exist in this country’s vaccine rollout, and we believe that minority and vulnerable communities should be prioritized.

What would be the best way to reduce healthcare inequities in the U.S.?

The best way would be to expand initiatives and funding to address social determinants of health. Nonclinical factors such as housing stability, economic status and access to transportation have a significant and long-lasting impact on one’s health. As payers, providers, community-based organizations and policy makers continue to recognize this impact and work closely together to improve health outcomes, we’ll be able to mitigate many of the healthcare disparities that exist in the United States.

Name a book or article that everyone in healthcare should read.

I recommend the book “Meditations” by Marcus Aurelius, which made me consider how someone’s leadership and service can enable innovation in healthcare.

HAROLD CARTER, PHARM.D.

Harold Carter, Pharm.D., vice president of pharma trade relations at Express Scripts in St. Louis

I grew up in St. Louis and received my doctorate of pharmacy in 2011 from the University of Health Sciences and Pharmacy in St. Louis.

I’m proud to have led the development of a number of Express Scripts’ solutions, including Express Scripts’ Patient Assurance Program, which increases adherence to critical diabetes medications by removing cost as a barrier to access, and Express Scripts’ SafeGuardRx Solutions, which leverages specialized clinical care and value-based contracting strategies. These solutions help lower prescription drug costs and reduce downstream medical events and costs.

Who has had the greatest influence on your life?

My grandfather, whom I was named after. He had a strong work ethic and funny personality, and he was always willing to assist others. Whether it was from his time in the military, in the St. Louis Fire Department, or simply lending a helping hand, I learned the importance and satisfaction that comes from giving back to your community. Regardless of the adversity that my grandfather faced, he never complained or made excuses.

Why did you pursue a career in healthcare?

One summer in high school, I had the unfortunate luck (or so I thought!) of not finding a summer job. Because my dad didn’t want me sitting around the house all summer, he suggested I volunteer at a local hospital. I gained exposure to all of the hospital’s different functions and was especially intrigued with pharmacy. I became enamored with the role that pharmacists played within the healthcare system, particularly the interactions they had with patients and other healthcare professionals on a daily basis. After that experience, I knew I wanted to pursue a career in healthcare.

Which career accomplishment has given you the greatest satisfaction?

My greatest career accomplishment is the privilege to mentor and develop students on pharmacy rotations as well as other colleagues across the organization. My mentors have been key to my career’s success. For me, being able to pass that wisdom and guidance forward to others is a gift within itself.

What has your organization’s role been in the rollout of COVID-19 vaccines?

During the rollout of the COVID-19 vaccine, Express Scripts played a critical role in supporting on-site vaccination clinics, educating clients and patients, and partnering with industry leaders. Our parent company, Cigna, has driven a number of incentive programs for U.S. employees, including a $200 well-being incentive award for employees in the Cigna Medical Plan who report that they are fully vaccinated and a drawing for an all-expenses-paid trip. We also have paid time off for vaccine appointments and recovery to encourage vaccine adoption and create healthy work sites.

What would be the best way to reduce healthcare inequities in the U.S.?

Too often in the U.S. a person’s health outcomes can be determined by the community they live in. To reduce inequities, we must do better at putting the appropriate resources — such as hospitals, clinics, food banks and literacy services — into underserved communities.

“For me, being able to pass that wisdom and guidance forward to others is a gift within itself.”

— Harold Carter, Pharm.D.
ANN MARY FERRIE, M.P.H.

Ann Mary Ferrie, M.P.H., director of public policy and strategy at Visiting Nurse Service of New York (VNSNY) in New York City

I grew up in Paramus, New Jersey. I completed my B.S. in biology and sociology at The College of New Jersey and then earned an M.P.H. from Columbia University.

At the Center for Health Care Strategies, a national nonprofit health policy resource center, I worked with state Medicaid agencies and health plans. I analyzed and advised them on innovative integrated care programs to improve care for Medicare-Medicaid (dually eligible) enrollees requiring long-term services and support. It was formative to work on new models across the country to address systemic fragmentation across Medicare and Medicaid for the highest-cost, highest-need cohort of either program.

At VNSNY, I advise on legislative, regulatory and strategic policy issues of interest to our organization. I also work with industry stakeholders within New York state and beyond to advocate for policy changes backed by VNSNY’s experience as an in-home healthcare provider and payer.

Who has had the greatest influence on your life?

My mother. She emigrated from India and has worked as a registered nurse for more than 30 years. She has never wavered in her commitment to caring, particularly when it came to her family.

Why did you pursue a career in healthcare?

I was drawn to healthcare because of my mother’s profession. The intersection of my two fields of study, biology and sociology, led to my focus on public health. I’ve always been inspired to make the greatest impact and found that healthcare policy can lead to impactful population-level improvements to care. I’m driven to make healthcare more equitable, accessible and effective.

Which career accomplishment has given you the greatest satisfaction?

I worked with VNSNY to inform CMS’ direct contracting demonstration opportunity for Medicaid managed-care organizations to improve care for Medicare-Medicaid enrollees in original Medicare. The model is currently under CMS review and has been paused, but it was satisfying to see what was once an idea be announced as an innovative demonstration opportunity to improve coordination, leveraging existing managed-care models.

What has your organization’s role been in the rollout of COVID-19 vaccines?

When vaccines first became available, VNSNY set up a clinic to vaccinate our frontline staff. We educated our staff throughout the pandemic and urged them to get vaccinated. In partnership with the NYC Homebound COVID-19 Vaccination Program, VNSNY also vaccinated homebound residents in their homes, prioritizing communities with low vaccination rates.

What would be the best way to reduce healthcare inequities in the U.S.?

Healthcare inequities have been driven by systemic societal issues that require multipronged, cross-sector approaches, so we need shared commitment and planning from healthcare, education, businesses and others. No more silos!

Name a book or article that everyone in healthcare should read.

Although its message is not unique to healthcare, I highly recommend the Harvard Business Review article “Management Time: Who’s Got the Monkey,” by William Oncken Jr. and Donald L. Wass for emerging leaders in any industry. Time management and understanding where to focus are extremely important skills for any leader. In an industry as complex as healthcare, we often face competing priorities that drive our day. This article teaches how to prioritize important work, how to empower your team to think critically and how to use effective communication to build trust.

“It was satisfying to see what was once an idea be announced as an innovative demonstration opportunity.”

—Ann Mary Ferrie, M.P.H.
Rachel Kotok Goldberg, B.S.N., RN, director of behavioral health client partnerships and product innovation at Horizon Blue Cross Blue Shield of New Jersey (BCBSNJ) in Newark

I grew up in Rochester, New York, earned a B.S. in nursing from the University of Pennsylvania (Hillman Scholar), and started my clinical career as a registered nurse in labor and delivery at Mount Sinai in New York City. Prior to joining Horizon BCBSNJ, I was an associate vice president of quality and compliance at ComplexCare Solutions, a supplier of in-home risk adjustment assessments and care management interventions for health plans.

Who has had the greatest influence on your life?

I am extremely fortunate to work for an amazing leader and mentor, Suzanne Kunis, vice president of behavioral health at Horizon. She empowers her team to be creative and effective and to push ourselves beyond our comfort zones to deliver for Horizon’s members. She has shaped my approach to leadership and the duty I feel to fight every day to put mental well-being on equal footing with physical health.

I also have to mention my husband, who is my greatest supporter, and my dad for always teaching me to think of problems as puzzles that need to be solved.

Why did you pursue a career in healthcare?

I knew that I would work in healthcare since I was a little girl. My mother is a nurse. I loved going to work with her and seeing how much her patients appreciated her efforts in helping them get through a challenging time. At Penn, my professors consistently highlighted how broad the nursing world is, challenging us to create our place and make a difference. It wasn’t until a few years into my career as a clinical nurse that I decided to heed their advice and take a leap beyond direct patient care.

Which career accomplishment has given you the greatest satisfaction?

My work at Horizon has been the role of a lifetime. I was the third employee hired to a new Horizon Behavioral Health team charged with charting the strategic direction and executing the development of our behavioral health capabilities. Suzanne empowered me to develop and launch from scratch a full continuum of evidence-based, outcomes-focused programs and services that guide members to the right behavioral health services for their individual needs.

What has your organization’s role been in the rollout of COVID-19 vaccines?

As the largest health insurer in New Jersey, Horizon has engaged with public and private partners statewide to help many people get vaccinated as quickly as possible. We put an emphasis on connecting with the state’s many racial and ethnic minorities and worked with community leaders to dispel myths, deliver facts and promote vaccination.

What would be the best way to reduce healthcare inequities in the U.S.?

At Horizon, we have made a companywide “Pledge to Achieve Lasting and Positive Change” and have joined with Blue plans across the country to confront racial health disparities. There is a significant underrepresentation of people of color and ethnic diversity within the behavioral health workforce. As of 2019, approximately 83% of the psychology workforce identified as White. This lack of diversity is even more acute in the context of the behavioral health clinician shortage that exists nationwide. Increasing the diversity of behavioral health clinicians is essential to addressing inequities in access to treatment, eliminating stigmas, and reducing racial and ethnic mental health inequities.

Name a book or article that everyone in healthcare should read.

Normalizing mental health and reducing stigma are fundamental to improving health and the healthcare system. In “Lift the Mask,” a documentary and book produced by The Quell Foundation, people reveal their experiences with mental health and substance use, taking the discussion beyond the clinical aspect. Only by raising awareness and acceptance and humanizing mental health can we create a society in which everyone feels as comfortable discussing anxiety as diabetes.
13 Emerging Industry Leaders

MELISSA HANNA, J.D., MBA

Melissa Hanna, J.D., MBA, co-founder and CEO of Mahmee in Los Angeles

I grew up in California’s San Fernando Valley and earned a B.A. in public policy and sociology at Pomona College, an MBA at Claremont Graduate University and a J.D. at Southwestern University School of Law.

Career highlights include securing an all-star lineup of investors in our seed fundraising, including Serena Williams and Mark Cuban, and establishing a first-of-its-kind public-private partnership with the DC Department of Health to serve new and expecting mothers in Washington, D.C.

Who has had the greatest influence on your life?
My mother, Linda Hanna, M.S.N./Ed., RNC, who is Mahmee’s other co-founder and whose work inspired its formation in 2014. As someone who delivers maternal and infant healthcare and also trains healthcare providers, my mother set an example of how integrated models of care could work at scale and where technology could make the greatest impact in this industry.

Why did you pursue a career in healthcare?
I did not initially decide to pursue a career in healthcare. Instead, I started my career in education, with a focus on policy and technology. After graduating from college, I worked for some educational tech startups. What I learned in those spaces about centering a student’s experience and needs in school informed my views on healthcare and led me to wonder where else these lessons could be applied. Centering maternity patients’ experiences and needs in healthcare was an exciting prospect for me despite the field’s known complexities.

Which career accomplishment has given you the greatest satisfaction?
Leading my current team at Mahmee. As Mahmee continues to grow, I take pride in sharing my passion for this work with new employees and leading them to find more effective ways to support patients and providers in maternal and infant health. Furthermore, I find myself in new and greater learning opportunities as I work toward improving my own skills as a strategic leader, which is incredibly satisfying.

What has your organization’s role been in the rollout of COVID-19 vaccines?
Earlier this year, we mandated that all 30 of Mahmee’s employees be fully vaccinated, which we achieved last spring. Because all types of expectant and new parents and providers use Mahmee, we have a unique reach into some of the most at-risk U.S. communities. Since the vaccine rollout began, Mahmee has promoted vaccinations among pregnant and postpartum mothers and continues to provide updated information on risks and considerations for birthing individuals based on guidelines and recommendations by local and federal public health officials.

What would be the best way to reduce healthcare inequities in the U.S.?
According to the CDC, (approximately) 700 pregnant women die during pregnancy or in the first postpartum year, and 50,000 women become injured or experience serious complications. What’s more, Black women are three times more likely to die from a pregnancy-related cause than White women, and in many cities pregnancy-related risk is disproportionately concentrated in certain areas.

The healthcare industry lacks the information technology infrastructure needed to connect professionals from different organizations to discuss cases and to follow and monitor patients across practices and health systems. This missing element creates serious gaps in care.

By zeroing in on these gaps and closing them, I believe we will make a massive impact on maternal health complications within the U.S.

Name a book or article that everyone in healthcare should read.
“Centering maternity patients’ experiences and needs in healthcare was an exciting prospect for me despite the field’s known complexities.”

— Melissa Hanna, J.D., MBA, co-founder and CEO of Mahmee

“Upstream: The Quest to Solve Problems Before They Happen,” by Dan Heath. The book delves into how to prevent or solve problems before they occur, which is a critical skill when running a business.
SHANTANU NUNDY, M.D., MBA

Shantanu Nundy, M.D., MBA, chief medical officer at Accolade in Plymouth Meeting, Pennsylvania

I was born in Canada but largely grew up in the Washington, D.C., metro area. I earned a B.S. from Massachusetts Institute of Technology (MIT), an M.D. from Johns Hopkins University and an MBA from the University of Chicago Booth School of Business. I completed my medical residency and fellowship in health disparities at the University of Chicago.

Previously, I served as a senior health specialist at the World Bank Group in its Health, Nutrition and Population Global Practice, where we advised developing countries across Africa, Asia and South America on health system innovation and technology. I served as the director of The Human Diagnosis Project, which we successfully built into the world’s largest open medical project spanning 80 countries. Prior to that, I was managing director for clinical innovation at Evolent Health, where we launched value-based care models and accountable care organizations around the country.

Who has had the largest influence on your life?

My mom. When I was in middle school, she was diagnosed with type 2 diabetes, which she struggled to manage for many years. Whenever I think about building innovative solutions for healthcare, I think about whether it would work for her.

Why did you pursue a career in healthcare?

When I was a college freshman, I taught English in a small village in India where my aunt ran a school and anti-poverty program. The first day I stood in front of the classroom, I was taken aback by the students’ health. Most had runny noses and many had open sores. I couldn’t understand how anyone could learn while sick.

The next week I found a local doctor who, to my delight, agreed to come to the school and examine all of the children for free. He prescribed preventive medications and supplements for many of them. Over the next three years, with support from MIT, we built a school-based clinic and public health program that still exists today, 20 years later.

The experience was exhilarating. It cemented my desire to serve individual patients as a physician and to scale access to high-quality healthcare as an entrepreneur.

Which career accomplishment has given you the greatest satisfaction?

I’m most proud of creating multiple new organizations and solutions from scratch and taking them to a point where they demonstrate clinical impact and have a pathway to sustainability. Healthcare is in urgent need of reinvention.

What has your organization’s role been in the rollout of COVID-19 vaccines?

Accolade provides personalized advocacy and healthcare services to more than 8 million working Americans and families through their employers. As a trusted partner to employers and families, we have sent evidence-based communications and email campaigns on the vaccine, hosted dozens of expert webinars, and directly provided nurse education and navigation on COVID-19 and the vaccine to Americans nationwide.

What would be the best way to reduce healthcare inequities in the U.S.?

Healthcare needs to meet people where they are physically and emotionally. Many vulnerable health populations either don’t have access to care or don’t trust their care options. To reduce healthcare inequities, healthcare needs to become distributed. Care needs to start at home and in the community at places such as churches and barbershops to meet patients where they are and in contexts they trust.

Name a book or article that everyone in healthcare should read.


“I’m most proud of creating multiple new organizations and solutions from scratch and taking them to a point where they demonstrate clinical impact.”

— Shantanu Nundy, M.D., MBA

Continued on page 28
Visit ManagedHealthcareExecutive.com

Get easy access to news, information, practice solutions, trusted perspectives through peer-based forums and opinions.

View in-depth interviews with industry experts.

Find healthcare management resources sorted by topic.

Medical World News®
Discover the 24-hour news channel for #healthcareprofessionals, by healthcare professionals.

Website Enhancements
- Streamlined, user-friendly navigation
- Improved mobile compatibility for easier viewing on phones
- Increased responsiveness and improved search capabilities
for an Enhanced Website Experience

Use our improved navigation and search.

Sign up to receive e-newsletters and the print publication.

Read keynote highlights, industry trends and policy updates.

Explore content relative to specific therapeutic areas or disease states.

Managed Healthcare®
The C-Suite Advisor
AN MHE life sciences BRAND
Michael Palantoni, vice president of platform services at Athenahealth in Watertown, Massachusetts

I grew up outside of New York City and graduated from Johns Hopkins University with a concentration in systems engineering. Prior to my current role at Athenahealth, I was a management consultant at Deloitte Consulting, where I specialized in healthcare and technology.

Some of my formative leadership experiences at Athenahealth have been leading our patient engagement teams and running the Athenahealth Marketplace (app store) business. These have been great opportunities to learn from consumer-focused executives and to have front-row seats to the explosive growth of the health-tech ecosystem over the past five years.

At Deloitte, I worked on the firm’s response to the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009, which involved building models for how meaningful use requirements and funding would impact the industry. This was my introduction into healthcare technology strategy.

Who has had the greatest influence on your life?
On a personal level, definitely my wife. We’ve been together since we were 19, and she has been my consultant for virtually every major decision of my adult life. She’s incredibly mission driven and really grounds me. From a pure career perspective, I was fortunate to work with a unique group of senior people at Deloitte who showed me what could be possible with technology in healthcare at an early career stage. That influenced me to consider how I could best use technology in the healthcare space.

Why did you pursue a career in healthcare?
My mom battled and ultimately passed away from cancer and its complications during the four years I was in high school. During those years, I struggled to find an outlet for processing this and ended up channeling it into my education at college, my career and my purpose.

I became very focused on healthcare and medicine. I shadowed staff in various medical areas at a hospital and worked on a project to evaluate provider-to-provider communication in a new hospitalist program. I believe they gave me this project as an internal experiment. Ultimately, I discovered I really enjoyed this type of “systems thinking” work as an outlet for both my purpose and strengths.

Which career accomplishment has given you the greatest satisfaction?
I built a platform services business that enables others to innovate in healthcare quickly and effectively. This involved starting with a business plan, selling it to initial customers and then leading the product team to grow its capabilities. Seeing it launch as a mainstream part of our business has been an incredible journey.

I can’t think of anything more rewarding than enabling others’ innovation in healthcare delivery and patient experiences.

What has your organization’s role been in the rollout of COVID-19 vaccines?
Over the past year, Athenahealth has built a significant number of COVID-19 vaccine workflows in real time to help provider organizations create and administer vaccine delivery programs.

What would be the best way to reduce healthcare inequities in the U.S.?
I don’t think there’s a single best way. If you look at the challenges the healthcare industry is facing in addressing inequalities and access to care, they are multifactorial. There must be a layered approach that looks at everything from social determinants of health to local healthcare access levels to addressing clinical biases.

Name a book or article that everyone in healthcare should read.
“The Square and the Tower: Networks and Power, From the Freemasons to Facebook” by Niall Ferguson is a great primer on network theory and strategies. A key insight in the book is how people and organizations that are connected to more things are generally more resilient and influential in times of change. For example, a supply chain with only one supplier is more likely to be very brittle and might create risks for that company during a crisis like COVID-19. In healthcare, there are many implications for how providers build referral networks and how their design impacts access, quality and costs for patients.

“I can’t think of anything more rewarding than enabling others’ innovation in healthcare delivery and patient experience.”
— Michael Palantoni, vice president of platform services at Athenahealth

Continued from page 25
EVIE POWELL, PH.D.

Evie Powell, Ph.D., virtual reality architect at Proprio, a med-tech company in Seattle

I grew up in Charlotte, North Carolina. I earned an M.Sc./B.S. in computer science and a Ph.D. in information technology, all from the University of North Carolina at Charlotte.

I am a games researcher and developer specializing in immersive interactions and prototype design. I integrate game design and UX (user experience) design to create meaningful experiences that help people learn, play, teach and work differently. In 2014, I founded Verge of Brilliance, an independent experimental games studio in Seattle, and I was a program manager at Microsoft on natural user interfaces and the Kinect technology at Xbox. At Proprio, I evaluate how we can create technology that supports surgeons in the operating room, and I am designing a suite of tools to help empower them to perform optimally.

Leadership highlights include leading external teams that won several hackathon awards, including Seattle VR 2018 Hackathon’s Best in Audio and 2016’s Best Technical Achievement.

I also co-led a successful Mobile Future Forward demonstration in which my team showed the possibilities of blending technology and the operating room through remote multiuser collaborative surgery by connecting a remote surgeon to an in-person practicing surgeon.

Who has had the greatest influence on your life? Everybody needs a champion who believes in you, challenges you and encourages you to pursue your goals. For me, that is Tiffany Barnes, Ph.D., my Ph.D. adviser and a professor at North Carolina State University.

Why did you pursue a career in healthcare? I’ve always been interested in technology and its impact on communities. When I was introduced to Proprio, I recalled reading the book “Ender’s Game” by Orson Scott Card and was excited about the possibilities of blending immersive technology with real-world scenarios. Although the story features a more dystopian view of technology and society, I could envision how intentionally designed technology could fundamentally change how important tasks are presented in a way to promote focus and performance. For example, by creating calm design through intentional data management and distillation, we can reduce anxiety, minimize overstimulating environments (like an operating room) and distill complex tasks for improved focus, well-being and results.

What has your organization’s role been in the rollout of COVID-19 vaccines? We have established a remote, safe working environment. The company provides transparency regarding vaccination rates and social distancing.

What would be the best way to reduce healthcare inequities in the U.S.? To reduce inequities in healthcare, we must recognize and reduce inequities in technological development. The concept of universal design is particularly important, as we need to design systems by a group that represents the people they are built for in order to ensure that quality of care is high for all patients and quality of experience is high for all surgeons.

Name a book or article that everyone in healthcare should read. “Homo Ludens” by Johan Huizinga is a book that focuses on the study of play in everything from law to language to other key aspects of culture. This book influenced a lot of the ways that I view how technology can blend into core aspects of our lives and how we can use early technology to assess which technologies and concepts will successfully permeate day-to-day life in the future.
SONIA SAMAGH, M.D., MBA

Sonia Samagh, M.D., MBA, vice president, The Center for Digital Health and Innovation at Optum Health in San Francisco

I was raised in San Diego. I earned an MBA from Stanford University and an M.D. from UCSF School of Medicine, and I currently practice as a hospital medicine physician.

I’m a founding member and vice president of The Center for Digital Health (CDH) and Innovation at Optum Health. For the past 10 years, I have worked at healthcare organizations, leading medical groups through value-based care transformation and serving in corporate strategy, operations and venture roles. I have led and implemented digital health strategy and innovation efforts across Optum, including digital health product development, corporate partnerships and clinical redesign for virtual care delivery.

Who has had the greatest influence on your life?

My parents. Watching them overcome incredible odds to both migrate to this country and overcome health issues has been a huge inspiration.

Why did you pursue a career in healthcare?

As an internal medicine physician, I see the effects of the healthcare system on patients and providers. I also see the amazing advancements made in technology and innovation. There is such potential for the ways that we can care for one another and create a health system where feeling better is a result of many ways that we interact with our bodies, minds and each other.

I believe physicians need a seat at the table to design our system of health and ensure that the system we create treats the whole person. I also believe that there is a chasm between what I am able to accomplish as a physician with my patients and what is possible with technology and innovation. My goal in healthcare is to close that gap.

Which career accomplishment has given you the greatest satisfaction?

When COVID-19 resulted in a rapid need to transition our 10,000 providers onto scalable, national telemedicine and remote patient monitoring systems, I founded and led Optum’s Digital Response Team (DRT). The DRT served as the foundation for our Optum Center for Digital Health and Innovation and consisted of 115 teammates rapidly deploying telehealth solutions and remote patient monitoring nationwide. We came together across our enterprise to support the infrastructure for rapid, coordinated, digital health scale, including launching a digital health support call center, local implementation teams and a digital nurse monitoring center. As a result, the DRT added more than 15,000 providers onto video visit platforms in eight weeks, completing more than 1.3 million virtual visits in 2020.

What has your organization’s role been in the rollout of COVID-19 vaccines?

Here are a just few examples of what Optum, along with its parent company UnitedHealth Group, has done to support the rollout of COVID-19 vaccines. We have worked with public health officials in California, Texas, North Carolina and Florida to set up community-based vaccination clinics. Through our care practices, community-based pharmacies and health services operations, Optum administered COVID-19 vaccines to patients, employees and other community members. And we created a COVID-19 vaccine resource locator to help people find vaccine eligibility and vaccination providers.

What would be the best way to reduce healthcare inequities in the U.S.?

To advance health equity, Optum Health is focused on delivering personalized care based on an individual’s needs, promoting equity and diversity in the health workforce, improving the health of underserved communities, and leveraging data and emerging analytics to monitor and address disparities in care.

Name a book or article that everyone in healthcare should read.

“Change by Design” by Tim Brown provides an introduction to the concept of design thinking and how it can transform organizations and inspire innovation. Design thinking’s tools and clear process steps help teams break free of human tendencies that can get in the way of innovation. I studied the elements of design thinking at Stanford Graduate School of Business and believe embracing the ethos of design thinking can truly help transform healthcare.

“Watching (my parents) overcome incredible odds to both migrate to this country and overcome health issues has been a huge inspiration.” — Sonia Samagh, M.D., MBA

Managed Healthcare Executive.com
ANDREW TOY, M.S.

Andrew Toy, M.S., president, chief technology officer and board member at Clover Health in Nashville, Tennessee

I was born and raised in Hong Kong and came to the United States to study computer science at Stanford University in 1996. Following my role as vice president of mobile applications at Morgan Stanley and then running mobile content for MTV, I co-founded Divide, a company focused on creating a split between work and personal data on mobile devices. At the time, as iPhone and Android devices were gaining popularity, it was common for folks to bring two devices to work — a work-assigned BlackBerry and a smartphone for personal use. We created Divide to fix the two-phone problem, and four years later Divide was acquired by Google for $120 million.

After serving as a director of Google's Android enterprise group, I saw the potential to both grow a great business and truly help people at Clover Health. I became chief technology officer in 2018. I helped create its breakthrough clinical support platform, the Clover Assistant. In February 2019, I was appointed president of Clover and also joined the board.

Who has had the greatest influence on your life?

My parents, who have always encouraged me to take the path less trodden. They are Australian-Chinese immigrants who raised me in a British school system in Hong Kong and encouraged me to pursue excellence by attending a university in the U.S. They taught me that talent and opportunity are distributed and that you should always push yourself to chase them wherever they are.

Why did you pursue a career in healthcare?

After I sold my last startup, I wanted to do something mission-oriented and build a great business. Healthcare seemed incredibly interesting and ripe for innovation but, as a technologist, I also saw it as a difficult task to create a business that could drive real change.

Then I met Clover's CEO Vivek Garipalli, who's been the most influential person in my healthcare journey. I've learned so much from him, and I'll never forget when he took a chance on me and said, "In a year, you'll be the technologist (who) knows the most about how healthcare actually works." I think that was a prescient observation because, in a short time, we've combined technology innovation with a deep understanding of how the wheels of healthcare actually turn to create real change.

Which career accomplishment has given you the greatest satisfaction?

My time at Divide has by far been my most satisfying accomplishment to date. Divide technology is built into every Android device in the world. That said, I fully expect Clover to be the most satisfying career journey I'll go on — but only after we truly make momentous progress on our goal to fundamentally transform healthcare.

What would be the best way to reduce healthcare inequities in the U.S.?

Free internet access for every home in the U.S. would go a long way toward reducing healthcare inequities. The pandemic highlighted just how intertwined internet access and health and wellness are as telehealth took off.

Name a book or article that everyone in healthcare should read.

“StrengthsFinder 2.0” by Tom Rath is about understanding how to value people who are good at what you aren’t and leaning on their strengths to augment your weaknesses. Diverse opinions and strengths are key to a strong team and company.
In patients with severe COVID-19 infection, a phenomenon called a cytokine storm is often the underlying reason for complications such as pneumonia and lung failure. Cytokine storms occur when a person’s body releases too many cytokines — a broad group of small proteins integral to the immune system — too quickly. The result is a hyperinflammatory response that may injure tissues in many parts of the body. As reports of the syndrome emerged at the beginning of the pandemic, drugmakers began combing through their drug portfolios, looking for possible treatments.

Physicians are treating hospitalized patients with COVID-19 with dexamethasone, a powerful steroid that quells inflammation, and remdesivir (the Gilead drug sold under the brand name Veklury). However, there’s a need for more effective treatment that could result in fewer patients needing mechanical ventilation and improve outcomes of severe cases of COVID-19. NRx Pharmaceuticals, which is based in Wilmington, Delaware, has an application pending for an EUA of its treatment that targets the cytokine IL-6. In July, the company shared more promising data about the treatment, Zyesami (aviptadil), that suggest it may prevent cytokine storm in patients with COVID-19.

Throughout the phase 2b/3 trial, patients receiving Zyesami did not have a large rise in cytokine level, whereas patients receiving placebo experienced a significant increase. The data showed the treatment yielded a survival benefit for patients, with a sizable drop in 60-day mortality from COVID-19.

Humanigen had shared data suggesting that the drug may be especially effective in Black patients, a group with a threefold increased risk of hospitalization and twofold increased risk of death from COVID-19. The company said that results from the phase 3 LIVE-AIR study showed that lenzilumab resulted in a ninefold increase of survival, without the need for ventilation, among Black patients with C-reactive protein levels less than 150 milligrams per/L. C-reactive protein is found in blood plasma and increases in response to inflammation. Across all patients in the study, lenzilumab yielded a more than twofold increased chance of survival without the need for ventilation, which was the basis for the company’s application for an EUA.

Meanwhile, researchers at I-Mab Biopharma, a biotech company based in China, announced positive results for plonmarlimab, which targets the same cytokines as lenzilumab. Results from a phase 2/3 study showed that plonmarlimab reduced the number of patients needing mechanical ventilation compared with placebo and also lowered death rates (4.9% versus 13.3%).

Jaime Rosenberg is a freelance writer based in Jersey City, New Jersey.

Drugmakers look to quell COVID-19 cytokine storms

The FDA rejected Humanigen’s application for an emergency use authorization, but the race is on to develop an effective therapy for the cytokine storms that affect patients with COVID-19. by J AIME ROSENBERG
LIBTAYO works with the immune system to help treat the following types of cancer:

- The first-line treatment of patients with non–small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression (tumor proportion score [TPS] ≥50%) as determined by an FDA-approved test, with no EGFR, ALK, or ROS1 aberrations, and is locally advanced where patients are not candidates for surgical resection or definitive chemoradiation OR metastatic

- The treatment of patients with locally advanced basal cell carcinoma (laBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate

- The treatment of patients with metastatic cutaneous squamous cell carcinoma (mCSCC) or locally advanced CSCC (laCSCC) who are not candidates for curative surgery or curative radiation

Visit LIBTAYOhcp.com for more information

Important Safety Information

Warnings and Precautions

Severe and Fatal Immune-Mediated Adverse Reactions

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue at any time after starting treatment. While immune-mediated adverse reactions usually occur during treatment, they can also occur after discontinuation. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously. Early identification and management are essential to ensuring safe use of PD-1/PD-L1–blocking antibodies. The definition of immune-mediated adverse reactions included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.
Important Safety Information (cont’d)

Warnings and Precautions (cont’d)

Severe and Fatal Immune-Mediated Adverse Reactions (cont’d)

No dose reduction for LIBTAYO is recommended. In general, withhold LIBTAYO for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue LIBTAYO for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids.

Withhold or permanently discontinue LIBTAYO depending on severity. In general, if LIBTAYO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Immune-mediated pneumonitis: LIBTAYO can cause immune-mediated pneumonitis. In patients treated with other PD-1/PD-L1–blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 4 (0.5%), Grade 3 (0.5%), and Grade 2 (2.1%). Pneumonitis led to permanent discontinuation in 1.4% of patients and withholding of LIBTAYO in 2.1% of patients. Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 58% of the 26 patients. Of the 17 patients in whom LIBTAYO was withheld, 9 reintiated after symptom improvement; of these, 3/9 (33%) had recurrence of pneumonitis. Withhold LIBTAYO for Grade 2, and permanently discontinue for Grade 3 or 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated colitis: LIBTAYO can cause immune-mediated colitis. The primary component of immune-mediated colitis was diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1–blocking antibodies. In cases of corticosteroid-refractory immune-mediated colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2.2% (18/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (1.1%). Colitis led to permanent discontinuation in 0.4% of patients and withholding of LIBTAYO in 1.5% of patients. Systemic corticosteroids were required in all patients with colitis. Colitis resolved in 39% of the 18 patients. Of the 12 patients in whom LIBTAYO was withheld, 4 reintiated LIBTAYO after symptom improvement; of these, 3/4 (75%) had recurrence. Withhold LIBTAYO for Grade 2 or 3, and permanently discontinue for Grade 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated hepatitis: LIBTAYO can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 2% (16/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (1.4%), and Grade 2 (0.2%). Hepatitis led to permanent discontinuation of LIBTAYO in 1.2% of patients and withholding of LIBTAYO in 0.5% of patients. Systemic corticosteroids were required in all patients with hepatitis. Additional immunosuppression with mycophenolate was required in 19% (3/16) of these patients. Hepatitis resolved in 50% of the 16 patients. Of the 5 patients in whom LIBTAYO was withheld, 3 reintiated LIBTAYO after symptom improvement; of these, none had recurrence.

For hepatitis with no tumor involvement of the liver: Withhold LIBTAYO if AST or ALT increases to more than 3 and up to 8 times the upper limit of normal (ULN) or if total bilirubin increases to more than 1.5 and up to 3 times the ULN. Permanently discontinue LIBTAYO if AST or ALT increases to more than 8 times the ULN or total bilirubin increases to more than 3 times the ULN.

For hepatitis with tumor involvement of the liver: Withhold LIBTAYO if baseline AST or ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN. Also, withhold LIBTAYO if baseline AST or ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN. Permanently discontinue LIBTAYO if AST or ALT increases to more than 10 times ULN or if total bilirubin increases to more than 3 times ULN. If AST and ALT are less than or equal to ULN at baseline, withhold or permanently discontinue LIBTAYO based on recommendations for hepatitis with no liver involvement.

Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated endocrinopathies: For Grade 3 or 4 endocrinopathies, withhold until clinically stable or permanently discontinue depending on severity.

- Adrenal insufficiency: LIBTAYO can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold LIBTAYO depending on severity. Adrenal insufficiency occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.4%). Adrenal insufficiency led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. LIBTAYO was not withheld in any patient due to adrenal insufficiency. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these, 67% (2/3) remained on systemic corticosteroids. Adrenal insufficiency had not resolved in any patient at the time of data cutoff.

Please see additional Important Safety Information and Brief Summary of Prescribing Information on the following pages.
Important Safety Information (cont’d)

Warnings and Precautions (cont’d)

Severe and Fatal Immune-Mediated Adverse Reactions (cont’d)

Immune-mediated endocrinopathies: (cont’d)

- **Hypophysitis:** LIBTAYO can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity. Hypophysitis occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.1%) adverse reactions. Hypophysitis led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient and withholding of LIBTAYO in 1 (0.1%) patient. Systemic corticosteroids were required in 67% (2/3) of patients with hypophysitis. Hypophysitis had not resolved in any patient at the time of data cutoff.

- **Thyroid disorders:** LIBTAYO can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity. Thyroiditis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including Grade 2 (0.2%) adverse reactions. No patient discontinued LIBTAYO due to thyroiditis. Thyroiditis led to withholding of LIBTAYO in 1 patient. Systemic corticosteroids were not required in any patient with thyroiditis. Thyroiditis had not resolved in any patient at the time of data cutoff. Blood thyroid stimulating hormone increased and blood thyroid stimulating hormone decreased have also been reported.

- **Hyperthyroidism:** Hyperthyroidism occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 2 (0.9%). No patient discontinued treatment and LIBTAYO was withheld in 0.5% of patients due to hyperthyroidism. Systemic corticosteroids were required in 3.8% (1/26) of patients. Hyperthyroidism resolved in 50% of 26 patients. Of the 4 patients in whom LIBTAYO was withheld for hyperthyroidism, 2 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hyperthyroidism.

- **Hypothyroidism:** Hypothyroidism occurred in 7% (60/810) of patients receiving LIBTAYO, including Grade 2 (6%). Hypothyroidism led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. Hypothyroidism led to withholding of LIBTAYO in 1.1% of patients. Systemic corticosteroids were not required in any patient with hypothyroidism. Hypothyroidism resolved in 8.3% of the 60 patients. Majority of the patients with hypothyroidism led to long-term thyroid hormone replacement. Of the 9 patients in whom LIBTAYO was withheld for hypothyroidism, 1 reinitiated LIBTAYO after symptom improvement; 1 required ongoing hormone replacement therapy.

- **Type 1 diabetes mellitus, which can present with diabetic ketoacidosis:** Monitor for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold LIBTAYO depending on severity. Type 1 diabetes mellitus occurred in 0.1% (1/810) of patients, including Grade 4 (0.1%). No patient discontinued treatment due to type 1 diabetes mellitus. Type 1 diabetes mellitus led to withholding of LIBTAYO in 0.1% of patients.

**Immune-mediated nephritis with renal dysfunction:** LIBTAYO can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 3 (0.1%), and Grade 2 (0.4%). Nephritis led to permanent discontinuation in 0.1% of patients and withholding of LIBTAYO in 0.4% of patients. Systemic corticosteroids were required in all patients with nephritis. Nephritis resolved in 80% of the 5 patients. Of the 3 patients in whom LIBTAYO was withheld, 2 reinitiated LIBTAYO after symptom improvement; of these, none had recurrence. Withhold LIBTAYO for Grade 2 or 3 increased blood creatinine, and permanently discontinue for Grade 4 increased blood creatinine. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

**Immune-mediated dermatologic adverse reactions:** LIBTAYO can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) has occurred with PD-1/PD-L1–blocking antibodies. Immune-mediated dermatologic adverse reactions occurred in 1.6% (13/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (0.6%). Immune-mediated dermatologic adverse reactions led to permanent discontinuation in 0.1% of patients and withholding of LIBTAYO in 1.4% of patients. Systemic corticosteroids were required in all patients with immune-mediated dermatologic adverse reactions. Immune-mediated dermatologic adverse reactions resolved in 69% of the 13 patients. Of the 11 patients in whom LIBTAYO was withheld for dermatologic adverse reactions, 7 reinitiated LIBTAYO after symptom improvement; of these, 43% (3/7) had recurrence of the dermatologic adverse reaction. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold LIBTAYO for suspected SJS, TEN, or DRESS. Permanently discontinue LIBTAYO for confirmed SJS, TEN, or DRESS. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

**Other immune-mediated adverse reactions:** The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in 810 patients who received LIBTAYO or were reported with the use of other PD-1/PD-L1–blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

- **Cardiac/vascular:** Myocarditis, pericarditis, and vasculitis. Permanently discontinue for Grades 2, 3, or 4 myocarditis.

- **Nervous system:** Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, and autoimmune neuropathy. Withhold for Grade 2 neurological toxicities and permanently discontinue for Grades 3 or 4 neurological toxicities. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.
Important Safety Information (cont’d)

Warnings and Precautions (cont’d)

Severe and Fatal Immune-Mediated Adverse Reactions (cont’d)

Other immune-mediated adverse reactions: (cont’d)

- **Ocular:** Uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada–like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss

- **Gastrointestinal:** Pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis, stomatitis

- **Musculoskeletal and connective tissue:** Myositis/polymyositis, rhabdomyolysis, and associated sequelae including renal failure, arthritis, polymyalgia rheumatica

- **Endocrine:** Hypoparathyroidism

- **Other (hematologic/immune):** Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection

Infusion-related reactions

Severe infusion-related reactions (Grade 3) occurred in 0.1% of patients receiving LIBTAYO as a single agent. Monitor patients for signs and symptoms of infusion-related reactions. The most common symptoms of infusion-related reaction were nausea, pyrexia, rash and dyspnea. Interrupt or slow the rate of infusion for Grade 1 or 2, and permanently discontinue for Grade 3 or 4.

Complications of allogeneic HSCT

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1–blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1–blocking antibody prior to or after an allogeneic HSCT.

Embryo-fetal toxicity

LIBTAYO can cause fetal harm when administered to a pregnant woman due to an increased risk of immune-mediated rejection of the developing fetus resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose.

Adverse Reactions

- In the pooled safety analysis of 810 patients, the most common adverse reactions (≥15%) with LIBTAYO were musculoskeletal pain, fatigue, rash, and diarrhea

- In the pooled safety analysis of 810 patients, the most common Grade 3-4 laboratory abnormalities (≥2%) with LIBTAYO were lymphopenia, hyponatremia, hypophosphatemia, increased aspartate aminotransferase, anemia, and hyperkalemia

Use in Specific Populations

- **Lactation:** Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO

- **Females and males of reproductive potential:** Verify pregnancy status in females of reproductive potential prior to initiating LIBTAYO

Please see Brief Summary of Prescribing Information on the following pages.

References:

1. LIBTAYO (cemiplimab-rwlc) injection full U.S. prescribing information. Regeneron Pharmaceuticals, Inc., and sanofi-aventis U.S. LLC.

©2021 Regeneron Pharmaceuticals, Inc., and sanofi-aventis U.S. LLC. All rights reserved. LB.21.08.0022 08/2021
LIBTAYO® (cemiplimab-rwlc) injection, for intravenous use

Brief Summary of Prescribing Information

1 INDICATIONS AND USAGE

1.1 Cutaneous Squamous Cell Carcinoma

LIBTAYO is indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma (mSCC) or locally advanced CSCC (lSCC) who are not candidates for curative surgery or curative radiation.

1.2 Basal Cell Carcinoma

LIBTAYO is indicated for the treatment of patients:

- with locally advanced basal cell carcinoma (lABCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.

1.3 Non-Small Cell Lung Cancer

LIBTAYO is indicated for the first-line treatment of patients with non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [Tumor Proportion Score (TPS) ≥ 50%] as determined by an FDA-approved test [see Dosage and Administration (2.1) in the full prescribing information], with no EGFR, ALK or ROS1 aberrations, and is:

- locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or
- metastatic.

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 Severe and Fatal Immune-Mediated Adverse Reactions

LIBTAYO is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting PD-1/PD-L1 blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1 blocking antibodies, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1 blocking antibodies. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue LIBTAYO depending on severity [see Dosage and Administration (2.3) in the full prescribing information]. In general, if LIBTAYO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

Immune-Mediated Pneumonitis

LIBTAYO can cause immune-mediated pneumonitis. The definition of immune-mediated pneumonitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. In patients treated with other PD-1/PD-L1 blocking antibodies the incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

Immune-mediated pneumonitis occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 4 (0.5%), Grade 3 (0.5%), and Grade 2 (2.1%) adverse reactions. Pneumonitis led to permanent discontinuation of LIBTAYO in 1.4% of patients and withholding of LIBTAYO in 2.1% of the patients.

Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 58% of the 26 patients. Of the 17 patients in whom LIBTAYO was withheld for pneumonitis, 9 reinitiated LIBTAYO after symptom improvement; of these, 3/9 (33%) had recurrence of pneumonitis.

Immune-Mediated Colitis

LIBTAYO can cause immune-mediated colitis. The definition of immune-mediated colitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. The primary component of the immune-mediated colitis was diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1 blocking antibodies. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Immune-mediated colitis occurred in 2.2% (18/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (1.1%) adverse reactions. Colitis led to permanent discontinuation of LIBTAYO in 0.4% of patients and withholding of LIBTAYO in 1.5% of patients.

Systemic corticosteroids were required in all patients with colitis. Colitis resolved in 39% of the 18 patients. Of the 12 patients in whom LIBTAYO was withheld for colitis, 4 reinitiated LIBTAYO after symptom improvement; of these, 3/4 (75%) had recurrence of colitis.

Immune-Mediated Hepatitis

LIBTAYO can cause immune-mediated hepatitis. The definition of immune-mediated hepatitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology.

Immune-mediated hepatitis occurred in 2% (16/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (1.4%), and Grade 2 (0.2%) adverse reactions. Hepatitis led to permanent discontinuation of LIBTAYO in 1.2% of patients and withholding of LIBTAYO in 0.5% of patients.

Systemic corticosteroids were required in all patients with hepatitis. Nineteen percent (19%) of these patients (3/16) required additional immunosuppression with mycophenolate. Hepatitis resolved in 50% of the 16 patients. Of the 5 patients in whom LIBTAYO was withheld for hepatitis, 3 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hepatitis.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

LIBTAYO can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold LIBTAYO depending on severity [see Dosage and Administration (2.3) in the full prescribing information]. Adrenal insufficiency occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.4%) adverse reactions. Adrenal insufficiency led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. LIBTAYO was not withheld in any patient due to adrenal insufficiency. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these 67% (2/3) remained on systemic corticosteroids. Adrenal insufficiency had not resolved in any patient at the time of data cutoff.

Hypophysitis

LIBTAYO can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity [see Dosage and Administration (2.3) in the full prescribing information]. Hypophysitis occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.1%) adverse reactions. Hypophysitis led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient and withholding of LIBTAYO in 1 (0.1%) patient. Systemic corticosteroids were required in 67% (2/3) patients with hypophysitis. Hypophysitis had not resolved in any patient at the time of data cutoff.

Thyroid Disorders

LIBTAYO can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hyperthyroidism can follow hypothyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue
Of the 4 patients in whom LIBTAYO was withheld for hyperthyroidism, receiving LIBTAYO, including Grade 2 (0.9%) adverse reactions. No patient of the dermatologic adverse reaction. LIBTAYO was withheld for dermatologic adverse reaction, 7 reinitiated Systemic corticosteroids were required in all patients with immune-mediated Immune-mediated dermatologic adverse reactions occurred in 1.6% depending on severity [see Dosage and Administration (2.3) in the full prescribing information]. Of the 4 patients in whom LIBTAYO was withheld for hyperthyroidism, 2 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hyperthyroidism. Hypothyroidism: Hypothyroidism occurred in 7% (60/810) of patients receiving LIBTAYO, including Grade 2 (6%) adverse reactions. Hypothyroidism led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. Hypothyroidism led to withholding of LIBTAYO in 1.1% of patients. Systemic corticosteroids were not required in any patient with hypothyroidism. Hypothyroidism resolved in 8.3% of the 60 patients. The majority of patients with hypothyroidism required long-term thyroid hormone replacement. Of the 9 patients in whom LIBTAYO was withheld for hypothyroidism, 1 reintiated LIBTAYO after symptom improvement; 1 required ongoing hormone replacement therapy. Type 1 Diabetes Mellitus, which can present with diabetic ketoacidosis. Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold LIBTAYO depending on severity [see Dosage and Administration (2.3) in the full prescribing information]. Type 1 diabetes mellitus occurred in 0.1% (1/810) of patients, including Grade 4 (0.1%) adverse reactions. No patient discontinued treatment due to Type 1 diabetes mellitus. Type 1 diabetes mellitus led to withholding of LIBTAYO in 0.1% of patients.

Immune-Mediated Nephritis with Renal Dysfunction

LIBTAYO can cause immune-mediated nephritis. The definition of immune-mediated nephritis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. Immune-mediated nephritis occurred in 0.6% (5/810) patients receiving LIBTAYO, including fatal (0.1%), Grade 3 (0.1%) and Grade 2 (0.4%) adverse reactions. Nephritis led to permanent discontinuation of LIBTAYO in 0.1% of patients and withholding of LIBTAYO in 0.4% of patients. Systemic corticosteroids were required in all patients with nephritis. Nephritis resolved in 80% of the 5 patients. Of the 3 patients in whom LIBTAYO was withheld for nephritis, 2 reintiated LIBTAYO after symptom improvement; of these, none had recurrence of nephritis.

Immune-Mediated Dermatologic Adverse Reactions

LIBTAYO can cause immune-mediated rash or dermatitis. The definition of immune-mediated dermatologic adverse reaction included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. Exfoliative rashes. Withhold or permanently discontinue LIBTAYO DRESS (Drug Rash with Eosinophilia and Systemic Symptoms), has absence of a clear alternate etiology. Exfoliative dermatitis, including Grade 2 (0.2%) adverse reactions. No patient continued treatment due to hyperthyroidism. Hyperthyroidism led to withholding of LIBTAYO in 0.5% of patients. Systemic corticosteroids were required in 3.8% (1/26) of patients with hyperthyroidism. Hyperthyroidism resolved in 50% of the 26 patients. Of the 4 patients in whom LIBTAYO was withheld for hyperthyroidism, receiving LIBTAYO, including Grade 2 (0.9%) adverse reactions. No patient of the dermatologic adverse reaction. LIBTAYO was withheld for dermatologic adverse reaction, 7 reinitiated Systemic corticosteroids were required in all patients with immune-mediated Immune-mediated dermatologic adverse reactions occurred in 1.6% depending on severity [see Dosage and Administration (2.3) in the full prescribing information]. Immune-mediated dermatologic adverse reactions occurred in 1.6% (13/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (0.6%) adverse reactions. Dermatologic adverse reactions led to permanent discontinuation of LIBTAYO in 0.1% of patients and withholding of LIBTAYO in 1.4% of patients. Systemic corticosteroids were required in all patients with immune-mediated dermatologic adverse reactions. Immune-mediated dermatologic adverse reactions resolved in 69% of the 13 patients. Of the 11 patients in whom LIBTAYO was withheld for dermatologic adverse reaction, 7 reintiated LIBTAYO after symptom improvement; of these 43% (3/7) had recurrence of the dermatologic adverse reaction.

Other Immune-Mediated Adverse Reactions

The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in 810 patients who received LIBTAYO or were reported with the use of other PD-1/PD-L1 blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

Cardiac/Vascular: Myocarditis, pericarditis, vasculitis.

Nervous System: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome / myasthenia gravis (including exacerbation), Guillain-Barre syndrome, nerve paresis, autoimmune neuropathy

Ocular: Uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

Gastrointestinal: Pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis, stomatitis

Musculoskeletal and Connective Tissue: Myositis/polymyositis, rhabdomyolysis and associated sequelae including renal failure, arthritis, polymyalgia rheumatica

Endocrine: Hypoparathyroidism

Other (Hematologic/Immune): Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection

5.2 Infusion-Related Reactions

Severe infusion-related reactions (Grade 3) occurred in 0.1% of patients receiving LIBTAYO as a single agent. Monitor patients for signs and symptoms of infusion-related reactions. The most common symptoms of infusion-related reaction were nausea, pyrexia, rash and dyspnea. Interrupt or slow the rate of infusion or permanently discontinue LIBTAYO based on severity of reaction [see Dosage and Administration (2.3) in the full prescribing information].

5.3 Complications of Allogeneic HSCT

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1 blocking antibody. Transplant-related complications include hyperacutegraft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT.

5.4 Embryo-Fetal Toxicity

Based on its mechanism of action, LIBTAYO can cause fetal harm when administered to a pregnant woman. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose [see Use in Specific Populations (8.1, 8.3)].

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling.

• Severe and Fatal Immune-Mediated Adverse Reactions [see Warnings and Precautions (5.1)]

• Infusion-Related Reactions [see Warnings and Precautions (5.2)]

• Complications of Allogeneic HSCT [see Warnings and Precautions (5.3)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described in Warnings and Precautions reflect exposure to LIBTAYO as a single agent in 810 patients in three open-label, single-arm, multicohort studies (Study 1423, Study 1540 and Study 1620), and one open-label randomized multi-center study (Study 1624). These studies included 219 patients with advanced CSCC (Studies 1540 and 1423), 152 patients with advanced BCC (Study 1620), 355 patients with NSCLC...
The safety of LIBTAYO was evaluated in 219 patients with advanced CSCC (metastatic or locally advanced disease) in Study 1423 and Study 1540 [see Clinical Studies (14.1) in the full prescribing information]. Of these 219 patients, 131 had mCSCC (nodal or distant) and 88 had laCSCC. Patients received LIBTAYO 1 mg/kg every 2 weeks (n=1), 3 mg/kg every 2 weeks (n=162) or 350 mg every 3 weeks (n=56) as an intravenous infusion until disease progression, unacceptable toxicity, or completion of planned treatment. The median duration of exposure was 38 weeks (2 weeks to 110 weeks).

The safety population characteristics were: median age of 72 years (38 to 96 years), 83% male, 96% White, and European Cooperative Oncology Group (ECOG) performance score (PS) of 0 (44%) and 1 (56%).

Serious adverse reactions occurred in 35% of patients. Serious adverse reactions that occurred in at least 2% of patients were pneumonitis, cellulitis, sepsis, and pneumonia. Permanent discontinuation due to an adverse reaction occurred in 8% of patients. Adverse reactions resulting in permanent discontinuation were pneumonitis, cough, pneumonia, encephalitis, aseptic meningitis, hepatitis, arthropathy, muscular weakness, neck pain, soft tissue necrosis, complex regional pain syndrome, lethargy, psoriasis, rash maculopapular, pruritus, and confusional state.

The most common (≥20%) adverse reactions were fatigue, rash, diarrhea, musculoskeletal pain, and nausea. The most common Grade 3 or 4 adverse reactions (≥2%) were cellulitis, anemia, hypertension, pneumonia, musculoskeletal pain, dermatitis, skin infection, and hypercalcemia. The most common (≥4%) Grade 3 or 4 laboratory abnormalities worsening from baseline were lymphopenia, anemia, hyperkalemia, and hyponatremia. Increased aspartate aminotransferase and increased alanine aminotransferase were seen in ≤2% of patients. Laboratory abnormalities associated with discontinuation included increased aspartate aminotransferase, anemia, and hyperkalemia.

The safety population for this pooled analysis consisted of 151 patients (56% male, 95% White) with a median age of 68 years (38 to 90 years), 90% of whom had advanced metastatic or locally advanced CSCC. The median duration of exposure was 10 weeks (0.5 to 52 weeks). The most common adverse reactions occurring in ≥10% of patients (at least 3 patients) included blood creatinine increased, diarrhea, colitis, pneumonia, and urinary tract infection.

Table 2: Adverse Reactions in at least 10% of Patients with Advanced CSCC Receiving LIBTAYO in Study 1423 and Study 1540

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>LIBTAYO N=219</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades %</td>
</tr>
<tr>
<td>General and Administration Site</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>34</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>31</td>
</tr>
<tr>
<td>Pruritus</td>
<td>18</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>25</td>
</tr>
<tr>
<td>Nausea</td>
<td>21</td>
</tr>
<tr>
<td>Constipation</td>
<td>13</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>24</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>11</td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>14</td>
</tr>
</tbody>
</table>

(continued)
Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03.

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03.

a. Composite term includes fatigue, asthenia, and malaise
b. Composite term includes arthralgia, back pain, myalgia, pain in extremity, musculoskeletal pain, neck pain, musculoskeletal stiffness, musculoskeletal chest pain, musculoskeletal discomfort, and spinal pain
c. Composite term includes rash maculo-papular, rash, dermatitis, dermatitis acneiform, erythema, rash pruritic, dermatitis bullous, dyshidrotic eczema, pemphigoid, rash erythematous, and urticaria
d. Composite term includes upper respiratory tract infection, nasopharyngitis, rhinitis, sinusitis, pharyngitis, respiratory tract infection, and viral upper respiratory tract infection
e. Composite term includes dyspnea and dyspnea exertional
f. Composite term includes hypertension and hypertensive crisis

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03.

Table 4: Adverse Reactions in ≥ 10% of Patients with Advanced BCC Receiving LIBTAYO in Study 1629

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>LIBTAYO N = 132</th>
<th>All Grades %</th>
<th>Grades 3-4 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue*</td>
<td>49</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal pain*</td>
<td>33</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>25</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>12</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>11</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>22</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>20</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection²</td>
<td>15</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>12</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>14</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>13</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>12</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>11</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Vascular disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension²</td>
<td>11</td>
<td>4.5</td>
<td></td>
</tr>
<tr>
<td>Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. Musculoskeletal pain is a composite term that includes back pain, arthralgia, pain in extremity, musculoskeletal pain, chest pain, bone pain, myalgia, neck pain, spinal pain, and musculoskeletal stiffness
b. Rash is a composite term that includes rash, dermatitis, urticaria, rash maculo-papular, erythema, rash erythematous, rash pruritic, psoriasis, autoimmune dermatitis, dermatitis acneiform, dermatitis atopic, dermatitis bullous, drug eruption, dyshidrotic eczema, lichen planus, and skin reaction
c. Fatigue is a composite term that includes fatigue, asthenia, and malaise
d. Pneumonia is a composite term that includes atypical pneumonia, embolic pneumonia, lower respiratory tract infection, lung abscess, paracancerous pneumonia, pneumonia, pneumonia bacterial, and pneumonia klebsiella
e. Cough is a composite term that includes cough and productive cough

Table 5: Grade 3 or 4 Laboratory Abnormalities Worsening from Baseline in ≥ 1% of Patients with Advanced BCC Receiving LIBTAYO in Study 1620

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>Grade 3-4 (%)</th>
<th>All Grades %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrolytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Coagulation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activated partial thromboplastin time prolonged</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocyte count decreased</td>
<td>2.3</td>
<td></td>
</tr>
</tbody>
</table>

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03.

a. Percentages are based on the number of patients with at least 1 post-baseline value available for that parameter

The safety of LIBTAYO was evaluated in 355 patients with locally advanced or metastatic NSCLC in Study 1624 [see Clinical Studies (14.3) in the full prescribing information]. Patients received LIBTAYO 350 mg every 3 weeks (n=355) or investigator’s choice of chemotherapy (n=342), consisting of paclitaxel plus cisplatin or carboplatin; gemcitabine plus cisplatin or carboplatin; or pemetrexed plus cisplatin or carboplatin followed by optional pemetrexed maintenance. The median duration of exposure was 27.3 weeks (9 days to 115 weeks) in the LIBTAYO group and 17.7 weeks (18 days to 86.7 weeks) in the chemotherapy group. In the LIBTAYO group, 54% of patients were exposed to LIBTAYO for ≥ 6 months and 22% were exposed for ≥ 12 months.

The safety population characteristics were: median age of 63 years (31 to 79 years), 44% of patients 65 or older, 88% male, 86% White, 82% had metastatic disease and 18% had locally advanced disease and ECOG performance score (PS) of 0 (27%) and 1 (73%).

LIBTAYO was permanently discontinued due to adverse reactions in 6% of patients; adverse reactions resulting in permanent discontinuation in at least 2% of patients were pneumonitis, pneumonia, ischemic stroke and increased aspartate aminotransferase. Serious adverse reactions occurred in 28% of patients. The most frequent serious adverse reactions in at least 2% of patients were pneumonia and pneumonitis.

Table 6 summarizes the adverse reactions that occurred in ≥ 10% of patients and Table 7 summarizes Grade 3 or 4 laboratory abnormalities in patients receiving LIBTAYO.

Table 6: Adverse Reactions in ≥ 10% of Patients with Locally Advanced or Metastatic NSCLC Receiving LIBTAYO in Study 1624

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>LIBTAYO N=355</th>
<th>Chemotherapy N=342</th>
<th>All Grades %</th>
<th>Grades 3-4 %</th>
<th>All Grades %</th>
<th>Grades 3-4 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal pain²</td>
<td>26</td>
<td>0.6</td>
<td>27</td>
<td>1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash²</td>
<td>15</td>
<td>1.4</td>
<td>6</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>15</td>
<td>3.4</td>
<td>50</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue²</td>
<td>14</td>
<td>1.1</td>
<td>26</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>12</td>
<td>0.6</td>
<td>18</td>
<td>0.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia²</td>
<td>11</td>
<td>5</td>
<td>12</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough²</td>
<td>11</td>
<td>0</td>
<td>8</td>
<td>0.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03.

a. Musculoskeletal pain is a composite term that includes back pain, arthralgia, pain in extremity, musculoskeletal pain, chest pain, bone pain, myalgia, neck pain, spinal pain, and musculoskeletal stiffness
b. Rash is a composite term that includes rash, dermatitis, urticaria, rash maculo-papular, erythema, rash erythematous, rash pruritic, psoriasis, autoimmune dermatitis, dermatitis acneiform, dermatitis atopic, dermatitis bullous, drug eruption, dyshidrotic eczema, lichen planus, and skin reaction
c. Fatigue is a composite term that includes fatigue, asthenia, and malaise
d. Pneumonia is a composite term that includes atypical pneumonia, embolic pneumonia, lower respiratory tract infection, lung abscess, paracancerous pneumonia, pneumonia, pneumonia bacterial, and pneumonia klebsiella
e. Cough is a composite term that includes cough and productive cough

Non-Small Cell Lung Cancer (NSCLC)

The safety of LIBTAYO was evaluated in 355 patients with locally advanced or metastatic NSCLC in Study 1624 [see Clinical Studies (14.3) in the full prescribing information]. Patients received LIBTAYO 350 mg every 3 weeks (n=355) or investigator’s choice of chemotherapy (n=342), consisting of paclitaxel plus cisplatin or carboplatin; gemcitabine plus cisplatin or carboplatin; or pemetrexed plus cisplatin or carboplatin followed by optional pemetrexed maintenance. The median duration of exposure was 27.3 weeks (9 days to 115 weeks) in the LIBTAYO group and 17.7 weeks (18 days to 86.7 weeks) in the chemotherapy group. In the LIBTAYO group, 54% of patients were exposed to LIBTAYO for ≥ 6 months and 22% were exposed for ≥ 12 months.

The safety population characteristics were: median age of 63 years (31 to 79 years), 44% of patients 65 or older, 88% male, 86% White, 82% had metastatic disease and 18% had locally advanced disease and ECOG performance score (PS) of 0 (27%) and 1 (73%).

LIBTAYO was permanently discontinued due to adverse reactions in 6% of patients; adverse reactions resulting in permanent discontinuation in at least 2% of patients were pneumonitis, pneumonia, ischemic stroke and increased aspartate aminotransferase. Serious adverse reactions occurred in 28% of patients. The most frequent serious adverse reactions in at least 2% of patients were pneumonia and pneumonitis.

Table 6 summarizes the adverse reactions that occurred in ≥ 10% of patients and Table 7 summarizes Grade 3 or 4 laboratory abnormalities in patients receiving LIBTAYO.
Table 7: Grade 3 or 4 Laboratory Abnormalities Worsening from Baseline in ≥1% of Patients with Locally Advanced or Metastatic NSCLC Receiving LIBTAYO in Study 1624

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>LIBTAYO N=355</th>
<th>Chemotherapy N=342</th>
<th>Grades 3-4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemistry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased aspartate</td>
<td>3.9</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>aminotransferase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased alanine</td>
<td>2.7</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>aminotransferase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased alkaline</td>
<td>2.4</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>phosphatase</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased blood</td>
<td>2.1</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>bilirubin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>1.8</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Increased creatinine</td>
<td>1.2</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>7</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>2.7</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Electrolytes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>6</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>4.2</td>
<td>1.9</td>
<td></td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>3.9</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>2.4</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>Hypermagnesemia</td>
<td>2.1</td>
<td>1.6</td>
<td></td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>1.5</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>1.2</td>
<td>2.2</td>
<td></td>
</tr>
</tbody>
</table>

Toxicity graded per NCI CTCAE v. 4.03

a. Percentages are based on the number of patients with at least 1 post-baseline value available for that parameter.

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to cemiplimab-rwlc in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

Anti-drug antibodies (ADA) were tested in 823 patients who received LIBTAYO. The incidence of cemiplimab-rwlc treatment-emergent ADAs was 2.2% using an electrochemiluminescent (ECL) bridging immunoassay; 0.4% were persistent ADA responses. In the patients who developed anti-cemiplimab-rwlc antibodies, there was no evidence of an altered pharmacokinetic profile of cemiplimab-rwlc.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on its mechanism of action, LIBTAYO can cause fetal harm when administered to a pregnant woman [see Clinical Pharmacology (12.1) in the full prescribing information]. There are no available data on the use of LIBTAYO in pregnant women. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus resulting in fetal death (see Data). Human IgG4 immunoglobulins (IgG4) are known to cross the placenta; therefore, LIBTAYO has the potential to be transmitted from the mother to the developing fetus. Advise women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

Animal reproduction studies have not been conducted with LIBTAYO to evaluate its effect on reproduction and fetal development. A central function of the PD-1/PD-L1 pathway is to preserve pregnancy by maintaining maternal immune tolerance to the fetus. In murine models of pregnancy, blockade of PD-L1 signaling has been shown to disrupt tolerance to the fetus and to result in an increase in fetal loss; therefore, potential risks of administering LIBTAYO during pregnancy include increased rates of abortion or stillbirth. As reported in the literature, there were no malformations related to the blockade of PD-1/PD-L1 signaling in the offspring of these animals; however, immune-mediated disorders occurred in PD-1 and PD-L1 knockout mice. Based on its mechanism of action, fetal exposure to cemiplimab-rwlc may increase the risk of developing immune-mediated disorders or altering the normal immune response.

8.2 Lactation

Risk Summary

There is no information regarding the presence of cemiplimab-rwlc in human milk, or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating LIBTAYO [see Use in Specific Populations (8.1)].

Contraception

LIBTAYO can cause fetal harm when administered to a pregnant woman [see Use in Specific Populations (8.1)].

Females

Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose.

8.4 Pediatric Use

The safety and effectiveness of LIBTAYO have not been established in pediatric patients.

8.5 Geriatric Use

Of the 810 patients who received LIBTAYO in clinical studies, 32% were 65 years up to 75 years and 22% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

Of the 219 patients with mCSCC or laCSCC who received LIBTAYO in clinical studies, 34% were 65 years up to 75 years and 41% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

Of the 132 patients with BCC who received LIBTAYO in Study 1620, 27% were 65 years up to 75 years, and 32% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

REGENERON | SANOFI GENZYME © 2021 Regeneron Pharmaceuticals, Inc., and sanofi-aventis U.S. LLC. All rights reserved.

LIB.21.02.0054 02/21
Network adequacy rules for cancer care are often inadequate

Vague standards may lead to networks with too few oncologists.

by KEITH LORIA

The ACA set national network adequacy standards, but since 2018 the responsibility has devolved to each state. The result is a patchwork of standards, many of them vague, according to a report published in JNCI Cancer Spectrum earlier this year.

Catherine Moore, M.D., at George Washington University School of Medicine in Washington, D.C., and David I. Shalowitz, M.D., M.S.H.P., of the Wake Forest School of Medicine, contacted representatives of the insurance departments in every state and Washington, D.C., and combed through information on state websites to gather network adequacy standards for cancer care.

They found that 16 states used only qualitative standards for access to an oncologist, such as health plan members must have “reasonable access” to oncologists or care. Seven states had quantitative elements, such as travel distance or a ratio of providers to members. Twenty-four states had network adequacy standards with both qualitative and quantitative elements.

“We found that states’ standards currently are highly variable,” Shalowitz says. “Unclear network adequacy standards for insurance plans may put patients at risk for poor access to cancer care.”

According to Shalowitz, it’s important for states to ensure that robust, transparent protections exist so that patients can access high-quality cancer care without having to go to a provider that is out of network, which may result in large medical bills that many people couldn’t afford to pay.

“While a single network adequacy standard may be neither possible nor desirable for all states and insurance markets, states should collaborate with patient advocates and cancer professionals who have knowledge of local markets and patients’ needs to develop basic standards for insurance coverage,” he says. “Transparent standards will also permit study of cancer care delivery outcomes related to network adequacy, improvement in access to high-quality care and minimization of the sometimes disastrous financial consequences of out-of-network billing.”

Shalowitz would also like to see additional research conducted to determine how network adequacy standards can be applied to rare or complex cancers and how they might improve equity in access to care.

Results of a number of studies have shown that nearly 1 in 5 emergency department visits involve a patient unknowingly being treated by an out-of-network provider, which led to unanticipated medical bills. The American Society of Clinical Oncology (ASCO) has pushed for legislation to address surprise billing for cancer patients. A spokesperson for ASCO confirmed that the organization is still pushing CMS to enact network adequacy standards for Medicaid managed care enrollees so they can access high-quality cancer care and all the oncology specialties in a timely fashion.

“Although our study did not address the issue of surprise billing specifically, we are concerned that patients may be at higher risk for receiving catastrophic medical bills if their insurance plan does not provide adequate access to cancer care,” Shalowitz says.

Network adequacy can be a major issue for patients with rare cancers. In a previous study, Shalowitz found that 27% of plans sold on insurance exchanges didn’t have an in-network specialist in gynecologic cancers, despite evidence that treatment by a specialist improves survival for patients with those types of cancers.

“Policy makers must ensure that insurance plans uniformly offer adequate coverage for cancer care to ensure that patients with these diseases are able to access high-quality treatment,” Shalowitz says.

Keith Loria is a freelance writer in the Washington, D.C., area.
COVID-19 ushers in a new era of health care delivery

The COVID-19 pandemic has forever changed how healthcare is and will be delivered in the future, Scott Gottlieb, M.D., former commissioner of the FDA, said during his keynote address.

The future of healthcare is going to be very different from what it is now, he said, and that doesn’t only mean accelerating the adoption of telehealth. It is broader than that, and bringing diagnostic testing for COVID-19 into the home was just the beginning of this change, opening up a range of possibilities for healthcare delivery.

“COVID has clearly changed the course of world history,” he said. “It’s had geopolitical consequences, and it’s impacted the economy in an irrecoverable way. But it has changed our culture around healthcare and changed our orientation to aspects of healthcare delivery that are fundamental. And it’s not going back.”

Healthcare in the home became the cultural norm during the pandemic, making telehealth, virtual visits, and home testing commonplace. “There was a time when the FDA would not allow people to self-diagnose for infectious disease. There was a perception that people wouldn’t engage in appropriate follow up,” he said.

In a wide-ranging, hourlong talk, Gottlieb sounded an optimistic note about the next six months of the COVID-19 pandemic and wove in some observations about missteps in the federal government’s response. Gottlieb’s book about the pandemic, “Uncontrolled Spread: Why COVID-19 Crushed Us and How We Can Defeat the Next Pandemic,” came out the week after his talk at the PBMI meeting. Gottlieb said the federal government was too slow in implementing and scaling up testing and that federal officials failed to contact companies in the private sector that could have helped: “That call just didn’t get made.”

He also said U.S. needs to maintain the capacity to respond to pandemics quickly. Gottlieb said the government should subsidize manufacturers so their facilities can quickly ramp up production.

When discussing the pandemic’s lasting effects on healthcare delivery, Gottlieb pointed to the example of home HIV testing. There was vigorous debate within the regulatory agency two decades ago about home HIV testing and whether patients would seek appropriate care.

“Now there has been a complete change. The FDA has embraced home testing with COVID and not worrying about how it will get reported to a public health authority. This is going to open up a whole new category for home testing,” Gottlieb said.

He discussed how in the future, routine care will be delivered in a whole new way, with home testing being coupled with virtual visits in a more robust way for many conditions. He pointed to Amazon’s construction of two CLIA labs that are far larger than what is needed for its employees: “Amazon is going to get into this in a more robust way, marrying their pharmacy business with their diagnostics business and build what they see as a missing link.”

But Amazon, Gottlieb said, is approaching this concept of care delivery as a logistic challenge they can solve. He said he sees this new era as a healthcare challenge, not simply a logistics issue. “The companies that are going to be able to capitalize on this new future and take advantage of this cultural change are healthcare companies that know how to couple diagnostic tests with the delivery of pharmacy in the home, build that relationship with the patient and overlay healthcare services,” he said. “The healthcare services companies don’t have all the tools to do that.”

PBMs, he said, are uniquely positioned to pull this all together, because their relationship to the patient is

Continued on page 46
How can we drive better health care choices?

By designing a better path to affordable benefits

At OptumRx®, we arm you with insights and options that give you more control over pharmacy costs and care.

optum.com/optumrx

©2021 Optum, Inc. All rights reserved.
Continued from page 44
through the pharmacy, and they are in are poised to build out the platforms need for this new care delivery system.
In discussing the short-term out-
look on the course of the pandemic, Gottlieb, who is on the board of direc-
tors of Pfizer, said the conventional wisdom is that delta variant of the COVID-19 will crowd out other vari-
ants such as mu and lambda. He also said the rate of mutation is likely to slowly. Citing data from Israel, he said a booster shot would likely increase people’s immunity to getting infected, not just the risk of serious disease, to levels that occurred after two shots of the Pfizer and Moderna vaccines. Gottlieb said he also foresees an emergency use authorization for a vaccine for children ages 5 to 11 by the end of October, and with that OK, some restoration normalcy. More childhood vaccines will need to become available, but Gottlieb said he expected the incorporation of COVID-19 vaccination into the CDC’s Advisory Committee on Im-
munization Practices schedule before the start of the school year in 2022. Gottlieb also predicted that COVID-19 would become endemic and that awareness of infectious respiratory ill-
ness — flu as well as COVID-19 — will change workplace and social norms. —Denise Myshko

Kerri Tanner, Pharm.D., RPh, Optum

Don’t take a piecemeal approach to specialty drug management

New, expensive specialty drugs have proliferated. But what also have increased are the challenges payers face in managing specialty cost trends along with the impact on patients and providers, said Kerri Tanner, Pharm.D., RPh, Optum’s senior vice president for specialty product.
Solutions that claim to address specialty spend have flourished, but not all approaches are the same. Although most solutions can help manage one or more aspects of specialty therapies, few address all the key challenges or simplify specialty management for multiple stakeholders.
“Payers need comprehensive, innovative solutions that go beyond traditional medical management and integrate with pharmacy cost-management levers,” Tanner said at the PBMI® meeting. She compared specialty drug management to a Jenga game with analytics at the base. Some new entrants in the pharmacy benefit management market are pulling out different elements, like removing blocks from a Jenga stack, and may do it well but are not mindful of the whole, Tanner said. By taking a broader approach, Optum’s efforts at managing specialty drug costs yield a saving of $16 per member per month, she said.
Solutions that claim to address specialty spend have flourished, but not all approaches are the same. Although most solutions can help manage one or more aspects of specialty therapies, few address all the key challenges or simplify specialty management for multiple stakeholders.
“Payers need comprehensive, innovative solutions that go beyond traditional medical management and integrate with pharmacy cost-management levers,” Tanner said. She mentioned Optum’s analytics that cover both the medical and pharmacy benefits and allow clients to compare how well they are managing spending on specialty drugs and related care. Tanner described an effort at Optum that she is leading that has pulled together the different services, efforts, and data at the company that are related to specialty pharmacy. A company model showed that this centralized, coordinated system, dubbed Optum Specialty Fusion, could save Optum clients $15 per member, per month in specialty drug spend.
Specialty medications are now half of the medication spending. Tanner often hears from health-
care professionals that their top concern is the rising cost of patient care.
“Most specialty patients see five or more providers and take 10 or more drugs that span both traditional and specialty medications,” she said. “Every specialty patient deserves a personalized health experience supported by clinicians, data and technology whenever they need it.”
These factors, plus the volume of new specialty drugs, make it difficult for providers to keep up with the best treatment options and nearly impossible for plan sponsors to control costs.
“Since specialty treatments can be covered across both the medical and pharmacy benefit, they bring additional
Continued on page 48
At Abarca, we have the team, technology and track record to provide payers with a real alternative to the big-three PBMs. We serve public and private sector organizations, including: Medicare & Commercial Health Plans, Self Insured Employers and State Medicaid Programs.

MAKING HEALTHCARE AWESOME FOR 15 YEARS

A SMARTER PLATFORM
Darwin™, Abarca’s technology platform was built from the ground up to be intelligent, flexible, fully integrated and infinitely scalable.

A BETTER EXPERIENCE
We are on a mission to find a better way, starting by taking the hassles out of pharmacy benefits for plans and members.

A HIGHER STANDARD
No shell games or word games. We take a straightforward business approach, and deliver on our promises.

To learn more about #PBMAwesome and Darwin™ visit www.abarcahealth.com.
Continued from page 46

complexity, health risk and cost to clinical decision-making,” Tanner said.

Tanner detailed how keeping up with the innovation in the specialty space requires industry-leading clinicians, aggressive analytics and technology.

“The management of specialty medications cannot be delivered in pieces, and we need to support clients in bringing components together to deliver more value,” Tanner said. “Optum sees an opportunity to deliver on this higher value when we combine our medical and pharmacy strategies together.”

Additionally, a solution must solve the current fragmentation, Tanner said. “It must solve it for our payers, our providers and our patients,” she noted.

“Optum has seen success when clients implement a multipronged approach for managing specialty medications,” Tanner said. “This starts with a foundation of excellence that allows us to manage specialty medication costs in three ways: pharmacy benefit management, medical benefit management and connected providers.”

“Keeping up with innovation in specialty requires organization of industry-leading clinicians, analytics and technology with the aim to reduce fragmentation and maintain high-quality care from an integrated benefit management system that is experienced in complex conditions,” she continued.

Tanner spoke of the “ridiculously large technology” group at OptumRx working on specialty drug management, and she forecast a future of management, not just of just of drugs, but also of many aspects of a patient’s therapy.

—Keith Loria

Kim Diehl-Boyd, CoverMyMeds

Digital tools, new standards will change healthcare and pharmacy access

Increased digital access in healthcare was already in the works when COVID-19 hit. But the pandemic turbocharged the trend, showing providers, payers and PBMs how they could improve service and efficiency by using more digital tools, said Kim Diehl-Boyd, vice president of industry relations and government affairs for CoverMyMeds.

Patients are looking for innovative partners to help them identify and afford the best treatment, Diehl-Boyd said, and COVID-19 complicated patients’ abilities to receive vital medications. During the pandemic, approximately 20% of patients, a majority with chronic conditions, experienced delays receiving their medications because of shortages or restrictions, according to results of a 2020 CoverMyMeds survey.

“We do know that even pre-COVID-19, patients were making considerable sacrifices to afford medications and therapies,” Diehl-Boyd said. Results of another CoverMyMeds survey showed that more than one-third of patients went without treatments or medications to pay other bills.

One of the COVID-19 success stories was rapid adoption of telehealth by providers and patients. “After COVID-19 hit, telehealth soared, peaking at a 6,000% increase compared (with) 2019,” Diehl-Boyd said. The pandemic also saw pharmacists expand their roles by administering vaccines and testing for COVID-19. “We will see pharmacists as a growing part of the care continuum team,” Diehl-Boyd said. More than two-thirds of pharmacists took on new responsibilities during the pandemic, such as checking with patients for adherence and refills, finding ways to help patients save money and starting prescription home-delivery programs, according to the 2020 CoverMyMeds survey.

Diehl-Boyd said she anticipates that PBMs and payers will focus on ways to transform member experiences beyond government regulations, providing more consumer-driven products. They can use technology to identify patient healthcare risks to develop prevention and intervention programs for a more holistic view of patient treatment.

This potentially could result in fewer duplicated services. By using data to innovate for more holistic care, PBMs and payers can improve retention and loyalty, said Diehl-Boyd.

True interoperability is a goal at federal and state levels. With adoption of newer standards such as the NCPDP Real-Time Prescription Benefit Standard, the E-Prescribing Standard, the Prior Authorization Standard, and work happening under HL7’s Da Vinci project, the community is seeing greater peer-to-peer

Continued on page 50

—Kim Diehl-Boyd, CoverMyMeds

Managed Healthcare Executive
How specialty pharmacies **lower** healthcare costs

Specialty pharmacies can prevent costly incidents and improve adherence through specialized patient-support services, making them uniquely positioned to help payers and PBMs lower costs.

Read our white paper to explore how specialty pharmacies maximize patients’ health so their overall healthcare spend is lower.

**BiologicsSP.com/payers**
Diehl-Boyd outlined five areas of future change:

**Access and affordability.** She noted the growth in the high-deductible health plans and growing enrollment in Medicaid and ACA plans.

**Innovation and digital transformation.** Telehealth and other digital transactions soared because of the pandemic and the relaxation of regulations. Although use of telehealth has slacked off some, Diehl-Boyd said that “telehealth is more than a temporary trend.”

**Pharmacy of the future.** Pharmacists will build on their role administering vaccines and become more central to the delivery of healthcare.

**Racial disparity.** Healthcare organizations are tackling the social determinants of health and also looking for long-term solutions.

**Growth in value-based care.** Providers are continuing to take on risk and are looking to reduce the financial risk fee-for-service exposure.

Diehl-Boyd also outlined the effects of two rules designed to bring out interoperability and “data fluidity” in health care, the Office of National Coordinator’s 21st Century Cures final rule and CMS’ final rule on data. The rules will force payers and providers to share information and equip patients with more information, particularly with respect to cost and coverage. “Health plans should be prepared for a radically empowered consumer,” Diehl-Boyd said.

---

**Javier Gonzalez, Pharm.D., Abarca**

**Smaller PBMs and insourcing**

are finding a place in a market dominated by major players

Many midsize health plans contract with the large PBMs that dominate the market and are owned by their rivals, such as CVS Health and Cigna, noted Javier Gonzalez, Pharm.D., chief growth officer at Abarca, a PBM based in Aventura, Florida, and San Juan, Puerto Rico.

But is that a smart thing for them to do? Now midsize plans are “starting to think about their competitive landscape,” Gonzalez said. By contracting with the large PBMs, they are contributing to the revenues of their large competitors. PBMs owned by CVS Health, UnitedHealthcare and Cigna control almost 80% of the market, and the five largest PBMs together hold about 90% of the market, he said.

But venture capital and private equity investors are supporting new PBMs that rely heavily on technology, noted Gonzalez, and some midsize insurers are thinking about alternatives to the major PBMs that might be available to them and are making requests for proposals from smaller PBMs. “They have enough scale to potentially make different types of investments,” Gonzalez said. Working with smaller PBMs “gives plans the opportunity to control more of the data so they can do a better job of leveraging that which they can actually control,” he said.

Plans don’t need to bring in all the services at once, he stressed: “It doesn’t have to be an all-you-can-eat out of the gate.” Companies are offering modular platforms that allow for a selective approach to bringing PBM services in-house. He also advised health plans to keep control of services like help centers that involve direct contact with members. “Don’t lose that opportunity — you’ve got to build your brand as a health plan,” Gonzalez said.

---

---

**Continued from page 48**

exchange in surfacing clinical information so that clinicians, care team and plans can have clinical information in real time, Diehl-Boyd said.

“We’ve seen this evolution in technology to bring about real time, clinical and administrative data exchange,” she continued. “We will continue to see that evolution tracking to payer-to-payer exchange, payer-to-consumer exchange, provider-to-provider exchange and provider-to-payer exchange.”

—Deborah Abrams Kaplan
A Simplified Platform for Payers

Our technology-based solutions solve access, adherence and affordability challenges throughout the prescription journey.

- Drive operational efficiencies by automating prior authorization requests
- Boost medication adherence surfacing real-time formulary and benefit information
- Improve patient health outcomes by accelerating speed to therapy

Contact CoverMyMeds to learn more about our payer-specific offerings:

covermymeds.com | 1-866-452-5017

CoverMyMeds is a registered trademark of CoverMyMeds LLC
The use of high-cost specialty drugs has put pressure on health plans and PBMs to better manage the pharmacy benefit, and innovative strategies are needed to deal with costs while also meeting patient needs, said WellDyne’s David Skomo, RPh, senior vice president and chief pharmacy operations officer, and Nick Page, Pharm.D., chief pharmacy officer.

Skomo and Page discussed how communication approaches that take into account patient preferences can lead to better care and pushing down the cost trend.

WellDyne has a care model that provides patients with a wide variety of options and communication channels to participate with the organization, including self-serve options through the telephone as well as a healthcare portal, Skomo explained.

He discussed the company’s efforts to tailor its messaging to patients grouped by “psychographic segmentation” and motivate them according to which segment they fall into. WellDyne has organized patients into five groups: direction takers, balance seekers, priority jugglers, self-achievers and willful endurers. Skomo stressed the importance of “marrying” the communication channel with these patient tendencies to motivate people to stay adherent to their medications.

“We’ve taken the technology to the next level and introduced digital capabilities through text messaging,” he said. “We can send a request to patients via text asking them to take action — for example, filling a prescription. By deploying that technology, along with additional communication channels, we provide convenience for the patient.”

Page reviewed some of the overall consequences of nonadherence, which he said includes 125,000 death per year and $600 billion in costs. Page said WellDyne’s efforts to more carefully monitor patients and meet their needs has resulted in company lowering specialty drug cost increases to 5%-6% per year, which he said is half the industry-wide rate of increase of 10%-20%.

WellDyne’s “push technology” has been useful during the COVID-19 pandemic because patients are using drive-thru and mail-order services more often, Page added. “Many pharmacies are reducing staff, which makes it very difficult for the consumer to be able to access a pharmacist to ask questions,” he said. “Patients may not feel comfortable asking a pharmacist a question with a lot of other people around.”

WellDyne clinicians use digital tools to send out patient assessment questionnaires, Skomo explained. “We find that the patients are much more likely to provide responses to those types of assessments,” he said. “It’s not us calling them. Patients can use their smartphones to provide those responses very easily at a time and place most convenient for them.”

Patient adherence has increased since WellDyne began using the digital technology; in fact, according to Skomo, medication adherence rates have increased 36%.

Consumers, Skomo said, are hungry for information. “The push technology tends to get read almost immediately,” he said. “We see much better engagement with that than we typically do with emails or print media mailed to the home.”

—Denise Myshko

---

**Thatcher Sloan, Confidio**

**Confidio to PBMs: Stop chasing rebates**

When PBMs focus too much on chasing rebates, they may miss out on the critical elements that provide true economic value to healthcare organizations and employers, said Thatcher Sloan, vice president, practice leader, at Confidio.

Sloan told conference attendees about Confidio’s net economic value assessment of PBMs that factors in how effective their formularies are in driving prescription to the most cost-effective choices and the rigor of their utilization management.

Applying formulary effectiveness and utilization management effectiveness to a PBM can paint a truer picture of how well it is managing drug costs, said Sloan. He walked through a real-world example of how applying formulary and utilization effectiveness could alter a comparison between two PBMs. Before applying formulary and utilization effectiveness, the projected annual drug costs, including rebates, with “PBM A” were about $127 million.

Continued on page 54
Yes, we serve millions of people in thousands of locations across the country. But what really matters is the size of our heart. Because every day, in every way, we are passionate about bringing our heart to every moment of your health.
Continued from page 52

and $132 million with “PBM B.” But once formulary and utilization effectiveness were factored in, the PBMs traded places, and drug costs were lower with PBM B ($116 million) than with PBM A ($134 million).

Sloan said Confidio developed this analysis of PBMs partly because of the difficulties of comparing pass-through PBMs to traditional ones. Another inspiration was when a PBM CEO complained that the conventional way that consultants evaluate PBM performance created an incentive to “chase rebates” and ignore other ways PBMs could manage drug costs for their clients. The PBM executive said that “we want to the right thing,” according to Sloan, “but the consulting community, in general, they are putting value on rebate — they are incentivizing us to do the wrong thing.”

Sloan said the approach was developed recently and that only a handful of clients have taken advantage of it so far. One byproduct might be a decrease in the PBM industry’s emphasis on rebates. PBMs, he said, are often evaluated by health plans and employers almost solely on the network discounts and rebates they can get from manufacturers. “In this way, they can show bigger rebates on their spreadsheet, which makes their deal look better than other PBMs,” Sloan said. “But that’s not real value.”

Rebates do create useful competition on price, Sloan noted. “For some products, the rebate negotiation is the only time throughout the whole supply chain where there’s any competition based on price. It may be the only time where that market factor comes in and is able to provide a lower price.”

—Denise Myshko, Peter Wehrwein

Doug Long, MBA, IQVIA

The pandemic effects and its aftershocks

The COVID-19 pandemic left no part of the American healthcare system untouched in 2020, and even as the U.S. healthcare system rebound, the pandemic’s influence is apparent and likely to be lasting, according to a stream of facts and figures presented by Doug Long, MBA, vice president of industry relations at IQVIA.

Using sales and other sorts of data assembled by IQVIA, Long showed that a billion fewer visits that resulted in a diagnosis occurred in 2020 than in the past, which works out to a 20% decrease. This year, people are starting to come back for visits, but Long shared data showing that “diagnostic visits” are still down significantly. Fewer diagnostic visits result in fewer prescriptions, and Long showed a wide assortment of data documenting various aspects of the effect on drug prescriptions and sales.

Lockdowns and people’s hesitancy to seek in-person healthcare contributed to the downturn in diagnostic visits, Long explained. But the dramatic decline in flu cases last year and first part of this year has also contributed. Long said one of the major question marks hanging over the coming months is whether the trend in flu cases will resume to normal levels or stay low. He showed data from Australia, which has a southern hemisphere flu season ahead of countries in the northern hemisphere, that suggests that they will stay low.

Long’s data also showed the much-discussed increase in telehealth usage. Telehealth visits have tended to generate fewer prescriptions than in-person visits because the lab and other tests that result in prescriptions are not done as often if a patient is seen remotely. As telehealth becomes a more established feature of U.S. healthcare delivery, that lack of testing and prescriptions may change. “What is going to be interesting to watch is how digital plays into the marketplace,” Long said.

Here are some of the other topics that Long touched upon:

Specialists with gaps in claims in 2020, particularly ophthalmologists and dermatologists, are working through the patient backlog. Long showed data for new-to-brand prescriptions (NBRx) — a metric that the pharma industry tracks to gauge drug sales — and claims comparing the first half of 2020 to the first half of 2021. Both NBRx and claims have increased for ophthalmology, dermatology and obstetrics and gynecology.

The nonretail channel is recovering from the effects of COVID-19. Nonretail growth in sales dipped to 1.8% in 2020, but Long showed a chart based on IQVIA data that show a rebound to 6.1% during the first half of 2021.

Specialty drug growth is outpacing traditional growth and now accounts for just under half of the nondiscounted spend. Almost every speaker at the meeting referenced the growth in spending on specialty drugs. In 2017, the specialty-traditional share of sales split was 43.1% specialty and 56.9% traditional, according to the IQVIA sales data shown by Long. In the 12 months prior to June of this year (MAT June), the split was 48.9% specialty, 51.1% traditional.

Growing payer control continues to challenge patient access. Specialty patients are 20% more likely to not fill a prescription today than they were in 2013, according to IQVIA data shared by Long, and 60% of specialty patients with a step edit (coverage of a less expensive medication before a more expensive one will be covered) are not able to overcome the restriction within 30 days.

—Peter Wehrwein
Discover a Better Rx Benefit Solution

We’re reinventing pharmacy benefits, helping plan sponsors across the nation save 10-15% on their prescription costs, while improving member health.

Contact us today to find out how we can help reinvent your pharmacy benefits.

sales@navitus.com | 877.571.7500 | www.navitus.com

© 2021 Navitus Health Solutions, LLC
Joshua Fredell, Pharm.D., and Tierra Ford, Pharm.D., CVS Health

What “next gen” specialty drug management looks like

Healthcare costs are increasing, but when it comes to drug expenditures, it’s just a small fraction of utilizers that account for more than half of their clients’ pharmacy spend, explained Joshua Fredell, Pharm.D., vice president of product development for CVS Health, and his co-presenter, Tierra Ford, Pharm.D., senior clinical adviser, specialty client solutions.

New specialty treatments that can transform the lives of some patients are coming to market with increasingly higher price tags — some costing hundreds of thousands per year, Fredell noted.

“This means that cost-management strategies must evolve to meet next-generation needs: a deliberate focus on curbing specialty spend without compromising plan member outcomes,” said his co-presenter.

In their presentation, Fredell and Ford stressed how digital tools and platforms and connectivity are key to an...
IDIOPATHIC HYPERSOMNIA

is a rare condition distinct from other sleep disorders\(^1\)-\(^3\)

In idiopathic hypersomnia (IH)...

IH is different from other sleep disorders like narcolepsy\(^1\)

IH is a unique condition with specific AASM ICSD-3 criteria\(^4\)

ICD-10-CM codes: G47.11, G47.12\(^4,6\)

There are currently no FDA-approved treatments indicated for IH\(^7\)

Good Sleep Outweighs More Sleep

People with IH are getting plenty of sleep, but still feel excessively sleepy during the day\(^4,5\)

To learn more about IH, contact your Jazz Pharmaceuticals Account Manager or visit SleepCountsHCP.com

References:

©2021 Jazz Pharmaceuticals plc or its subsidiaries
US-SLE-2100143 Rev0621
Fredell and Ford also discussed how clinically rigorous utilization management builds the foundation for a strong specialty cost-management program.

“Electronic health record connectivity enables greater visibility to accurate clinical data, including the exact diagnosis and most appropriate therapy for each member,” Ford said. The pharmaceutical marketplace is dynamic, and specialty cost-management tactics must evolve to help payer stay ahead of trends and manage rapidly rising costs, Fredell said. “Doing so effectively demands new approaches that go beyond traditional strategies and aggressive therapy denials, which may not deliver lasting savings,” Fredell continued. “Starting on the most appropriate therapy, ongoing monitoring, and intervening when needed to prevent and eliminate wasteful spend throughout the duration of therapy can help lower payer costs and support plan member health.”

—Keith Loria, Peter Wehrwein

Fredell and Ford also discussed how clinically rigorous utilization management builds the foundation for a strong specialty cost-management program.

“Electronic health record connectivity enables greater visibility to accurate clinical data, including the exact diagnosis and most appropriate therapy for each member,” Ford said. The pharmaceutical marketplace is dynamic, and specialty cost-management tactics must evolve to help payer stay ahead of trends and manage rapidly rising costs, Fredell said. “Doing so effectively demands new approaches that go beyond traditional strategies and aggressive therapy denials, which may not deliver lasting savings,” Fredell continued. “Starting on the most appropriate therapy, ongoing monitoring, and intervening when needed to prevent and eliminate wasteful spend throughout the duration of therapy can help lower payer costs and support plan member health.”

—Keith Loria, Peter Wehrwein

Fredell and Ford also discussed how clinically rigorous utilization management builds the foundation for a strong specialty cost-management program.

“Electronic health record connectivity enables greater visibility to accurate clinical data, including the exact diagnosis and most appropriate therapy for each member,” Ford said. The pharmaceutical marketplace is dynamic, and specialty cost-management tactics must evolve to help payer stay ahead of trends and manage rapidly rising costs, Fredell said. “Doing so effectively demands new approaches that go beyond traditional strategies and aggressive therapy denials, which may not deliver lasting savings,” Fredell continued. “Starting on the most appropriate therapy, ongoing monitoring, and intervening when needed to prevent and eliminate wasteful spend throughout the duration of therapy can help lower payer costs and support plan member health.”

—Keith Loria, Peter Wehrwein

Fredell and Ford also discussed how clinically rigorous utilization management builds the foundation for a strong specialty cost-management program.

“Electronic health record connectivity enables greater visibility to accurate clinical data, including the exact diagnosis and most appropriate therapy for each member,” Ford said. The pharmaceutical marketplace is dynamic, and specialty cost-management tactics must evolve to help payer stay ahead of trends and manage rapidly rising costs, Fredell said. “Doing so effectively demands new approaches that go beyond traditional strategies and aggressive therapy denials, which may not deliver lasting savings,” Fredell continued. “Starting on the most appropriate therapy, ongoing monitoring, and intervening when needed to prevent and eliminate wasteful spend throughout the duration of therapy can help lower payer costs and support plan member health.”

—Keith Loria, Peter Wehrwein

Fredell and Ford also discussed how clinically rigorous utilization management builds the foundation for a strong specialty cost-management program.

“Electronic health record connectivity enables greater visibility to accurate clinical data, including the exact diagnosis and most appropriate therapy for each member,” Ford said. The pharmaceutical marketplace is dynamic, and specialty cost-management tactics must evolve to help payer stay ahead of trends and manage rapidly rising costs, Fredell said. “Doing so effectively demands new approaches that go beyond traditional strategies and aggressive therapy denials, which may not deliver lasting savings,” Fredell continued. “Starting on the most appropriate therapy, ongoing monitoring, and intervening when needed to prevent and eliminate wasteful spend throughout the duration of therapy can help lower payer costs and support plan member health.”

—Keith Loria, Peter Wehrwein

Fredell and Ford also discussed how clinically rigorous utilization management builds the foundation for a strong specialty cost-management program.

“Electronic health record connectivity enables greater visibility to accurate clinical data, including the exact diagnosis and most appropriate therapy for each member,” Ford said. The pharmaceutical marketplace is dynamic, and specialty cost-management tactics must evolve to help payer stay ahead of trends and manage rapidly rising costs, Fredell said. “Doing so effectively demands new approaches that go beyond traditional strategies and aggressive therapy denials, which may not deliver lasting savings,” Fredell continued. “Starting on the most appropriate therapy, ongoing monitoring, and intervening when needed to prevent and eliminate wasteful spend throughout the duration of therapy can help lower payer costs and support plan member health.”

—Keith Loria, Peter Wehrwein

Fredell and Ford also discussed how clinically rigorous utilization management builds the foundation for a strong specialty cost-management program.

“Electronic health record connectivity enables greater visibility to accurate clinical data, including the exact diagnosis and most appropriate therapy for each member,” Ford said. The pharmaceutical marketplace is dynamic, and specialty cost-management tactics must evolve to help payer stay ahead of trends and manage rapidly rising costs, Fredell said. “Doing so effectively demands new approaches that go beyond traditional strategies and aggressive therapy denials, which may not deliver lasting savings,” Fredell continued. “Starting on the most appropriate therapy, ongoing monitoring, and intervening when needed to prevent and eliminate wasteful spend throughout the duration of therapy can help lower payer costs and support plan member health.”

—Keith Loria, Peter Wehrwein

Fredell and Ford also discussed how clinically rigorous utilization management builds the foundation for a strong specialty cost-management program.

“Electronic health record connectivity enables greater visibility to accurate clinical data, including the exact diagnosis and most appropriate therapy for each member,” Ford said. The pharmaceutical marketplace is dynamic, and specialty cost-management tactics must evolve to help payer stay ahead of trends and manage rapidly rising costs, Fredell said. “Doing so effectively demands new approaches that go beyond traditional strategies and aggressive therapy denials, which may not deliver lasting savings,” Fredell continued. “Starting on the most appropriate therapy, ongoing monitoring, and intervening when needed to prevent and elimina