REFORMING HOSPICE

Experts call for more at-home hospice care funding

INDUSTRY ANALYSIS
Part D redesign

CHRONIC DISEASE
New weight-loss drugs

POPULATION HEALTH
Capping insulin OOP

FORMULARY DEVELOPMENT
ICER eyeing payers
For adults at risk of rapid disease progression,
TARPEYO: First and only treatment FDA approved
to reduce proteinuria in IgA Nephropathy

TARPEYO™ (budesonide) delayed release capsules is designed to deliver
treatment to an area of the ileum to target mucosal B cells, which are
responsible for the production of galactose-deficient IgA1 antibodies,
cauising immunoglobulin A Nephropathy (IgAN).  

*Drug release is initiated in the ileum by the pH-dependent disintegration of the enteric coat.

**Indication**
TARPEYO™ (budesonide) delayed release capsules is a corticosteroid indicated to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g.

This indication is approved under accelerated approval based on a reduction in proteinuria. It has not been established whether TARPEYO slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

**Important Safety Information**

**Contraindications**: TARPEYO is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of TARPEYO. Serious hypersensitivity reactions, including anaphylaxis, have occurred with other budesonide formulations.

**Warnings and Precautions**

**Hypercorticism and adrenal axis suppression**: When corticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur. Corticosteroids can reduce the response of the hypothalamic-pituitary-adrenal (HPA) axis to stress. In situations where patients are subject to surgery or other stress situations, supplementation with a systemic corticosteroid is recommended. When discontinuing therapy (see Dosing and Administration) or switching between corticosteroids, monitor for signs of adrenal axis suppression. Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C, respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure to oral budesonide. Avoid use in patients with severe hepatic impairment (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B).

**Risks of immunosuppression**: Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in susceptible patients or patients on immunosuppressive doses of corticosteroids. Avoid corticosteroid therapy in patients with active or quiescent tuberculosis infection; untreated fungal, bacterial, systemic viral, or parasitic infections; or ocular herpes simplex. Avoid exposure to active, easily transmitted infections (eg, chicken pox, measles). Corticosteroid therapy may decrease the immune response to some vaccines.
Described to deploy in the ileum\(^1,2,4\)
- Designed to deliver treatment to the area of the ileum, including the Peyer’s patches, where mucosal B cells are located
- Mucosal B cells express glucocorticoid receptors and produce galactose-deficient IgA1 antibodies, causing IgAN
- Through anti-inflammatory and immunosuppressive effects at the glucocorticoid receptor, TARPEYO can modulate B cell numbers and activity

Statistically significant reduction in UPCR with TARPEYO plus RASI vs RASI alone at 9 months\(^{1,5}\)
- **Primary endpoint:** Significant reduction (34%) in UPCR from baseline was achieved in the TARPEYO plus renin-angiotensin system inhibitor (RASI)-treated group (n=97) vs 5% with RASI alone (n=102) at 9 months\(^{1,2}\)
  - After 3 months of observational follow-up, a 53% reduction from baseline in UPCR was seen in the TARPEYO plus RASI-treated group (n=97) vs 9% with RASI alone (n=102)\(^{1,4}\)

Additional data presented beyond the primary endpoint of 9 months should be interpreted cautiously.

eGFR data with TARPEYO plus RASI vs RASI alone at 9 months
- **Secondary endpoint:** At 9 months, absolute change in eGFR was -0.6 mL/min/1.73 m\(^2\) with TARPEYO plus RASI (n=97) vs -4.0 mL/min/1.73 m\(^2\) with RASI alone (n=102)\(^{1,4}\)
  - These interim secondary endpoint data were not prospectively controlled for multiplicity and need cautious interpretation. The clinical significance of these results is unknown. Confirmatory clinical trial results are required to draw any conclusions. It has not been established whether TARPEYO has demonstrated a benefit in slowing kidney function decline in patients with IgAN.\(^3\)

Demonstrated safety profile
- 87% of patients in the TARPEYO plus RASI-treated group reported adverse reactions vs 73% of patients on RASI alone\(^1,3\)
- In clinical studies, the most common adverse reactions of TARPEYO plus RASI (occurring in ≥10% of patients treated with TARPEYO plus RASI and at a higher incidence than RASI alone) were: hypertension, peripheral edema, muscle spasms, and acne\(^1,3\)
- The safety profile is generally consistent with the well-established safety profile of the active ingredient, budesonide\(^2\)

**Study Design:** NEFIBARD is an ongoing, phase 3, randomized, double-blind, multicenter study to evaluate the efficacy and safety of TARPEYO 16 mg/day vs placebo in patients with primary IgAN as an addition to optimized RASI blockade therapy. Part A of the study (n=199) included a 9-month blinded treatment period and a 3-month follow-up period. The primary endpoint was UPCR at 9 months; eGFR was a secondary endpoint. Part B, a confirmatory validation study in which no treatment will be administered, will assess eGFR over 2 years.\(^1,4\)

It has not been established to what extent the efficacy of TARPEYO is mediated via local effects in the ileum vs systemic effects.\(^1\)

1% reduction (95% CI, 16-42) in UPCR from baseline was achieved in the TARPEYO plus RASI-RASI alone (P=0.0003).\(^1,5\)

Adjusted geometric least squares mean ratio of UPCR relative to baseline were based on a longitudinal repeated measures model.\(^1\)

*Primary endpoint:* 87% of patients in the TARPEYO plus RASI-treated group reported adverse reactions vs 73% of patients on RASI alone\(^1,3\)

All patients with a UPCR/eGFR reading regardless of use of prohibited medication at 9 months and 12 months.\(^1,3\)

All patients with a UPCR/eGFR reading regardless of use of prohibited medication at 9 months.\(^1,3\)

Statistically significant reduction in UPCR with TARPEYO plus RASI vs RASI alone at 9 months\(^1,2\)

Part B, a confirmatory validation study in which no treatment will be administered, will assess eGFR over 2 years.\(^1,4\)

**Introduction:** Designed to deploy in the ileum by the pH-dependent disintegration of the enteric coat.\(^1,3\)

- Through anti-inflammatory and immunosuppressive effects at the glucocorticoid receptor, TARPEYO can modulate B cell numbers and activity

**Learn more about how TARPEYO works at TARPEYOhcp.com**

**Warnings and Precautions (cont’d)**

**Other corticosteroid effects:** TARPEYO is a systemically available corticosteroid and is expected to cause related adverse reactions. Monitor patients with hypertension, prediabetes, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma, cataracts, a family history of diabetes or glaucoma, or with any other condition in which corticosteroids may have unwanted effects.

**Adverse reactions:** In clinical studies, the most common adverse reactions with TARPEYO (occurring in ≥5% of TARPEYO patients and ≥2% higher than placebo) were hypertension (16%), peripheral edema (14%), muscle spasms (13%), acne (11%), dermatitis (7%), weight increase (7%), dyspnea (6%), face edema (6%), dyspepsia (5%), fatigue (5%), and hirsutism (5%).

**Drug interactions:** Budesonide is a substrate for CYP3A4. Avoid use with potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, erythromycin, and cyclosporine. Avoid ingestion of grapefruit juice with TARPEYO. Intake of grapefruit juice, which inhibits CYP3A4 activity, can increase the systemic exposure to budesonide.

**Use in specific populations**

**Pregnancy:** The available data from published case series, epidemiological studies, and reviews with oral budesonide use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with IgAN. Infants exposed to in utero corticosteroids, including budesonide, are at risk for hypoaldosteronism. Please see brief summary of Full Prescribing Information on the adjacent pages.


*Drug release is initiated in the ileum by the pH-dependent disintegration of the enteric coat.\(^1,3\)*
TARPEYO™ (budesonide) delayed release capsules

Brief Summary of Prescribing Information

4 CONTRAINDICATIONS

TARPEYO is contraindicated in patients with hypersensitivity to budesonide or any of the ingredients of TARPEYO. Serious hypersensitivity reactions, including anaphylaxis, have occurred with other budesonide formulations.

5 WARNINGS AND PRECAUTIONS

5.1 Hypercorticism and Adrenal Axis Suppression

When corticosteroids are used chronically, systemic effects such as hypercorticism and adrenal suppression may occur. Corticosteroids can reduce the response of the hypothalamus-pituitary-adrenal (HPA) axis to stress. In situations where patients are subject to surgery or other stress situations, supplementation with a systemic corticosteroid is recommended. When discontinuing therapy [see Dosing and Administration (2)] or switching between corticosteroids, monitor for signs of adrenal axis suppression.

Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure of oral budesonide. Avoid use in patients with severe hepatic impairment (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B) [see Use in Specific Populations (8.6), Clinical Pharmacology (12.3)].

5.2 Risks of Immunosuppression

Patients who are on drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in susceptible patients or patients on immunosuppressant doses of corticosteroids. Avoid corticosteroid therapy in patients with active or quiescent tuberculosis infection, untreated fungal, bacterial, systemic viral or parasitic infections, or ocular herpes simplex. Avoid exposure to active, easily-transmitted infections (e.g., chickenpox, measles). Corticosteroid therapy may decrease the immune response to some vaccines.

How the dose, route, and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, consider therapy with varicella zoster immune globulin (VZIG) or pooled intravenous immunoglobulin (IVIG). If exposed to measles, consider prophylaxis with pooled intramuscular immunoglobulin (IG). If chickenpox develops, consider treatment with antiviral agents.

5.3 Other Corticosteroid Effects

TARPEYO is a systemically available corticosteroid and is expected to cause related adverse reactions. Monitor patients with hypertension, prediabetes, diabetes mellitus, osteoporosis, peptic ulcer, glaucoma or cataracts, or with a family history of diabetes or glaucoma, or with any other condition where corticosteroids may have unwanted effects.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypercorticism and adrenal suppression [see Warnings and Precautions (5.1)]
- Risks of immunosuppression [see Warnings and Precautions (5.2)]
- Other corticosteroid effects [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 safety of TARPEYO has been evaluated in a randomized controlled study in 197 patients. The most common adverse reactions reported in greater than or equal to 5% of TARPEYO-treated patients are listed in Table 1. The majority of adverse reactions were mild or moderate in severity.

Table 1: Reported adverse reactions occurring in greater than or equal to 5% of TARPEYO treated patients, and greater than or equal to 2% higher than Placebo

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>TARPEYO 16 mg (N=97)</th>
<th>Placebo (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>13 (13)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Nausea</td>
<td>14 (14)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>19 (19)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>21 (21)</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Face edema</td>
<td>12 (12)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Weight increased</td>
<td>14 (14)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>9 (9)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>8 (8)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Nervous system</td>
<td>7 (7)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Headache</td>
<td>4 (4)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Anorexia</td>
<td>6 (6)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4 (4)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Infection</td>
<td>3 (3)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Most adverse reactions that occurred at a greater incidence for TARPEYO compared to placebo were consistent with hypercortisolism.

7 DRUG INTERACTIONS

7.1 Interaction with CYP3A4 Inhibitors

Budesonide is a substrate for CYP3A4. Avoid use with potent CYP3A4 inhibitors; e.g., ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, erythromycin, and cyclosporine. Avoid ingestion of grapefruit juice with TARPEYO. Intake of grapefruit juice, which inhibits CYP3A4 activity, can increase the systemic exposure to budesonide.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary The available data from published case series, epidemiological studies and reviews with oral budesonide use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. There are risks to the mother and fetus associated with IgA Nephropathy. Infants exposed to in-utero corticosteroids, including budesonide, are at risk for hypoadrenalism (see Clinical Considerations). In animal reproduction studies with pregnant rats and rabbits, administration of subcutaneous budesonide during...
organogenesis at doses approximately 0.3 times or 0.03 times, respectively, the maximum recommended human dose (MRHD), resulted in increased fetal loss, decreased pup weights, and skeletal abnormalities. Maternal toxicity was observed in both rats and rabbits at these dose levels (see Data).

The estimated background risk of major birth defects and miscarriage of the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. 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.

Clinical Considerations Disease-Associated Maternal and/or Embryo/Fetal Risk IgA nephropathy in pregnancy is associated with adverse maternal outcomes, including increased rates of cesarean section, pregnancy-induced hypertension, pre-eclampsia and preterm delivery, and adverse fetal/neonatal outcomes, including stillbirth and low birth weight.

Fetal/Neonatal Adverse Reactions Hypoadrenalism may occur in infants born to mothers receiving corticosteroids during pregnancy. Infants should be carefully observed for signs of hypoadrenalism, such as poor feeding, irritability, weakness, and vomiting, and managed accordingly (see Warnings and Precautions [5.1]).

Data

Animal Data Budesonide was teratogenic and embryolethal in rabbits and rats. In an embryo-fetal development study in pregnant rats dosed subcutaneously with budesonide during the period of organogenesis on gestation days 6 to 15 there were effects on fetal development and survival at subcutaneous doses up to approximately 500 mcg/kg in rats (approximately 0.3 times the maximum recommended human dose (MRHD) on a body surface area basis).

In an embryo-fetal development study in pregnant rabbits dosed during the period of organogenesis on gestation days 6 to 18, there was an increase in maternal abortion, and effects on fetal development and reduction in litter weights at subcutaneous doses of approximately 25 mcg/kg (approximately 0.03 times the MRHD on a body surface area basis).

Maternal toxicity, including reduction in body weight gain, was observed at subcutaneous doses of 5 mcg/kg in rabbits (approximately 0.006 times the maximum recommended human dose on a body surface area basis) and 500 mcg/kg in rats (approximately 0.3 times the maximum recommended human dose on a body surface area basis).

In a peri- and post-natal development study, subcutaneous treatment of pregnant rats with budesonide during the period from Day 15 post coitum to Day 21 post partum, budesonide had no effects on delivery, but did have an effect on growth and development of offspring. In addition, offspring survival was reduced and surviving offspring had decreased mean body weights at birth and during lactation at exposures ≥ 0.012 times the MRHD (on a mg/m² basis at maternal subcutaneous doses of 20 mcg/kg/day and higher). These findings occurred in the presence of maternal toxicity.

8.2 Lactation

Risk Summary Breastfeeding is not expected to result in significant exposure of the infant to TARPEYO. Lactation studies have not been conducted with oral budesonide, including TARPEYO, and no information is available on the effects of the drug on the breastfed infant or the effects on the drug on milk production. One published study reports that budesonide is present in human milk following maternal inhalation of budesonide (see Data). Routine monitoring of linear growth in infants is recommended with chronic use of budesonide in the nursing mother. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for TARPEYO and any potential adverse effects on the breastfed infant from TARPEYO, or from the underlying maternal condition.

Data One published study reports that budesonide is present in human milk following maternal inhalation of budesonide, which resulted in infant doses approximately 0.3% to 1% of the maternal weight-adjusted dosage and a milk to plasma ratio of approximately 0.5. Budesonide was not detected in plasma, and no adverse events were noted in the breastfed infants following maternal use of inhaled budesonide.

Assuming a daily average milk intake of about 150 mL/kg/day and a milk to plasma ratio of 0.5, the estimated oral dose of budesonide for a 5-kg infant is expected to be less than 2 mcg/day for a maternal dose of 16 mg TARPEYO. Assuming 100% bio-availability in the infant this is about 0.1% of the maternal dose and about 3% of the highest inhaled dose used clinically for asthma in infants.

8.4 Pediatric Use

The safety and efficacy of TARPEYO in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of TARPEYO did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

8.6 Hepatic Impairment

Patients with moderate to severe hepatic impairment (Child-Pugh Class B and C, respectively) could be at an increased risk of hypercorticism and adrenal axis suppression due to an increased systemic exposure to budesonide (see Warnings and Precautions [5.1] and Clinical Pharmacology [12.3]). Avoid use in patients with severe hepatic impairments (Child-Pugh Class C). Monitor for increased signs and/or symptoms of hypercorticism in patients with moderate hepatic impairment (Child-Pugh Class B).

10 OVERDOSAGE

Reports of acute toxicity and/or death following overdosage of corticoids are rare. In the event of acute overdosage, no specific antidote is available. Treatment consists of supportive and symptomatic therapy.

Please see Full Prescribing Information for TARPEYO at TARPEYOhcp.com

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Hospice care. It’s complicated.

So many issues and beliefs divide Americans these days that it is surprising to come upon any areas of agreement. But as Robert Calandra reports in this issue’s cover story, hospice care might be one small patch of common ground. Polling shows that Americans support hospice care and that it enjoys a good reputation. The law that extended Medicare coverage for hospice care goes back 40 years. The proportion dipped slightly in 2020 but about half (47.8% in 2020) of Medicare beneficiaries who die each year have received hospice care. There is wide acceptance of the general premise of hospice: Medical care needs to pivot near the end of life. Comfort, not cure, becomes the goal.

This isn’t to say that everything is tidy and settled about hospice care. Far from it. As Calandra reports, some physicians on the front lines of hospice and end-of-life care want to see more done — and more funding — to support care at home. They say that even if spending were increased (the Medicare program spent more than $22 billion on hospice care in 2020), it would be a bargain compared with inpatient hospital care. But others argue that strong beliefs about the advantages of dying at home have overshadowed the real advantages that inpatient hospice care has for some patients and their families and loved ones.

About three-quarters of hospice providers are now for-profit businesses. Do for-profit providers bring efficiency and some market discipline to hospice care? Or are they more likely to skimp on services? There’s back and forth on those questions.

Many hospice providers and experts say people tend to wait too long before getting hospice care that would have improved their quality of life and helped their families. Yet there’s also concern about people spending too much time in hospice. According to the Medicare Payment Advisory Commission (MedPAC), nearly 60% of Medicare spending on hospice in 2020 was for patients whose hospice care exceeded 60 days. Of course, there is great uncertainty about the end of life and how long people will live. And, ironically, hospice care can extend life by easing individuals’ pain and distress. But longer stays mean larger margins for providers. “Financial incentives likely play a role in why some providers treat more patients with very long stays,” MedPAC said in a report to Congress earlier this year.

As with so many things, scratch beneath the surface and hospice care gets complicated and has its fair share of controversies.
REFORMING HOSPICE

Experts call for more at-home hospice care funding

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NOW APPROVED

Olumiant is the **first and only** approved systemic treatment for adults with severe alopecia areata\(^1\)
INDICATION
Olumiant is a Janus kinase (JAK) inhibitor indicated for the treatment of adult patients with severe alopecia areata.

Limitations of Use: Not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, cyclosporine or other potent immunosuppressants.

SELECT IMPORTANT SAFETY INFORMATION: WARNING RELATED TO SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS, AND THROMBOSIS

SERIOUS INFECTIONS: Olumiant-treated patients are at increased risk of serious bacterial, fungal, viral and opportunistic infections leading to hospitalization or death, including tuberculosis (TB). Interrupt treatment with Olumiant if a serious infection occurs until the infection is controlled. Olumiant should not be given to patients with active tuberculosis. Test for latent TB before and during therapy, except for COVID-19; treat latent TB prior to use. Monitor all patients for active TB during treatment, even patients with initial negative, latent TB test.

MORTALITY: Higher rate of all-cause mortality, including sudden cardiovascular death was observed with another Janus kinase (JAK) inhibitor vs. tumor necrosis factor (TNF) blockers in rheumatoid arthritis (RA) patients.

MALIGNANCIES: Malignancies have also occurred in patients treated with Olumiant. Higher rate of lymphomas and lung cancers was observed with another JAK inhibitor vs. TNF blockers in RA patients.

MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE): Higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) was observed with another JAK inhibitor vs. TNF blockers in RA patients.

THROMBOSIS: Thrombosis has occurred in patients treated with Olumiant. Increased incidence of pulmonary embolism, venous and arterial thrombosis was observed with another JAK inhibitor vs. TNF blockers.

Please see the following pages for Important Safety Information, including Boxed Warning about Serious Infections, Mortality, Malignancy, Major Adverse Cardiovascular Events, and Thrombosis, and Brief Summary of Prescribing Information.
IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS, AND THROMBOSIS

SERIOUS INFECTIONS

Patients treated with Olumiant are at risk for developing serious infections that may lead to hospitalization or death. Most patients with rheumatoid arthritis (RA) who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. If a serious infection develops, interrupt Olumiant until the infection is controlled. Reported infections include:

- Active tuberculosis (TB), which may present with pulmonary or extrapulmonary disease. Olumiant should not be given to patients with active tuberculosis. Test patients, except those with COVID-19, for latent TB before initiating Olumiant and during therapy. If positive, start treatment for latent infection prior to Olumiant use.
- Invasive fungal infections, including candidiasis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.
- Bacterial, viral, and other infections due to opportunistic pathogens.

Carefully consider the risks and benefits of Olumiant prior to initiating therapy in patients with chronic or recurrent infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with Olumiant including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

The most common serious infections reported with Olumiant included pneumonia, herpes zoster, and urinary tract infection. Among opportunistic infections, tuberculosis, multidermalomat herpes zoster, esophageal candidiasis, pneumocystosis, acute histoplasmosis, cryptococcosis, cytomegalovirus, and BK virus were reported with Olumiant. Some patients have presented with disseminated rather than localized disease, and were often taking concomitant immunosuppressants such as methotrexate or corticosteroids.

Avoid use of Olumiant in patients with an active, serious infection, including localized infections. Consider the risks and benefits of treatment prior to initiating Olumiant in patients with chronic or recurrent infection; who have been exposed to TB; with a history of a serious or an opportunistic infection; who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or with underlying conditions that may predispose them to infection.

Consider anti-TB therapy prior to initiation of Olumiant in patients with a history of latent or active TB in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent TB but who have risk factors for TB infection.

Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical studies with Olumiant. If a patient develops herpes zoster, interrupt Olumiant treatment until the episode resolves. The impact of Olumiant on chronic viral hepatitis reactivation is unknown. Screen for viral hepatitis in accordance with clinical guidelines before initiating Olumiant.

MORTALITY

In a large, randomized, postmarketing safety study in RA patients 50 years of age and older with at least one cardiovascular risk factor comparing another Janus kinase (JAK) inhibitor to tumor necrosis factor (TNF) blockers, a higher rate of all-cause mortality, including sudden cardiovascular death, was observed with the JAK inhibitor.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Olumiant.

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with Olumiant. In RA patients treated with another JAK inhibitor, a higher rate of malignancies (excluding non-melanoma skin cancer [NMSC]) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. A higher rate of lymphomas was observed in patients treated with the JAK inhibitor compared to those treated with TNF blockers. A higher rate of lung cancers and an additional increased risk of overall malignancies were observed in current or past smokers treated with the JAK inhibitor compared to those treated with TNF blockers.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Olumiant, particularly in patients with a known malignancy (other than successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers.

NMSCs have been reported in patients treated with Olumiant. Periodic skin examination is recommended for patients who are at increased risk for skin cancer.

MAJOR ADVERSE CARDIOVASCULAR EVENTS

In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with another JAK inhibitor, a higher rate of major adverse cardiovascular events (MACE) (defined as cardiovascular death, myocardial infarction [MI], and stroke) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Discontinue Olumiant in patients that have experienced a myocardial infarction or stroke.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Olumiant, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Inform patients about the symptoms of serious cardiovascular events and the steps to take if they occur.
THROMBOSIS

Thrombosis, including deep venous thrombosis (DVT) and pulmonary embolism (PE), has been observed at an increased incidence in patients treated with Olumiant compared to placebo. In addition, there were cases of arterial thrombosis. Many of these adverse events were serious and some resulted in death. In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with another JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid Olumiant in patients at risk. Discontinue Olumiant and promptly evaluate patients with symptoms of thrombosis.

HYPERSENSITIVITY

Reactions such as angioedema, urticaria, and rash that may reflect drug hypersensitivity have been observed in patients receiving Olumiant, including serious reactions. If a serious hypersensitivity reaction occurs, promptly discontinue Olumiant while evaluating the potential causes of the reaction.

GASTROINTESTINAL PERFORATIONS

Gastrointestinal perforations have been reported in Olumiant clinical studies. Monitor Olumiant-treated patients who may be at increased risk for gastrointestinal perforation (e.g., patients with a history of diverticulitis). Promptly evaluate patients who present with new onset abdominal symptoms for early identification of gastrointestinal perforation.

LABORATORY ABNORMALITIES

Neutropenia – Olumiant treatment was associated with an increased incidence of neutropenia (absolute neutrophil count [ANC] <1000 cells/mm³) compared to placebo. Evaluate at baseline and thereafter according to routine patient management. In patients with RA or alopecia areata (AA), avoid initiation or interrupt Olumiant treatment in patients with an ANC <1000 cells/mm³.

Lymphopenia – Absolute lymphocyte count (ALC) <500 cells/mm³ were reported in Olumiant clinical trials. Lymphocyte counts less than the lower limit of normal were associated with infection in patients treated with Olumiant, but not placebo. Evaluate at baseline and thereafter according to routine patient management. In patients with RA or AA, avoid initiation or interrupt Olumiant treatment in patients with ALC <500 cells/mm³.

Anemia – Decreases in hemoglobin levels to <8 g/dL were reported in Olumiant clinical trials. Evaluate at baseline and thereafter according to routine patient management. In patients with RA or AA, avoid initiation or interrupt Olumiant treatment in patients with hemoglobin <8 g/dL.

Liver Enzyme Elevations – Olumiant treatment was associated with increased incidence of liver enzyme elevation compared to placebo. Increases of alanine transaminase (ALT) ≥5x upper limit of normal (ULN) and increases of aspartate transaminase (AST) ≥10x ULN were observed in patients in Olumiant clinical trials.

Evaluate at baseline and thereafter according to routine patient management. Promptly investigate the cause of liver enzyme elevation to identify potential cases of drug-induced liver injury. If increases in ALT or AST are observed and drug-induced liver injury is suspected, interrupt Olumiant until this diagnosis is excluded.

Lipid Elevations – Treatment with Olumiant was associated with increases in lipid parameters, including total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol. Assess lipid parameters approximately 12 weeks following Olumiant initiation in patients with RA or AA. Manage patients according to clinical guidelines for the management of hyperlipidemia.

VACCINATIONS

Avoid use of live vaccines with Olumiant. Update immunizations in patients with RA or AA prior to initiating Olumiant therapy in accordance with current immunization guidelines.

ADVERSE REACTIONS

In RA trials, the most common adverse reactions (≥1%) reported with Olumiant were: upper respiratory tract infections, nausea, herpes simplex, and herpes zoster.

In AA trials, the most common adverse reactions (≥1%) reported with Olumiant were: upper respiratory tract infections, headache, acne, hyperlipidemia, creatine phosphokinase increase, urinary tract infection, liver enzyme elevations, folliculitis, fatigue, lower respiratory tract infections, nausea, genital Candida infections, anemia, neutropenia, abdominal pain, herpes zoster, and weight increase.

PREGNANCY AND LACTATION

Based on animal studies, Olumiant may cause fetal harm when administered during pregnancy. Advise pregnant women and women of reproductive potential of the potential risk to a fetus. Consider pregnancy planning and prevention for women of reproductive potential. Advise women not to breastfeed during treatment with Olumiant and for 4 days after the last dose.

HEPATIC AND RENAL IMPAIRMENT

Olumiant is not recommended in patients with RA or AA and severe hepatic impairment or severe renal impairment (estimated glomerular filtration rate [eGFR] <30 mL/min/1.73m²).

Please see the following pages for Brief Summary of Prescribing Information, including Boxed Warning about Serious Infections, Mortality, Malignancy, Major Adverse Cardiovascular Events, and Thrombosis.

BA HCP ISI RA-AA 13JUN2022

Reference: 1. Olumiant. Prescribing Information. Lilly USA, LLC.

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Olumiant® (baricitinib) TABLETS BRIEF SUMMARY OF PRESCRIBING INFORMATION
Consult the package insert for complete prescribing information.

INDICATIONS AND USAGE
Rheumatoid Arthritis: Olumiant is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more tumor necrosis factor (TNF) blockers. Limitations of Use: Not recommended for use in combination with other Janus kinase (JAK) inhibitors, biologic disease-modifying antirheumatic drugs (DMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine.

Coronavirus Disease 2019 (COVID-19): Olumiant is indicated for the treatment of COVID-19 in hospitalized adults requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

Alopecia Areata: Olumiant is indicated for the treatment of adult patients with severe alopecia areata. Limitations of Use: Not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, cyclosporine or other potent immunosuppressants.

WARNING: SERIOUS INFECTIONS, MORTALITY, MALIGNANCY, MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE), AND THROMBOSIS
SERIOUS INFECTIONS
Patients treated with Olumiant are at risk for developing serious infections that may lead to hospitalization or death. Most patients with rheumatoid arthritis (RA) who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

If a serious infection develops, interrupt Olumiant until the infection is controlled. Reported infections include:
• Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Olumiant should not be given to patients with active tuberculosis.

Patients, except those with COVID-19, should be tested for latent tuberculosis before initiating Olumiant and during therapy. If positive, start treatment for latent infection prior to Olumiant use.

Invasive fungal infections, including candidiasis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.

Bacterial, viral, and other infections due to opportunistic pathogens. The risks and benefits of treatment with Olumiant should be carefully considered prior to initiating therapy in patients with chronic or recurrent infections. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Olumiant including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

MORTALITY
In a large, randomized, postmarketing safety study in RA patients 50 years of age and older with at least one cardiovascular risk factor comparing another JAK inhibitor to tumor necrosis factor (TNF) blockers, a higher rate of all-cause mortality, including sudden cardiovascular death, was observed with the JAK inhibitor.

MALIGNANCIES
Lymphoma and other malignancies have been observed in patients treated with Olumiant. In RA patients treated with another JAK inhibitor, a higher rate of malignancies (excluding non-melanoma skin cancer (NMSC)) was observed when compared with current or past smokers who are at additional increased risk.

MAJOR ADVERSE CARDIOVASCULAR EVENTS
In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with another JAK inhibitor, a higher rate of major adverse cardiovascular events (MACE) (defined as cardiovascular death, myocardial infarction, and stroke) was observed when compared with TNF blockers. Patients who are current or past smokers are at additional increased risk. Discontinue Olumiant in patients that have experienced a myocardial infarction or stroke.

THROMBOSIS
Thrombosis, including deep venous thrombosis and pulmonary embolism, has been observed at an increased incidence in patients treated with Olumiant compared to placebo. In addition, there were cases of arterial thrombosis. Many of these adverse events were serious and some resulted in death. In RA patients 50 years of age and older with at least one cardiovascular risk factor treated with another JAK inhibitor, a higher rate of thrombosis was observed when compared with TNF blockers. Avoid Olumiant in patients at risk. Patients with symptoms of thrombosis should discontinue Olumiant and be promptly evaluated.

WARNINGS AND PRECAUTIONS
Serious Infections—Serious and sometimes fatal infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens have been reported in patients with rheumatoid arthritis receiving Olumiant. The most common serious infections reported with Olumiant included pneumonia, herpes zoster, and urinary tract infection. Among opportunistic infections, tuberculosis, multidrug resistant tuberculosis, hepatitis C, and Candida infections have been reported.

Avoid use of Olumiant in patients with an active, serious infection, including localized infections. Consider the risks and benefits of treatment prior to initiating Olumiant in patients:
• with chronic or recurrent infection
• who have been exposed to tuberculosis
• with a history of a serious or an opportunistic infection
• who have resided or traveled in areas of endemic tuberculosis or endemic mycoses; or
• with underlying conditions that may predispose them to infection.

In patients with rheumatoid arthritis or alopecia areata, closely monitor for the development of signs and symptoms of infection during and after treatment with Olumiant. Interrupt Olumiant in patients with rheumatoid arthritis or alopecia areata, if the patient develops a serious infection, an opportunistic infection, or sepsis. A patient who develops a new infection during treatment with Olumiant should undergo prompt and complete diagnostic testing appropriate for an immunocompromised patient; appropriate antimicrobial therapy should be initiated, the patient should be closely monitored, and Olumiant should be interrupted if the patient is not responding to therapy. Do not resume Olumiant until the infection is controlled.

In patients with COVID-19, monitor for signs and symptoms of new infections during and after treatment with Olumiant. There is limited information regarding the use of Olumiant in patients with COVID-19 and concomitant active serious infections. The risks and benefits of treatment with Olumiant in COVID-19 patients with other concurrent infections should be considered.

Tuberculosis—Evaluate patients for active infection prior to administration of Olumiant. Olumiant should not be given to patients with active tuberculosis (TB).

Test patients with rheumatoid arthritis or alopecia areata for latent tuberculosis before initiating Olumiant. Patients with rheumatoid arthritis or alopecia areata and latent TB should be treated with standard antituberculosis therapy before initiating Olumiant. Consider anti-TB therapy prior to initiation of Olumiant in patients with a history of latent or active TB in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent TB but who have risk factors for TB infection. Consider consulting with a physician with expertise in the treatment of TB is recommended to aid in the decision about whether initiating anti-TB therapy is appropriate for an individual patient.

During Olumiant use, monitor patients for the development of signs and symptoms of TB, including patients who tested negative for latent TB infection prior to initiating therapy.

Viral Reactivation—Viral reactivation, including cases of herpes virus reactivation (e.g., herpes zoster), were reported in clinical studies with Olumiant. If a patient develops herpes zoster interrupt Olumiant treatment until the episode resolves.

The impact of Olumiant on chronic viral hepatitis reactivation is unknown. Patients with evidence of active hepatitis B or C infection were excluded from clinical trials. In clinical trials in patients with rheumatoid arthritis or alopecia areata, patients who were positive for hepatitis C antibody but negative for hepatitis C virus RNA were permitted to enroll. Patients with positive hepatitis B surface antibody and hepatitis B core antibody, without hepatitis B surface antigen, were permitted to enroll; such patients should be monitored for expression of hepatitis B virus (HBV) DNA. Should HBV DNA be detected, consult with a hepatologist. Perform screening for viral hepatitis in accordance with clinical guidelines before starting therapy with Olumiant.

Mortality—In a large, randomized, postmarketing safety study of another JAK inhibitor in RA patients 50 years of age and older with at least one cardiovascular risk factor, a higher rate of all-cause mortality, including sudden cardiovascular death, was observed in patients treated with the JAK inhibitor compared with TNF blockers. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Olumiant.

Malignancy and Lymphoproliferative Disorders—Malignancies were observed in clinical studies of Olumiant. In a large, randomized, postmarketing safety study of another JAK inhibitor in RA patients, a higher rate of malignancies (excluding non-melanoma skin cancer (NMSC)) was observed in patients treated with the JAK inhibitor compared to those treated with TNF blockers. A higher rate of lymphomas was observed in patients treated with the JAK inhibitor compared to those treated with TNF blockers. A higher rate of lung cancers was observed in current or past smokers treated with the JAK inhibitor compared to those treated with TNF blockers. In this study, current or past smokers had an additional increased risk of overall malignancies. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Olumiant, particularly in patients with a known malignancy (other than successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers.
Non-melanoma skin cancers—NMSCs have been reported in patients treated with Olumiant. Periodic skin examination is recommended for patients who are at increased risk for skin cancer.

Major Adverse Cardiovascular Events—In a large, randomized, postmarketing safety study of another JAK inhibitor for RA patients 50 years of age and older with at least one cardiovascular risk factor, a higher rate of major adverse cardiovascular events (MACE) defined as cardiovascular death, non-fatal myocardial infarction (MI), and non-fatal stroke was observed with the JAK inhibitor compared to those treated with TNF blockers. Patients who are current or past smokers are at additional increased risk.

Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Olumiant, particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur. Discontinue Olumiant in patients who have experienced a myocardial infarction or stroke.

Thrombosis—Thrombosis, including deep venous thrombosis (DVT) and pulmonary embolism (PE), has been observed in an increased incidence in patients treated with Olumiant compared to placebo. In addition, arterial thrombosis events in the extremities have been reported in clinical studies with Olumiant. Many of these adverse events were serious and some resulted in death. There was no clear relationship between platelet count elevations and thrombotic events. In a large, randomized, postmarketing safety study of another JAK inhibitor in RA patients 50 years of age and older with at least one cardiovascular risk factor, higher rates of overall thrombosis, DVT, and PE were observed compared to those treated with TNF blockers.

If clinical features of DVT/PE or arterial thrombosis occur, patients should discontinue Olumiant and be evaluated promptly and treated appropriately. Avoid Olumiant in patients that may be at increased risk of thrombosis.

Hypersensitivity—Reactions such as angioedema, urticaria, and rash that may reflect drug hypersensitivity have been observed in patients receiving Olumiant, including serious reactions. If a serious hypersensitivity reaction occurs, promptly discontinue Olumiant while evaluating the potential causes of the reaction.

Gastrointestinal Perforations—Gastrointestinal perforations have been reported in clinical studies with Olumiant. Monitor Olumiant-treated patients who may be at increased risk for gastrointestinal perforation (e.g., patients with a history of diverticulitis). Evaluate promptly patients presenting with new onset abdominal symptoms for early identification of gastrointestinal perforation.

Laboratory Abnormalities Neutropenia—Treatment with Olumiant was associated with an increased incidence of neutropenia (absolute neutrophil count [ANC] less than 1000 cells/mm³) compared to placebo.

In patients with rheumatoid arthritis or alopecia areata, avoid initiation or interrupt Olumiant treatment in patients with an ANC less than 1000 cells/mm³.

In patients with COVID-19, there is limited information regarding use of Olumiant in patients with an ANC less than 1000 cells/mm³. Avoid initiation or interrupt Olumiant treatment in patients with COVID-19 and an ANC less than 500 cells/mm³.

Evaluate at baseline and thereafter according to routine patient management. Adjust dosing based on ANC.

Lymphopenia—Absolute lymphocyte count (ALC) less than 500 cells/mm³ were reported in Olumiant clinical trials. Lymphocyte counts less than the lower limit of normal were associated with infection in patients treated with Olumiant, but not placebo.

In patients with rheumatoid arthritis or alopecia areata, avoid initiation or interrupt Olumiant treatment in patients with an ALC less than 500 cells/mm³.

In patients with COVID-19, there is limited information regarding use of Olumiant in patients with an ALC less than 500 cells/mm³.

Evaluate at baseline and thereafter according to routine patient management. Avoid initiation or interrupt Olumiant treatment in patients with COVID-19 and an ALC less than 200 cells/mm³.

Evaluate at baseline and thereafter according to routine patient management. Adjust dosing based on ALC.

Anemia—Decreases in hemoglobin levels to less than 8 g/dL were reported in Olumiant clinical trials. In patients with rheumatoid arthritis or alopecia areata, avoid initiation or interrupt Olumiant treatment in patients with hemoglobin less than 8 g/dL. Evaluate at baseline and thereafter according to routine patient management. Avoid initiation or interrupt Olumiant treatment in patients with hemoglobin levels of less than 8 g/dL.

Liver Enzyme Elevations—Treatment with Olumiant was associated with increased incidence of liver enzyme elevation compared to placebo. Increases of ALT ≥5 times upper limit of normal (ULN) and increases of AST ≥10 times ULN were observed in patients in Olumiant clinical trials. Evaluate at baseline and thereafter according to routine patient management. Prompt investigation of the cause of liver enzyme elevation is recommended to identify potential cases of drug-induced liver injury. If increases in ALT or AST are observed and drug-induced liver injury is suspected, interrupt Olumiant until this diagnosis is excluded.
23,000 cells/mm³ in patients treated with baricitinib 4 mg.

Other Adverse Reactions
- Vein thrombosis or pulmonary embolism were reported in 0 patients treated with placebo, 0 patients treated with Olumiant 2 mg, and 3 patients (0.3% per 100 patient-years) treated with baricitinib 4 mg.
- In the 0 to 52-week treatment period, arterial thromboses were reported in 3 patients (0.9 per 100 patient-years) treated with Olumiant 2 mg and 3 patients (0.3 per 100 patient-years) treated with baricitinib 4 mg.

Laboratory Abnormalities
- Neutropenia—During the 16-week treatment period, neutrophil counts below 1000 cells/mm³² occurred in 0% of patients treated with placebo, 0.6% of patients treated with Olumiant 2 mg, and 0.3% of patients treated with baricitinib 4 mg. There were no neutrophil counts below 500 cells/mm³ in any treatment group.

Platelet Elevations—During the 16-week treatment period, increases in platelet counts above 600,000 cells/mm³ were reported in 1.1% of patients treated with placebo, 1.1% of patients treated with Olumiant 2 mg, and 2.0% of patients treated with baricitinib 4 mg. Mean platelet count increased by 3000 cells/mm³ at 16 weeks in patients treated with placebo by 15,000 cells/mm³ at 16 weeks in patients treated with Olumiant 2 mg and by 23,000 cells/mm³ in patients treated with baricitinib 4 mg.

Liver Enzyme Elevations—Events of increases in liver enzymes ≥3 times the ULN were observed in patients treated with Olumiant:
- During the 16-week treatment period, ALT elevations ≥3 times the ULN occurred in 1.0% of patients treated with placebo, 1.7% of patients treated with Olumiant 2 mg, and 1.4% of patients treated with baricitinib 4 mg.
- During the 16-week treatment period, AST elevations ≥3 times the ULN occurred in 0.6% of patients treated with placebo, 1.3% of patients treated with Olumiant 2 mg, and 0.9% of patients treated with baricitinib 4 mg.
- In a phase 3 study of DMARD naïve patients, during the 24-week treatment period, ALT and AST elevations ≥3 times the ULN occurred in 1.9% and 0% of patients treated with methotrexate monotherapy, 1.9% and 1.3% of patients treated with baricitinib 4 mg monotherapy, and 4.7% and 1.9% of patients treated with baricitinib 4 mg plus methotrexate.

Lipid Elevations—In controlled clinical trials, Olumiant treatment was associated with dose-related increases in lipid parameters, including total cholesterol, triglycerides, LDL cholesterol, and HDL cholesterol. Elevations were observed at 12 weeks and remained stable thereafter. During the 12-week treatment period, changes in lipid parameters are summarized below:
- Mean LDL cholesterol increased by 8 mg/dL in patients treated with Olumiant 2 mg and by 14 mg/dL in patients treated with baricitinib 4 mg.
- Mean HDL cholesterol increased by 7 mg/dL in patients treated with Olumiant 2 mg and by 9 mg/dL in patients treated with baricitinib 4 mg.
- The mean LDL/HDL ratio remained stable.
- Mean triglycerides increased by 7 mg/dL in patients treated with Olumiant 2 mg and by 15 mg/dL in patients treated with baricitinib 4 mg.

Creatine Phosphokinase (CPK)—Olumiant treatment was associated with increases in CPK within one week of starting Olumiant and plateauing after 8 to 12 weeks. At 16 weeks, the mean change in CPK for Olumiant 2 mg and baricitinib 4 mg was 37 IU/L and 52 IU/L, respectively.

Cerebrovascular Adverse Reactions—In a phase 3 study of devices-related increases in serum creatinine were observed with Olumiant treatment. At 52 weeks, the mean increase in serum creatinine was less than 0.1 mg/dL, with baricitinib 4 mg. The clinical significance of the observed serum creatinine increases is unknown.

Other Adverse Reactions—Other adverse reactions are summarized in the following table.

Adverse Reactions That Occurred in Greater Than or Equal to 1% of Patients Treated with Olumiant 4 mg During the First 29 Days in Placebo-Controlled Trials for COVID-19

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Placebo N=1310 (%)</th>
<th>Olumiant 4 mg N=1307 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT ≥3 x ULN³</td>
<td>201 (16.0)</td>
<td>230 (18.1)</td>
</tr>
<tr>
<td>AST ≥3 x ULN³</td>
<td>117 (9.4)</td>
<td>149 (11.8)</td>
</tr>
<tr>
<td>Thrombocytosis &gt;600,000 cells/mm³²</td>
<td>34 (2.6)</td>
<td>59 (7.9)</td>
</tr>
<tr>
<td>Creatine phosphokinase (CPK) &gt;5 x ULN¹¹</td>
<td>38 (4.7)</td>
<td>36 (4.5)</td>
</tr>
<tr>
<td>Neutropenia &lt;1000 cells/mm³³</td>
<td>22 (1.8)</td>
<td>26 (2.2)</td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td>18 (1.4)</td>
<td>20 (1.5)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>11 (0.8)</td>
<td>20 (1.5)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>13 (1.0)</td>
<td>19 (1.5)</td>
</tr>
</tbody>
</table>

* As assessed by measured values within the clinical trial database. Frequencies are based on study size adjusted percentages.

Adverse Reactions That Occurred in ≥1% of Patients Treated with Olumiant 2 mg and Baricitinib 4 mg Treated in Placebo-Controlled Trials for Rheumatoid Arthritis

Additional adverse drug reactions occurring in fewer than 1% of patients: acne.

Adverse Reactions in Patients with COVID-19—The safety of Olumiant was evaluated in two randomized, double-blind, placebo-controlled clinical trials of hospitalized adults with COVID-19 for up to 29 days, in which 1307 patients received at least one dose of Olumiant 4 mg once daily, and 1310 patients received placebo, up to 14 days or until hospital discharge, whichever occurred first. In these studies, prophylaxis for venous thromboembolic event (VTEs) was recommended or required for all patients unless a major contraindication was noted.

Overall, the safety profile observed in patients with COVID-19 treated with Olumiant was consistent with the safety profile in patients with rheumatoid arthritis.

Overall Infections—During the first 29 days of the randomized clinical trials, infections were reported in 194 patients (14.6%) treated with Olumiant 4 mg and by 219 patients (16.7%) treated with placebo. The most commonly reported infection with Olumiant was pneumonia (3.1%).

Serious Infections—During the first 29 days of the randomized clinical trials, serious infections were reported in 98 patients (7.5%) treated with Olumiant 4 mg and 120 patients (9.2%) treated with placebo. The most commonly reported serious infections with Olumiant were COVID-19 pneumonia (2.1%) and septic shock (2.1%).

Opportunistic Infections—During the first 29 days of the randomized clinical trials, opportunistic infections were reported in 12 patients (0.9%) treated with Olumiant 4 mg and 14 patients (1.1%) treated with placebo. Tuberculosis was reported in 1 patient (0.1%) treated with Olumiant 4 mg and 0 patients treated with placebo.

Venous Thrombosis Events—During the first 29 days of the randomized clinical trials, pulmonary embolism was reported in 20 patients (1.5%) treated with Olumiant 4 mg and 11 patients (0.8%) treated with placebo. Deep vein thrombosis was reported in 20 patients (1.5%) treated with Olumiant 4 mg and 18 patients (1.4%) treated with placebo.

Adverse drug reactions in greater than or equal to 1% of patients in trials for COVID-19 are summarized in the following table.

Adverse Reactions That Occurred in Greater Than or Equal to 1% of Patients Treated with Olumiant 4 mg During the First 29 Days in Placebo-Controlled Trials for COVID-19

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Placebo N=371 (%)</th>
<th>Olumiant 2 mg N=365 (%)</th>
<th>Olumiant 4 mg N=540 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper respiratory tract infections (URTs)²</td>
<td>19.9</td>
<td>15.4</td>
<td>21.3</td>
</tr>
<tr>
<td>Headache</td>
<td>5.4</td>
<td>5.5</td>
<td>6.6</td>
</tr>
<tr>
<td>Acne³</td>
<td>2.2</td>
<td>5.8</td>
<td>5.9</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>3.0</td>
<td>3.6</td>
<td>5.9</td>
</tr>
<tr>
<td>Blood creatinine phosphokinase increased</td>
<td>1.3</td>
<td>0.8</td>
<td>4.3</td>
</tr>
<tr>
<td>Urinary tract infections (UTIs)²</td>
<td>2.2</td>
<td>3.8</td>
<td>3.7</td>
</tr>
</tbody>
</table>

a Includes acute sinusitis, acute tonsillitis, chronic tonsillitis, epiglottitis, laryngitis, nasopharyngitis, oropharyngeal pain, pharyngitis, pharyngotonsillitis, rhinitis, sinobronchitis, sinusitis, tonsillitis, tracheitis, and upper respiratory tract infection.

b Includes eczema herpeticum, genital herpes, herpes simplex, aphthous herpeticum simplex, and oral herpes.

OLUMIANT® (baricitinib) BA HCP BS 13JUN2022
During the 12-week treatment period, changes in lipid parameters are summarized below:

- Neutropenia
- Abdominal pain
- Herpes zoster
- Weight increased

Adverse Reactions That Occurred in ≥1% of Patients Treated with Olumiant 2 mg or Olumiant 4 mg in Alopecia Areata Trials (Cont.)

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=371) (%)</th>
<th>Olumiant 2 mg (n=365) (%)</th>
<th>Olumiant 4 mg (n=540) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver enzyme elevations</td>
<td>2.4 1.1 3.0</td>
<td>1.9 2.2 2.7</td>
<td>2.4 2.2 2.2</td>
</tr>
<tr>
<td>Foliculitis</td>
<td>0.8 1.4 2.2</td>
<td>0.9 1.8 2.2</td>
<td>0.8 1.8 2.2</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1.1 0.8 2.2</td>
<td>1.4 1.3 2.2</td>
<td>1.1 1.0 2.2</td>
</tr>
<tr>
<td>Lower respiratory tract infections (LRTI)</td>
<td>0.8 2.2 2.0</td>
<td>0.9 1.3 1.3</td>
<td>1.0 1.3 1.3</td>
</tr>
<tr>
<td>Nausea</td>
<td>1.5 1.0 2.0</td>
<td>1.6 1.5 2.0</td>
<td>1.6 1.6 2.0</td>
</tr>
<tr>
<td>Genital Candida infections</td>
<td>0.3 2.2 1.3</td>
<td>0.3 2.2 1.3</td>
<td>0.4 2.2 1.3</td>
</tr>
<tr>
<td>Anemia</td>
<td>0.9 0.5 1.0</td>
<td>0.9 0.5 1.0</td>
<td>0.9 0.5 1.0</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>0.8 0.7 1.3</td>
<td>0.8 0.7 1.3</td>
<td>0.8 0.7 1.3</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>2.2 3.8 0.9</td>
<td>2.2 3.8 0.9</td>
<td>2.2 3.8 0.9</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>0.5 1.4 0.9</td>
<td>0.5 1.4 0.9</td>
<td>0.5 1.4 0.9</td>
</tr>
<tr>
<td>Weight increased</td>
<td>0.3 1.6 0.9</td>
<td>0.3 1.6 0.9</td>
<td>0.3 1.6 0.9</td>
</tr>
</tbody>
</table>

a % - study size adjusted percentages.
b URT includes: acute sinusitis, influenza, laryngitis, nasopharyngitis, oropharyngeal pain, pharyngitis, pharyngotonsillitis, rhinitis, sinusitis, tonsillitis, upper respiratory tract infection, viral upper respiratory tract infection, viral sinusitis, viral pharyngitis, respiratory tract infection viral, rhinovirus infection and adenoviruses
c Acne includes: acne and dermatitis acneiform.
d Hyperlipidemia includes: hyperlipidaemia, hypercholesterolaemia, hypertriglyceridaemia, dyslipidemia, lipids increased, low density lipoprotein increased, blood cholesterol increased, and blood triglycerides increased.
e UTI includes: cystitis, urinary tract infection, white blood cells urine positive, urinary tract infection bacterial, and pyelonephritis.
f Liver enzyme elevations includes: transaminases increased, aspartate aminotransferase increased, alanine aminotransferase increased, hepatic enzyme increased, gamma-glutamyl transferase increased, and hepatic function abnormal.
g Felicitus was most commonly localized in the scalp region associated with hair regrowth.
h LRTI includes: bronchitis, bronchiolitis, lower respiratory tract infection, pneumonia, COVID-19 pneumonia, and respiratory tract infection.
i Genital Candida infections includes: vulvovaginal candidiasis, vulvovaginal mycotic infection, and genitourinary fungal infection.
j Neutropenia includes: neutropenia and neutrophil count decreased.
k Abdominal pain includes: abdominal pain, abdominal pain lower, abdominal pain upper, and abdominal discomfort.

In patients treated with any dose of baricitinib, adverse reactions that occurred in fewer than 1% of patients included arterial thrombosis, B cell lymphoma, lymphoproliferative, and fungal skin infections. Additional adverse reactions observed after Week 52: venous thromboembolic events (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE), and malignancy including non-melanoma skin cancer.

Overall, the adverse reactions observed in patients with alopecia areata treated with Olumiant were consistent with the adverse reactions in patients with rheumatoid arthritis.

Postmarketing Experience—The following adverse reactions have been identified during post-approval use of Olumiant. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

**Immune System Disorders:** Drug hypersensitivity (events such as rash, urticaria, and angioedema have been observed).

**Drug Interactions**

- Strong CYP3A4 Inhibitors—Baricitinib exposure is increased when Olumiant is co-administered with strong Organic Anion Transporter 3 (OAT3) inhibitors (such as probenecid), hence the dosage of baricitinib should be reduced by half the recommended dose.
- Other JAK Inhibitors or Biologic DMARDs—Olumiant has not been studied in combination with other JAK inhibitors or with biologic DMARDs.

**Use in Specific Populations**

**Pregnancy**

**Risk Summary**—Based on the findings from animal reproduction studies, Olumiant may cause fetal harm during pregnancy. Available data from clinical trials and postmarketing case reports with Olumiant exposure in pregnancy are insufficient to inform a drug- associated risk for major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are no human data on chronic baricitinib exposure throughout pregnancy. There are risks to the mother and the fetus associated with rheumatoid arthritis in pregnancy. Consider the risks and benefits with chronic use of Olumiant during pregnancy.

**In animal embryo-fetal development studies, oral baricitinib administration to pregnant rats and rabbits at exposures equal to and greater than approximately 11 and 46 times the maximum recommended human dose (MRHD) of 4 mg/day, respectively, resulted in reduced fetal body weights, increased embryolethality (rabbis only), and dose-related increases in skeletal malformations. No developmental toxicity was observed in pregnant rats and rabbits treated with oral baricitinib during organogenesis at approximately 2 and 7 times the exposure at the MRHD, respectively. In a pre- and post-natal development study in pregnant female rats, oral baricitinib administration at exposures approximately 24 times the MRHD resulted in reduction in pup viability (increased incidence of stillborn pups and early neonatal deaths), decreased fetal birth weight, reduced fetal body weight gain, decreased cytoxic T cells on post-natal day (PND) 35 with evidence of recovery by PND 65, and developmental delays that might be attributable to decreased body weight gain. No developmental toxicity was observed at an exposure approximately 5 times the exposure at the MRHD.**

The background risks of major birth defects and miscarriage for the indicated population(s) are unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2%-4% and 15%-20%, respectively.

Report pregnancies to Eli Lilly and Company at 1-800-LillyRx (1-800-545-5979).

**Clinical Considerations—** Disease-Associated Maternal and/or Embryo/Fetal Risk: Published data suggest that increased disease activity is associated with the risk of developing adverse pregnancy outcomes in women with rheumatoid arthritis. Adverse pregnancy outcomes include preterm delivery (before 37 weeks of gestation), low birth weight (less than 2500 g) infants, and small for gestational age at birth.

**Data—Animal Data:** In an embryofetal development study in pregnant rats, dosed orally during the period of organogenesis from gestation days 6 to 17, baricitinib was teratogenic (skeletal malformations that consisted of bent limb bones and rib anomalies) at exposures equal to or greater than approximately 11 times the MRHD (on an AUC basis at maternal oral dose of 10 mg/kg/day and higher). No developmental toxicity was observed in rats at an exposure approximately 2 times the MRHD (on an AUC basis at a maternal oral dose of 2 mg/kg/day).

In an embryofetal development study in pregnant rabbits, dosed orally during the period of organogenesis from gestation days 7 to 20, embryolethality, decreased fetal body weights, and skeletal malformations (rib anomalies) were observed in the presence of maternal toxicity at an exposure approximately 48 times the MRHD (on an AUC basis at a maternal oral dose of 30 mg/kg/day). Embryolethality consisted of increased post-implantation loss that was due to elevated incidences of both early and late resorptions. No developmental toxicity was observed in rabbits at an exposure approximately 7 times the MRHD (on an AUC basis at a maternal oral dose of 10 mg/kg/day).

In a pre- and post-natal development study in pregnant female rats dosed orally from gestation day 6 through lactation day 20, adverse findings observed in pups included decreased survival from birth to post-natal day 4 (due to increased stillbirths and early neonatal deaths), decreased birth weight, decreased body weight gain during the pre-weaning phase, increased incidence of malrotated forelimbs during the pre-weaning phase, and decreased cytoxic T cells on PND 35 with recovery by PND 65 at exposures approximately 24 times the MRHD (on an AUC basis at a maternal oral dose of 25 mg/kg/day). Developmental delays (that may be secondary to decreased body weight gain) were observed in males and females at exposures approximately 24 times the MRHD (on an AUC basis at a maternal oral dose of 25 mg/kg/day). These findings included decreased forelimb and hindlimb grip strengths, and delayed mean age of sexual maturity. No developmental toxicity was observed in rats at an exposure approximately 5 times the MRHD (on an AUC basis at a maternal oral dose of 5 mg/kg/day).

**Lactation**

**Risk Summary—** No information is available on the presence of Olumiant in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Baricitinib is present in the milk of lactating rats. Because of the potential for serious adverse reactions in nursing infants advise women not to breastfeed during treatment with Olumiant and for 4 days after the last dose (approximately 5 to 6 half-lives).

**Data—** A single oral dose of 25 mg/kg radiolabeled baricitinib was administered to lactating female Sprague-Dawley rats on post-partum day 13. Drug exposure was approximately 45-fold greater in milk than in plasma based on AUC.<values>

**Females and Males of Reproductive Potential**

**Contraception—** Based on animal studies, Olumiant may cause fetal harm when administered during pregnancy. Consider pregnancy planning and prevention for females of reproductive potential.

**Pediatric Use—** The safety and effectiveness of Olumiant in pediatric patients have not been established.

**Geriatric Use—** Of the 3100 patients treated in the rheumatoid arthritis clinical trials, a total of 537 patients were 65 years of age and older, including 71 patients 75 years of age and older. Of the 2558 patients treated in the COVID-19 clinical trials, a total of 781 were 65 years of age and older, including 295 patients 75 years and older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.
and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Of the 1200 patients in the alopecia areata trials, a total of 29 patients were 65 years of age or older. The number of patients aged 65 years and older was not sufficient to determine whether they respond differently from younger patients.

Olumiant is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because geriatric patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

**Hepatic Impairment**—No dose adjustment is necessary in patients with mild or moderate hepatic impairment.

The use of Olumiant has not been studied in patients with rheumatoid arthritis or alopecia areata and severe hepatic impairment and is therefore not recommended. Olumiant has not been studied in patients with COVID-19 and severe hepatic impairment. Olumiant should only be used in patients with COVID-19 and severe hepatic impairment if the potential benefit outweighs the potential risk.

**Renal Impairment**—Renal function was found to significantly affect baricitinib exposure.

Rheumatoid Arthritis and Alopecia Areata—The recommended dosage of Olumiant in patients with moderate renal impairment (estimated glomerular filtration rate [GFR] between 30 and <60 mL/min/1.73 m²) should be reduced by half the recommended dose. Olumiant is not recommended for use in patients with rheumatoid arthritis or alopecia areata and severe renal impairment (estimated GFR of less than 30 mL/min/1.73 m²).

COVID-19—The recommended dosage of Olumiant in patients with moderate renal impairment (estimated GFR between 30 and <60 mL/min/1.73 m²) or severe renal impairment (estimated GFR between 15 and <30 mL/min/1.73 m²) is 2 mg once daily and 1 mg once daily, respectively. Olumiant is not recommended for use in patients who are on dialysis, have end-stage renal disease (ESRD), or with estimated GFR of <15 mL/min/1.73 m².

**OVERDOSE**

Single doses up to 40 mg and multiple doses of up to 20 mg daily for 10 days have been administered in clinical trials without dose-limiting toxicity. Pharmacokinetic data of a single dose of 40 mg in healthy volunteers indicate that more than 90% of the administered dose is expected to be eliminated within 24 hours.

In case of an overdose, it is recommended that the patient should be monitored for signs and symptoms of adverse reactions. Patients who develop adverse reactions should receive appropriate treatment.

Additional information can be found at www.Olumiant.com
**Mission** Managed Healthcare Executive® provides healthcare executives at health plans and provider organizations with analysis, insights and strategies to pursue value-driven solutions.

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In Brief

CVS returns Eliquis to its formularies

Following objections from patient groups and professional organizations, CVS Caremark put Eliquis (apixaban) back on its formularies starting July 1.

“This is about decisions between doctors and patients being respected,” says Beth Joyner Waldron, a patient advocate in North Carolina who used Twitter and other social media to criticize the pharmacy benefit manager (PBM) and its initial formulary decision.

CVS Caremark issued a statement on June 22 that said Eliquis was re-added after being taken off the formularies at the beginning of this year because it had negotiated a lower net cost from drug manufacturer. “Anticoagulant therapies are among the nonspecialty products where we are seeing the fastest cost increases from drug manufacturer. Anti-coagulant therapies are among the nonspecialty products where we are seeing the fastest cost increases from drug manufacturers, and we will continue to push back on unwarranted price increases,” said the statement.

A company spokesman said Eliquis was restored to the PBM’s Value Formulary along with its Standard and Advanced control formularies.

Eliquis is in a class of drugs called direct oral anticoagulants (DOACs) that are taken by people to prevent blood clots. Other DOACs include Xarelto (rivaroxaban), Pradaxa (dabigatran), Savaysa (edoxaban) and Beyvxxa (betrixaban). For years, warfarin was the mainstay of anticoagulation. But the risk of bleeding is lower for patients taking DOACs, and they don’t need to be monitored as closely as patients on warfarin. Introduced in 2010, DOACs have taken off. But they are far more expensive than warfarin, so payers have looked for ways to manage spending on DOACs.

Waldron, who was diagnosed with venous thromboembolism about 20 years ago, has been taking Eliquis for eight years. Waldron says she managed to stay on the drug because of a fortunate combination of reasons: She had a large supply on hand; she got a copay card from the manufacturer; and she benefited from a decision by the North Carolina State Health Plan to put the drug back on its formulary for its members.

The American College of Cardiology (ACC) and the American Society of Hematology have been involved in pushing back on CVS Caremark’s formulary decision. In January 2022, the ACC posted a news story on its website that said the group, along with the American Society of Hematology, had met with CVS Caremark to discuss the PBM’s decision to prefer Xarelto — the article on the website uses the generic name, rivaroxaban — over other DOACs on its formularies. The ACC article says that CVS Caremark pointed atrial fibrillation guidelines issued jointly by the ACC, the American Society of Hematology and the Heart Rhythm Society in 2019, as justifying the decision to drop Eliquis from its formularies. The 2019 guidelines do not tier DOACs and their intent was to “encourage discussion between physicians and patients so an informed decision can be made based on medical history and preferences,” the article said.

The ACC published another news story in June about Eliquis getting back on the CVS Caremark formularies. The article says that the ACC and the American Society of Hematology “engaged” with CVS Caremark about taking Eliquis off its formularies and “the potential impact on patients and practice staff.”

Waldron says she knows of eight medical events in five states that are related to people losing coverage of Eliquis because of the CVS Caremark change. Waldron says some of the events may be the result of gaps in anticoagulation therapy, adding that it would take research to determine the link between the events to CVS’ Eliquis formulary decision.

—Peter Wehrwein

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WELLBEING CHECKUP

Patricia Jakel, MN, RN, AOCN, of the UCLA Health System, discussed burnout and compassion fatigue among those delivering cancer care.

Did you know that dry eye disease (DED) can impact individuals irrespective of age, gender, and race and currently affects between 5% and 15% of people in the United States?

To learn more, watch Laura Periman, MD, as she shares her knowledge about DED in this multipart video series.

During the series, you’ll discover:
- Information about DED and its clinical burden
- The population health implications of DED
- The evolving treatment landscape for the condition

Featuring:
Laura M. Periman, MD
Periman Eye Institute
Seattle, Washington

WATCH NOW
visit https://bit.ly/DryEyeDis or scan the QR code.
Multiple myeloma is a form of cancer characterized by the proliferation of plasma cells in the bone marrow. Although relatively rare, accounting for less than 2% of all cancer cases each year, multiple myeloma is the second most common blood cancer in the United States. The National Cancer Institute estimates that approximately 34,500 cases will be diagnosed this year and that 12,640 people in the U.S. will die from the multiple myeloma.

Clinicians and patients have a growing number of treatment options for multiple myeloma from which to choose, both for patients whose disease comes back after responding to treatment (relapse) and isn’t responding to treatment (refractory). A cohort of newer treatments featuring innovative mechanisms of action are currently under development, including chimeric antigen receptor T-cell (CAR-T) therapy and bispecific antibodies.

**Off the shelf**

CAR-T therapy has involved using the patient’s own T cells to attack cancer cells. The T cells, which are the mainstays of the body’s immune system, are collected from the patient’s blood and re-engineered in a laboratory to produce proteins on their surfaces that recognize and attach to specific antigens on the surface of cancer cells. These proteins are called chimeric antigen receptors (CARs). Millions of CAR-altered T cells are grown in the laboratory, then infused back into the patient, where they seek out and bind to antigens on cancer cells and destroy them. Typically, CAR-T cell therapies target CD19 antigens or B-cell maturation antigens (BCMAs). CAR-T therapy is complicated and expensive; the price of the primary treatment and the associated treatment typically exceeds $500,000.

Poseida Therapeutics, a San Diego biotech company, is developing an allogeneic version of CAR-T therapy. Instead of using the patient’s own cells, the allogeneic version of CAR-T uses T cells from donors to create CAR-T cells for use in multiple patients. Allogeneic products carry an increased risk of host-graft and graft-versus-host reactions, but they can be created more easily to meet off-the-shelf demand. Poseida’s product, provisionally named P-BCMA-ALLO1, is currently in a phase 1 study evaluating its safety in patients with relapsed/refractory multiple myeloma. Preliminary results are expected in June 2023.

Cartesian Therapeutics, based in Gaithersburg, Maryland, is developing the first CAR-T cell therapy to potentially treat newly diagnosed multiple myeloma. The investigational agent, Descartes-08, is currently in a phase 2 study evaluating its use in patients with high-risk multiple myeloma. Primary study results are expected in February 2023.

OriCAR-017, developed by Shanghai-based OriCell Therapeutics, is a second-generation CAR-T cell therapy targeting GPRC5D, a surface receptor on myeloma cells. The findings from a phase 1 trial were presented at the 2022 American Society of Clinical Oncology (ASCO) annual meeting in June. Efficacy results were positive with no dose-limiting toxicities reported.

**Matchmaking tumor, T cells**

Bispecific antibodies are monoclonal antibodies with two targets. Typically, one is on tumor cells and the other on the surface of cells the immune system. Bispecific antibody targets include BCMAs on myeloma cells and CD3 proteins on the surface of T cells.

Pfizer’s elranatamab is a BCMA, CD3-targeted bispecific antibody under investigation for the potential treatment of relapsed/refractory multiple myeloma. The FDA has granted the drug an orphan drug and fast-track designation. Interim results from a phase 2 were presented at the 2022 ASCO meeting. Patients with refractory multiple myeloma received a 76-milligram dose of elranatamab weekly via subcutaneous injection. Of the 94 patients evaluated, 90% responded positively to the treatment. Based on results, Pfizer says it plans to move ahead with the drug. Also moving through the pipeline is Cartesian’s Descartes-25. This novel bispecific antibody targets BCMA and the cytokine interleukin-12. The drug is currently in a phase 1/2 study as a treatment for relapsed/refractory multiple myeloma.

Rosanna Sutherby, Pharm. D., is a medical writer and community pharmacist in High Point, North Carolina.
INSULIN PRICES:
Lowering them is a group effort

As Congress considers legislation that would cap out-of-pocket costs for insulin, Walmart and Civica Rx are taking steps that could make less expensive versions of the diabetes medication more available. by DENISE MYSHKO

If it were a popularity contest, putting a $35-per-month cap on out-of-pocket insulin costs would win, no problem. About 87% of voters surveyed by think tank Data for Progress support the idea. President Joseph Biden is on board. He mentioned it in the State of the Union address and has talked about it since. The Build Back Better legislation that passed the U.S. House of Representatives in November 2021 but stalled in the Senate included a $35 monthly insulin cap among its drug-pricing provisions. A separate bill, the Affordable Insulin Now Act, which would also limit the price of insulin, passed the House in March.

Some drugmakers have taken steps to blunt the criticism about insulin prices. For example, Sanofi announced in late June that it limit its insulin prices to $35 per month for people without health insurance.

The political momentum to cap insulin prices comes as out-of-pocket prices for the medication continue to be high and are rising. The average cash price for insulins climbed approximately 55% from 2014 to 2019, from $0.22 to $0.34 per insulin unit, according to GoodRx (an insulin unit is a measure used for dosing; for example, a concentration of U-100 has 100 insulin units per milliliter). Since then, it has dropped some, $0.33 to $0.31, which works out to 5%.

Most of this current decline is a result of recent approvals of generics and biosimilars. But not all insulins saw decreases, according to GoodRx’s January 2022 report on insulins. GoodRx tracked 28 insulins across all manufacturers and insulin types. A package of five generic insulin lispro KwikPens, for example, still costs about $300 compared with the $700 price for a similar package of brand-name Humalog KwikPens.

In December 2021, the House Committee on Oversight and Reform’s minority staff issued a report on pharmacy benefit managers’ (PBMs) practices and drug pricing that found that drug prices overall have risen three times faster than inflation and that patient out-of-pocket costs have increased by 53%.

Manufacturers are charging what the market will bear, Allan Coukell, senior vice president of public policy at Civica Rx, said in an interview with Managed Healthcare Executive. “The retail distribution system for drugs is a system that incentivizes very high list prices; it is also not transparent about negotiated prices. A lot of what you’re looking at is a profit margin with those products,” Civica Rx is a nonprofit generic company that recently announced a new initiative in the insulin space. The company has entered into a co-development and commercial agreement with GeneSys Biologics for three insulins it plans to sell at a major discount. Civica Rx anticipates that the first insulin, glargine, will be available by early 2024.

Legislative action
The Build Back Better Act that the House of Representatives passed in November included several provisions that would lower prescription drug costs. Those concerning insulin would have capped monthly insulin costs for people covered by Medicare and private insurance. Sen. Raphael Warnock (D-Ga.) introduced the Affordable Insulin Now Act, which would cap insulin prices at $35 per month, in the Senate.

In June, Sens. Susan Collins (R-Maine) and Jeanne Shaheen (D-New Hampshire) announced...
that they would be introducing a different bill that takes several steps to improve access to insulin, including the $35 cap on out-of-pocket costs featured in the other bills.

Kaiser Family Foundation research found that 26% of those with an insulin prescription who have bought health insurance coverage in the individual market (primarily through the Affordable Care Act exchanges) would benefit from a limit of $35 on monthly out-of-pocket costs for insulin. Currently, more than 1 in 20 insulin users in the private insurance markets pay more than $150 per month per insulin product, according to a recent review by the foundation.

In the large group market, the researchers found that if insulin was capped at $35 a month, median savings would be $19 per month, and one-quarter of patients would save at least $42 per month. The researchers also reported that in the small group market, median savings would also be $19 per month, and one-quarter would save at least $48 per month. The researchers also reported that in the small group market, median savings would also be $19 per month, and one-quarter would save at least $48 per month.

A different analysis from the Health Care Cost Institute, an independent, nonprofit healthcare research organization, found that a $35 cap on insulin would benefit about 70% of patients with commercial insurance who pay for insulin. The institute’s analysis, which used 2019 claims data, determined that almost 30% of individuals in the sample had average monthly out-of-pocket spending on insulin between $51 and $100, 16% had average monthly spending between $101 and $200, and close to 9% had average monthly spending over $200.

Coukell points out that efforts to cap insulin prices would lower costs only for those with insurance and wouldn’t help those without it. The National Center for Health Statistics estimates that between January 2021 and June 2021, about 31.1 million people, or 9.6% of the population, were uninsured.

“One of the ways that uninsured patients get hurt the most is that their out-of-pocket cost is driven by a very high list price, which PBMs and insurance companies don’t pay,” Coukell. “They all negotiate a lower price. But if you’re somebody who doesn’t have insurance, they will be charged $300 a vial.” A 2020 report from The Commonwealth Fund found that uninsured people are also much more likely to pay full list price for insulin (68%) than those who are privately insured (9%) or have coverage through Medicaid (3%).

Walmart, which has said that 14% of its shoppers have diabetes, introduced its own brand of insulin in 2021 that could help those without insurance. Available through Walmart’s private ReliOn brand, the company announced that analog insulin vials would be priced at $72.88 and a FlexPen option at $83.88. A few months later, the retailer began offering an equivalent of the combination NovoLog Mix 70/30 for the same price. Walmart is also working directly with Novo Nordisk, which sells the NovoLog brand, to develop a private-label version.

Civica Rx announced in March that it will sell insulins for no more than $30 per vial and no more than $55 for a box of five pen cartridges. The company said it will manufacture glargine, lispro and aspart that are interchangeable with their brand-name products, Lantus, Humalog and Novolog, respectively. In June, Civica announced that Profil, a German company, will be its “clinical trial partner” in developing the insulin. But patients will have to be patient: The company said the first insulin, glargine, won’t be available until early 2024.

“We’re not going to have a high price and a subsequent discount or rebate that’s only available to some purchasers,” Coukell said in his interview with MHE. “We hope that if Civica insulin is out there for no more than $30 a vial, other manufacturers will have to respond to that,” he added. “It will become difficult or impossible for anybody to try to charge patients hundreds of dollars for an identical product.”

Denise Myshko is senior editor of Formulary Watch®, a news website affiliated with Managed Healthcare Executive®.
PBM are creating GPOs, and stirring debate as to why

The Big Three all set up group purchasing organizations recently, but some industry observers question the timing of the move and who will benefit. by DEBORAH ABRAMS KAPLAN

In 2019, Express Scripts PBM (pharmacy benefit manager) formed Ascent Health Services GPO (group purchasing organization), based in Switzerland. In 2020, CVS Caremark formed Zine GPO. And in 2021, OptumRx formed Emisar Pharma Services, based in Ireland. With pharmacy benefits for approximately 75% of U.S.-covered lives under their control, why would these PBMs need GPOs — to capitalize on their scale to get better drug prices?

"In each case, there’s what the PBM said, and then you have to do your best to fill in the blanks of what could possibly be going on," says Howard Deutsch, principal at ZS Associates, a global professional services firm with offices in Boston. "They haven’t said a heck of a lot. They’ll say things about serving customer needs, but nowhere will you find some particular customer need that is better being served by the existence of this new entity."

With the Big Three PBMs already covering a majority of prescription claims, "the idea that they needed to create some sort of new entities so they can have some bargaining power is kind of ludicrous," Deutsch says. "They already had plenty of bargaining power and were using that quite effectively. It’s unclear from what they’ve publicly said what the value proposition is to the rest of the healthcare system. The value proposition to the PBM is somewhat clear."

Pricing is one reason Ken Paulus, president and CEO of Prime Therapeutics, gave in an interview last year with Managed Healthcare Executive*. Prime entered into an agreement with Express Scripts three years ago whereby Express Scripts handles some of the negotiations with pharmaceutical manufacturers. As a minority owner of Ascent GPO, Prime has direct access to all the GPO contracts and received savings it would not have gotten otherwise, Paulus said in the interview. Prime still processes its own claims and performs utilization management, Paulus said, but the GPO was "a fairly elegant solution for us to save significant dollars for clients and members and employers, but do so without giving up our strategic optionality, which is continuing to run our own business."

Alan Lotvin, president of CVS Caremark, CVS Health’s PBM, said in a recent interview with Managed Healthcare Executive* that the GPO was a way for CVS Caremark to "separate out all the different lines of business onto separate contracts" and gain some bargaining power.

"It wasn’t, at least in our minds, so much about regulation," Lotvin said. "I thought about more that if we have a single rebate contract that covers multiple lines of business, if one line of business is impacted by a decision, if I have to go back to pharma and renegotiate, I am renegotiating from a position of weakness. So, if I disaggregate proactively, now I’ve taken a tool away from the manufacturers."

With the consolidation in the PBM industry and with large payers now integrated with PBMs, "the payer value proposition is pretty important," observes Ashraf Shehata, national sector leader for healthcare and life sciences for KPMG, a consulting and accounting firm. Over the years, PBMs have moved into a shared services role within their health plan owner systems. The PBM would typically be the largest single entity in the shared services business. But Shehata anticipates seeing other capabilities like care management, IT services and data analytics moving into various shared services buckets as these frameworks for large multitenant payer enterprises mature.
GPOs negotiate prices of drugs, medical products and devices for members. In healthcare, the members have traditionally been hospitals and nursing homes. The idea is to lower prices and reduce transaction costs by increasing the purchasing power of a larger group. The GPOs are often member-owned and funded by administrative fees.

**Suspicious of the timing**

The spate of GPO launches by PBMs came as Congress was debating legislation that would establish new transparency requirements for PBMs, notes James Gelfand, executive vice president, public affairs, of the ERISA Industry Committee, a trade association representing large employers. Transparency language was included in the Lower Health Care Costs Act in 2019, which the PBMs lobbied against, according to Gelfand. PBM transparency provisions are also included in the now-defunct Build Back Better bill.

Gelfand finds the timing for forming GPOs suspicious. "Are you creating another intermediary in the supply chain to prepare for transparency requirements that are going to be specific to the PBM?" he asks. Many have worked to bring more transparency to the drug supply chain and healthcare system in recent years. With so many entities involved in the drug supply chain, such as insurance companies, PBMs and vendors that set up and run the plans, adding another intermediary — the GPO — risks losing some of the progress made, Gelfand believes.

Employers want to know whether the new GPO entity will retain rebates or discounts instead of them going back to plan sponsors, Gelfand says. Will this new layer add costs? Will GPOs be able to negotiate better than the PBMs? Will the PBM use the excuse that it cannot provide the requested data or information because the GPO has it and there is a firewall?

"We have moved pretty far ahead in terms of making sure that the plan sponsor owns the plan and the data in the plan. But this could be a setback depending on how it’s implemented," Gelfand says.

Vendors will always say they are performing better and overall savings have improved. But plan sponsors need to do complex data reconstruction and analysis to be sure. "Vendors are going to guarantee us that we’re reaping the benefits of lower prices, but it’s a trust-but-verify situation. I haven’t had time to verify," Gelfand says.

Deutsch suspects that the new GPO layer will keep some of the rebates and only pass through a percentage to the PBMs. With PBMs, "almost every single penny on the dollar is passed through to the plan sponsors now," so PBMs do not have that revenue stream. The GPO can take a cut through an administrative or data-use fee to retain some of the rebate, he said.

Ultimately, many experts anticipate prices going up. "I don’t see how you can add another middleman and not add more cost to the system," says Kevin Young, co-founder and chief product officer of Prescriptive, a prescription data platform with a PBM product.

"It’s going to be up to the plan sponsor to evaluate the benefits and the value they’re getting from the PBM relationship," says Shehata. If the overall benefit is good, they will not care about individual fees, he says.

"Most buyers of PBM services and most consultants that evaluate (PBM contracts) look at the total value rather than separating individual fees."

Outside experts also have questions about why Express Scripts located its GPO in Switzerland and OptumRx did so in Ireland. "They stand to lose a lot if they get regulated on rebates," notes Young. "Creating another organization that’s offshore, they can protect their interests, protect their shareholders’ interests. Europe does not make much sense as a location for U.S. healthcare entities, says Deutsch: "Switzerland is not exactly a hotbed of U.S. pharmaceutical activity."

But Shehata thinks placing the GPOs outside the U.S. makes sense: "Going back to that shared services model, the belief is that many organizations build shared services structures at a global scale to actually optimize their ability to work at scale." He says many payers run organizations in multiple countries and have global businesses ranging from infrastructure to call centers. "I think of this as consistent with their global delivery model and less of a short-term move to try to reduce liabilities."

No matter where a vendor is located, Gelfand wants to make sure it is still subject to transparency and accountability rules. "I don’t know that basing your company in another country gets you out of any of that," he says. "If being based in Ireland or Switzerland gives you a better tax rate, that’s not our business as customers. We don’t care about that. We care about what effect will it have on patients and our ability to provide the best benefits for the patients."

GPO creation "could be a really good thing or it could be a really bad thing. And ... it’s too early for us to tell," Gelfand says.  

Deborah Abrams Kaplan is a freelance writer who covers medical and practice management topics.
ICER looking at payer policies

Cost-effectiveness research has been the Institute for Clinical and Economic Review’s reason to be. Now it is looking at whether coverage policies align with FDA approvals and treatment guidelines.

The Institute for Clinical and Economic Review (ICER) in Boston has conducted cost-effectiveness studies throughout its entire 16-year history. But now the organization is branching out into assessing payer coverage policies to determine whether they provide “fair” access.

More specifically, ICER is looking at whether the formulary limitations and utilization management tactics used by insurers and their pharmacy benefit managers (PBMs) align with the FDA-approved labels of the drug and treatment guidelines.

In May, ICER released the protocol for the second such review, which will evaluate whether 15 large commercial payers, the two largest state health exchange plans and the Department of Veterans Affairs have formularies and procedures that provide appropriate access to the prescription drugs reviewed by the organization in 2020. The review will consider drugs used to treat cystic fibrosis, hemophilia A, migraine, sickle cell disease and ulcerative colitis. Results are expected to be published in November.

This research is funded in the same way as ICER’s cost-effectiveness research. ICER says nearly 75% of its annual budget of about $10 million comes from nonprofit foundations, 12% from drugmakers and 8% from health plans. The remaining 5% is from a variety of sources.

Molly Beinfeld, M.P.H., senior research lead, evidence synthesis, says there are eight members on the team involved in conducting the fair-access reviews, although the exact staffing varies depending on the stage of the analysis.

Similar to the way it conducts cost-effectiveness, ICER will provide a payer review period, as well as a working group review, before publishing a final report. The goal of ICER’s first assessment, which was released in December 2021, was to show the organization’s methods. “There were a lot of limitations, so the second annual report will build on that initial body of work,” Beinfeld says.

In that report, ICER analysts found that most of the payer pharmacy and medical policies available for review were structured to support fair access to medications. In 67 of 70, ICER rated the payer’s policies as consistent for all fair-access criteria. But ICER reviewers were unable to assess the full set of information for all drugs for all insurers. The database they used, Managed Market Insight & Technology’s market-access analytics solution, did not include all the coverage policies.

“The biggest issue we found was the lack of transparency,” Beinfeld says. “We’re trying to do this in a systematic way, and we’re trying to get an equal amount of information for each payer. That just wasn’t possible. We call on insurers to make both their prior authorization criteria and cost-sharing information available to consumers prior to enrollment. This way, they can make informed decisions.”

The 2021 assessment reviewed drugs that ICER deemed cost-effective. The next review will include both therapies that are cost-effective as well as those with prices that haven’t met ICER’s cost-effectiveness thresholds. “We believe there is a relationship between cost and access. So, the higher the cost, the more access issues,” says Beinfeld. “Some of the areas that we’re looking at moving forward, such as cystic fibrosis and sickle cell disease, [include] drugs that were priced very high.”

Any limitations on access should be based on evidence, Beinfeld says. “Oftentimes, we did find examples where payers would limit the eligible population to something that isn’t a part of the label.”

After ICER’s review last year, several payers changed their policies. In some cases, the changes were minor clarifications, but others were more substantial. One insurer, for example, was limiting access to Dupixent (dupilumab) to patients who had moderate-to-severe atopic dermatitis for more than three years. “The three-year requirement was arbitrary,” Beinfeld says.

Denise Myshko is senior editor of Formulary Watch®, a news website affiliated with Managed Healthcare Executive.
A lexis Drutchas, M.D., does not claim to be a health insurance or Medicare payment hospice expert. Her expertise, says the palliative care physician at Massachusetts General Hospital in Boston, is caring for patients in their dwindling days of life. "A lot of our work is talking about being present in the moment with families and sort of witnessing and hearing about their sufferings," Drutchas says. "And that does help people to be seen and heard, even if we can’t fix the problem."

It’s not unusual that once a week or so, a patient will confide in her that they would like to spend their remaining time at home. It’s a wish that families desperately want to fulfill. But for a variety of reasons, many can’t. "They don’t have the family support, or they work full time and can’t be at home," Drutchas explains. "Or they don’t have the financial means to pay for extra help, and they can’t honor that end-of-life desire of loved ones. That’s incredibly heartbreaking."

Drutchas can only reassure families that "it’s not their fault that they can’t bring their mom home."

**Coming back home**
The Tax Equity and Fiscal Responsibility Act of 1982 created the Medicare hospice benefit that entitles...
beneficiaries to Medicare coverage of end-of-life care. There is no debate that it was an important addition to Medicare’s coverage policies. Patients, families and medical professionals alike endorse the provision of hospice care, which can occur at home, in an assisted living facility, nursing home, hospital or stand-alone hospice facility.

Hospice does not have a reputation problem. A 2017 Kaiser Family Foundation survey found that 70% of Americans said they know at least a little about hospice. A large majority (85%) of that group had a positive opinion of hospice care and almost half (47%) said their opinion was very positive.

Dying at home was the norm before healthcare became more technology-driven in the 20th century. Now, it is more common. In a research letter published in the New England Journal of Medicine in 2019, Sarah H. Cross, M.S.W., M.P.H., of Duke University’s Sanford School of Public Policy, reported that in 2017, at-home deaths had edged out hospital deaths, 30.7% to 29.8%, for the first time since the early 20th century. But the trend comes at a time when families are scattered across the U.S., making caregiving logistically challenging. Meanwhile, advances in medical treatments and technology are helping people with terminal and chronic illnesses to live longer. Families, say palliative care physicians and hospice advocates, need help.

More specifically, they want Medicare to increase its at-home hospice payment, which is currently $203 a day, and reconsider its policy that limits hospice coverage to people with a life expectancy of less than six months. As the difference between curative and comfort care becomes more nebulous, some experts and advocates also want Medicare to reconsider the rules that require hospice patients to forgo curative treatments that may help relieve symptoms.

“What we really need is for the hospice benefit that was defined and implemented over 40 years ago to be redefined and delivered in a way that meets the needs of those who experience serious illness and end of life today,” says Ben Marcantonio, M.S., M.Ed., LMFT, chief operating officer for the National Hospice and Palliative Care Organization (NHPCO).

Medicare coverage of hospice was, by design, rather limited. Changing it now to be more responsive to 21st-century needs — especially care at home — is likely to be expensive. Lawmakers may be shocked by the price tag. But hospice advocates believe the money can be found. As a country, America spends an estimated $80,000 a year per person for medical care in the last year of life. Compare that with the current cap of $31,297.61 per year per person on Medicare hospice payments. Could some of that money be used to help families who want to bring their loved ones home to die? Drutchas thinks it could.

It is heartbreaking, she says, to see patients — with their families in agreement — who want to die at home but don’t for a number of reasons, “I don’t think it feels good to be part of a system that can’t meet patient needs,” she says.

According to the Medicare Payment Advisory Commission’s (Med-PAC) 2022 Report to the Congress, the main hospice location for 47% of the Medicare beneficiaries who received hospice care in 2020 was someplace other than at home: a nursing home, assisted living facility, hospital, or hospice facility. The report also showed how the use — and cost — of hospice services have risen steadily in the last decade. Between 2010 and 2020, spending grew 5.7% annually, going from $12.9 billion to $22.4 billion. Between 2019 and 2020 alone, spending rose 7.4%, largely reflecting the number of people using hospice.

In 2020 Medicare was the largest payer of hospice services, covering 90% of all patient days for 1.7 million beneficiaries deemed terminally ill with a life expectancy of six months. That year, $500 million went to 5,058 hospice providers, a 4.5% increase in

<table>
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<tr>
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<td>For profit</td>
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<tr>
<td>Government</td>
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<td>3%</td>
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hospice providers over the previous year. The entire increase, according to CMS, came from for-profit companies rushing into the provision of hospice services. In 2020, 73% (3,680 of 5,058) of hospice providers are for-profit businesses, according to the 2022 MedPAC report.

By definition, for-profit hospice providers are moneymaking ventures with an eye to delivering a return for investors or shareholders. Medicare’s daily rate makes for tight margins. That concerns Mass General’s Drutchas. “If you are for-profit and you only get $203 a day, then what you could theoretically do is think about picking and choosing the patients with fewer physical needs so that you don’t spend your resources on them and get to keep more of that money,” she says.

NHPCO’s Marcantonio understands, saying that the influx of for-profit hospices has been a “challenge” for the healthcare field and his industry. But for-profit and quality, he says, are reinforcing, not mutually exclusive. “As a for-profit provider, if we are not quality, we won’t be able to be successful financially or otherwise,” he says. “So, we had better be committed to quality.”

NHPCO has implemented a program focused on a commitment to quality among its members. There are also several accrediting organizations that oversee the industry, including Medicare.

The $500 million that Medicare spent on hospice care in 2020 (and the money that it spends every year) pays for physician services, nursing care, counseling and social worker services, hospice aides and homemaker services. Medicare funds also pay for care planning, drugs, medical equipment, a 24-hour call center, crisis response and transporting patients between sites for care.

The organizations and companies that provide hospice services receive daily payment from Medicare every day a patient is enrolled in a hospice program. Patients get, on average, just three to five hours of in-person care a week. But Marcantonio stresses that is an average. Visits are “determined by the needs of that patient at that time.”

Study shows racial differences in hospice use, hospitalizations among dementia patients

Study after study has found major differences between the healthcare services received by Black and Hispanic patients and the services received by White patients.

Findings reported in JAMA Network Open in June show that the pattern extends to people with dementia in the final months of life.

Meanwhile, results of an unrelated study reported in the June issue of Health Affairs showed that hospice enrollment among people living with dementia was associated with higher-quality end-of-life care compared with not being enrolled in hospice.

The study published in JAMA Network Open included approximately 5,000 Medicare beneficiaries with a dementia diagnosis and focused on people’s final 180 days of life.

Lead author Pei-Jung Lin, Ph.D., M.S., an associate professor at Tufts Medical Center in Boston and a researcher at its Center for the Evaluation of Value and Risk in Health, and her colleagues found that 309 of 809, or 38.2%, of Black patients and 153 of 357, or 42.9%, of Hispanic patients used hospice services compared with 1,967 of 3,892, or 50.5%, of White patients. They also found that Black and Hispanic beneficiaries were more likely to have had an emergency department (ED) visit or an inpatient admission than their White counterparts. The difference in inpatient admissions resulted in a 60% difference between expenditures on inpatient care for Black ($23,279) and Hispanic ($23,471) beneficiaries and expenditures on inpatient care for White beneficiaries ($14,609).

Lin and her co-researchers also looked at differences in advanced planning and the expressed wishes for health care. They found that that 20.7% of Black beneficiaries and 21.4% of Hispanic beneficiaries with dementia had completed advanced care planning documents compared with 57.1% of White beneficiaries. Of those who had advanced care plans, a larger proportion of Black and Hispanic beneficiaries indicated that they wanted all care possible to prolong life than did White beneficiaries.

The reasons for these differences in planning and preferences were beyond the scope of this study, but the researchers referenced other research documenting mistrust of the U.S. healthcare system that is associated with “medical racism” and healthcare inequalities. The mistrust “may lead more non-White patients to perceive hospice care as ‘giving up’ and motivate them to request more aggressive, life-sustaining interventions,” wrote Lin and her colleagues.
given time, he says. “When someone comes on the service, they may get 10 hours or more during the week to make sure they are set up well and that they are comfortable and have what they need. When their condition stabilizes and they reach a level of comfort, then it does go down to three to five hours a week.”

The amount of the daily payment to hospice organizations or companies depends on where they fall among Medicare’s four levels of care: routine home care, continuous home care, respite care and general inpatient care. Routine home care is reimbursed at $203 a day for 60 days and then drops to $161 daily for up to six months. Starting this year, hospice providers are eligible

Other studies have examined the use of hospice services among people with dementia. Lin and her colleagues said their study had the advantage of including a broader group of patients, namely, those living in the community as well as the nursing home population that other studies have focused on.

Krista Harrison, Ph.D., the lead author of the study published in Health Affairs, and her colleagues also said their findings plugged a gap in research because their study included patients living outside nursing homes. Hospice care and its payment was originally designed for people dying of cancer, noted Harrison, an associate professor at University of California, San Francisco, and her colleagues. Now, they said, almost half of the older adults receiving hospice care have dementia. Just under half (951 of 2,059) of the patients in their study had dementia.

Harrison and her colleagues investigated assessments of the quality of care during the last month of life by proxies (loved ones and caregivers). Their takeaway finding is that the proxies of patients with dementia who were enrolled in hospice rated the quality of the care that the patients received higher than did proxies of the patients with dementia who were not enrolled in hospice. Their analysis also suggests that care improves as people spend more time enrolled in hospice.

To qualify for the Medicare hospice benefit, two physicians must attest that the patient is terminally ill with a prognosis of six months or less. Prognostic challenges in dementia make certifying eligibility for this benefit difficult, note Harrison and her colleagues. Meanwhile, they said, CMS has implemented policies designed to curb long-term hospice enrollment due to concerns about for-profit hospices and private equity funding, resulting in dementia patients being disproportionately discharged from hospice.

Lin and her co-authors said in *JAMA Network Open* that their research shows that the timing of hospital enrollment is often suboptimal. One in 3 beneficiaries with dementia entered hospice very close to the end of life (i.e., within 7 days before death), a higher proportion than the general Medicare population.

Additionally, some dementia beneficiaries in hospice were subsequently admitted to the ED or hospital before death, especially Black and Hispanic beneficiaries.

“They hospitalizations are necessary and expected as part of the natural course of treatment,” wrote Lin and her colleagues, “whereas others may be considered low value at the end of life.”

They said that alternative payment models, such as bundled payments for episodes of care, are one way to counteract hospitalizations that are expensive and don’t improve the quality of life of the patients with dementia who are enrolled in hospice.

—Lindsey Mulrooney

### Hospice, trending up

Medicare Spending, number of users and other hospice indices have increased since 2010

<table>
<thead>
<tr>
<th>Category</th>
<th>2010</th>
<th>2018</th>
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<tr>
<td>Total spending (in billions)</td>
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<tr>
<td>Number of hospice users</td>
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<td>Number of hospice days for all hospice beneficiaries (in millions)</td>
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<td>Average lifetime length of stay among decedents (in days)</td>
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<tr>
<td>Median lifetime length of stay among decedents (in days)</td>
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<td>18</td>
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</table>

Source: Medicare Payment Advisory Commission Report to the Congress, March 2022
for additional payments for registered nurses and social worker visits during the last seven days for patients in the routine home care category. The hourly payments are for up to four hours a day of care and are on top of base payment rate. The visits must be in person.

Continuous home care is layered on top of routine home care. A hospice worker is paid $61 an hour to be on site for eight to 24 hours to provide nursing care during brief periods of crisis to, for example, manage pain or other acute symptoms. The stated purpose of continuous care is to keep the person at home.

Respite care, designed to give the patient’s primary caregiver time off, is reimbursed at $474 a day. The current Medicare payment for general inpatient care is $1,068 a day and applies to hospice care delivered in a hospital, hospice inpatient facility or nursing home.

**Advantages of the hospital**

Less than 2% of all hospice care is delivered in an inpatient circumstance, Melissa Wachterman, M.D., M.P.H., noted during a recent a New England Journal of Medicine podcast. A palliative care physician and an assistant professor at Brigham and Women’s Hospital in Boston, Wachterman agrees that dying at home is the best option for many patients and their families and that “a lot of good comes from hospice.” But she is concerned that the decision to send someone home to die isn’t always best for the patient, despite the strong, overall preference.

“Hospitals get paid based on the diagnostic risk group, where they get a lump sum of money for a patient regardless of how long they stay in the hospital,” Wachterman said during the podcast. “So, if stays are shorter, they can save money, and oftentimes home is one of the easiest discharge destinations for a patient. Sending a patient home can save hospitals and Medicare money because it shifts the burden of around-the-clock care and out-of-pocket expenses to families and is paid out at the much lower routine home care rate.”

Dying in a hospital or at an inpatient hospice facility, she added, may be the better choice for families. Both offer support from nurses and aides who can respond quickly to issues like pain, incontinence or delirium, all common as death nears. The stereotype of someone dying in a hospital, hooked up to machines with monitors continually beeping, isn’t accurate, as a hospital death can be very peaceful, Wachterman said. “In these settings, patient families can focus on quality time together, which becomes more important where there isn’t a lot of time.”

Wachterman would like to see Medicare increase financial support for families. She said the Department of Veteran Affairs and some state Medicaid programs that pay for family caregiving are setting a good example. She also wants to see easier access for inpatient hospice because, she believes, it is the best option for some families. In Wachterman’s view, people who have severe symptoms and need great deal of care are strong candidates for inpatient care.

Drutchas agrees that everyone should have an option about where they want to die, including those who want to spend their final days at home but don’t have the necessary support network.

“It should be an option for everyone, not just those who have the money to pay for private care or those who are blessed to have multiple family members and friends in the exact geographic location who can help with that 24-hour care,” she says.

The main issue Marcantonio would like to see addressed is Medicare’s requirement that a patient have a life expectancy of six months or less.

“Is there a way to think about that and talk about that differently? Because these various illnesses and how they proceed is different,” he says. “There isn’t (always) a clear six-month prognosis. We need to evolve that in a thoughtful, meaningful way that is still efficient and uses our resources responsibly.”

Robert Calandra is an independent journalist in the Philadelphia area.
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Part D may be due for a redesign

The program started before specialty drugs became such a large expense for Medicare and its beneficiaries. Congress is considering legislation that would cap beneficiary out-of-pocket costs and require price discounts from manufacturers.

by JOSEPH BURNS

Carol Thompson is a 77-year-old retired payroll accountant in Lawrenceville, Georgia, who could not afford the medication her physician prescribed earlier this year for chronic lymphocytic leukemia, a form of blood cancer.

As retirees, Thompson and her husband, Tom, live on their Social Security income and some retirement savings and were pleased to learn the first-month prescription of Imbruvica (ibrutinib) from Janssen Pharmaceuticals (a unit of Johnson & Johnson) was free. But they could not afford the second-month charge of $3,200 even though each is enrolled in Medicare Advantage with Part D prescription drug coverage.

“This oral chemotherapy drug that my doctor recommended,” Thompson said, “is not designed for specialty drugs. One reason Part D redesign is needed is because the Medicare program has seen spending on expensive specialty medications skyrocket, notes Leigh Purvis, M.P.A., director of healthcare costs and access for the Public Policy Institute at AARP.

“The most important elements for Part D redesign are reducing beneficiary costs, which will be achieved primarily by setting an out-of-pocket maximum for seniors,” explains Ryan Urgo, managing director for consulting firm Avalere Health.

“The threshold for 2022 is $7,050. “The most important elements for Part D redesign are reducing beneficiary costs, which will be achieved primarily by setting an out-of-pocket maximum for seniors,” explains Ryan Urgo, managing director for consulting firm Avalere Health.

By giving health plans more liability for the cost of care in what’s
called the catastrophic phase, you could reduce the government’s role for spending in that phase by creating more skin in the game for plan sponsors,” Urgo says.

Shifting the cost burden of Part D coverage so that more of it falls on health plans and less on Medicare and beneficiaries could provide an incentive for health plans to be tougher about negotiating lower prices from drugmakers, in Urgo’s view.

“At the same time, you could free the federal government from being on the hook for what is the fastest-growing segment of the Part D program, which is that catastrophic phase,” he notes. “That increase in spending is driven in large part by the proliferation of specialty drugs and newer products for patients with specialty conditions that tend to have high price tags.”

However, shifting costs to health plans raises the prospect of a common trade-off in health insurance: Ask insurers to shoulder more costs or expand coverage, and they will soon be asking for higher premiums. But Urgo says, “Part D is an extremely competitive market, where premium is king.” Rather than increasing premiums, plans may limit access to certain drugs, seek higher rebates from manufacturers or reevaluate their provider networks, he says. There are also other provisions of the Part D benefit redesign proposals that would work against premium increases.

Will drug companies increase their prices? With patients insulated, to some extent, from the cost of expensive medications if there was a “hard” cap on out-of-pocket costs, drugmakers might face less public pressure about setting high list prices.

But Urgo says there might still be some pushback from the Part D plans. “Depending on the details of a final Part D redesign package, some

“The most important elements for Part D redesign are reducing beneficiary costs, which will be achieved primarily by setting an out-of-pocket maximum for seniors.”

-RYAN URGO, AVALERE HEALTH

Medicare’s spending on Part D drug benefits more than doubled since 2006, when the benefit started

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<thead>
<tr>
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<th>Amount</th>
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<tr>
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<td>2019</td>
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Source: 2021 report from The Commonwealth Fund titled, “Medicare Part D Redesign.”
manufacturers’ costs will be higher than others,” Urgo observes. Therefore, some drug companies may try to raise prices, he says, but if they do, the largest Part D health plans would likely push back and seek higher drug rebates.

**Skyrocketing costs**

When the Part D benefit was designed, a relatively small number of beneficiaries had drug expenses that pushed them into the catastrophic phase of the coverage, when Medicare pays 80% of the expense; the Part D plans, 15%; and beneficiaries, 5%.

That 5% share may seem small, but with many drugs priced at $100,000 a year or more, a small proportion of a large expense ends up being a large amount. “For high-cost medications for cancer and other conditions, patient costs in Part D are so high that the lack of a true out-of-pocket cap on spending can create a financial strain on beneficiaries throughout the whole year,” Urgo says. Under this arrangement, health plans, drug companies and pharmacy benefit managers have limited incentives to contain drug costs.

In a *Health Affairs* article published in April 2022, Stacie B. Dusetzina, Ph.D., a researcher at Vanderbilt University Medical Center, and her colleagues found that many beneficiaries who weren’t eligible for subsidies that offer some financial protection from the 5% coinsurance did not start a prescribed therapy. More specifically, Dusetzina and her colleagues found that 50% did not start drug treatment for either immune system disorders or high cholesterol, 30% did not pick up their first prescriptions for cancer drugs and 22% did not start their medications for hepatitis C.

The fact that so many Medicare beneficiaries with serious illnesses cannot afford their treatments shows that the design of Part D is outdated, Dusetzina noted in a medical center press release about the research reported in *Health Affairs*. Almost all other health plans in the United States include out-of-pocket limits to protect members from unlimited spending on prescriptions, she added. When Part D members do not start their medications, their symptoms get worse, driving up healthcare costs, she and her colleagues wrote.

Purvis at AARP says it is “a huge source of concern when a Medicare beneficiary with income of about $30,000 a year has to pay upwards of $10,000 for prescriptions. That’s just not sustainable.”

—LEIGH PURVIS, M.P.A., AARP PUBLIC POLICY INSTITUTE

**High prices for specialty drugs**

and the growing number of prescriptions for them resulted in a doubling of Medicare spending on Part D coverage of patients who had hit the catastrophic phase between 2013 and 2017, according to the 2021 Commonwealth Fund report. Even when beneficiaries in the catastrophic phase are required to pay 5% of their drug costs, many do not fill their prescriptions, the report authors added.

**Joseph Burns** is an independent journalist in Brewster, Massachusetts, who covers healthcare, health policy and health insurance.
Today’s Oncology Care Journey: Augmenting Value-Based Care with Empathetic Support

The future of oncology care is going beyond traditional, fee-for-service delivery models by investing in an agile, patient-first, value-based care model. This approach places patients at the center of care to improve their experience and outcomes while creating value. Jasper Health embodies a value-based care model with data-driven, and empathetic, human-led guidance for people affected by cancer.

A new standard for oncology care

Despite novel breakthroughs in treatment options and clinical research, cancer remains the second leading cause of death in the US today¹, prematurely taking the lives of over half a million individuals each year. With a new cancer diagnosis every 30 seconds² and incidence rates on the rise, healthcare is on a transformational journey to tackle the issue of how we treat patients to improve patient experiences and outcomes. The Center for Medicare and Medicaid Innovation (CMMI), a part of CMS, is setting the standard for changing care delivery from the traditional fee-for-service model to patient-centered, value-based care through its guidelines in Oncology Care Model (OCM)³.

The OCM is defined by coordination of care with a multidisciplinary approach, breaking through barriers around payors and costs and driven by interoperative data, predictive analytics, and patient needs. Strategically refocusing revenue into continuous enhancement of patient care along with strong, data-driven best practices and information-sharing across a multi-payor structure are key components to the model. The goal of this approach is to achieve a higher quality care experience while also lowering extraneous costs.

Jasper Health further innovates the model

Jasper Health was founded on the value-based care approach, but with a true focus on the person dealing with cancer and living with the day-to-day struggle and strain. What does this person or their non-medical caregiver (be it a relative or a friend) really need to help in this unthinkable time?

Jasper Health has found that outcomes and experience improve when psychosocial support and guidance is empathetic and personalized to the patient from diagnosis through remission and beyond. Through an intelligent application, Jasper members have access to a hybrid, coordinated care model that provides support via personalized information, and in-between-visit coaching via chat or phone around psychosocial needs, clinical trial guidance, social determinants of health, and more. Jasper Health also works with providers by delivering an easy-to-use clinician dashboard, connecting care and driving seamless communication between the patient and their doctors across all payors.

Every Jasper Health interaction provides patient data insights gathered not on the traditional periodic, visit-by-visit cadence, but continuously and in real-time. This produces a 360-degree view of patient health and well-being enhancing continuous learning algorithms and patient-reported psychosocial outcomes data. Results show powerful insights that break through barriers to care to improve quality and lower unnecessary costs. Moreover, Jasper Health's per member, per month approach focuses revenue on raw patient needs around improving experiences and outcomes.

All people deserve empathetic support

Patient-centered, value-based care is a delivery model that patients deserve. Innovators like CMMI set and encourage standards and best practices, while Jasper Health continues to maintain the patient-centric model as the cornerstone of our approach as we help those through their cancer journey and beyond.

Visit hello.jasper.com to request a conversation about how Jasper Health can improve cancer care experiences and reduce costs.

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¹ Centers for Disease Control and Prevention
https://www.cdc.gov/chronicdisease/resources/publications/factsheets/cancer.htm

² National Cancer Institute
https://training.seer.cancer.gov/disease/war/

³ Oncology Care Model
The Oncology Care Model and its successor

Although the Oncology Care Model produced some positive results, the value-based care model cost Medicare money. Now attention is turning to its successor, the Enhancing Oncology Model.

The Oncology Care Model (OCM) was introduced in 2016 by the Centers for Medicare & Medicaid Services (CMS) in an effort to improve the quality and coordination of care for cancer patients. It aimed to do so by bundling payments for care and encouraging collaboration among providers. Practices could bill Medicare for a $160 monthly enhanced oncology service (MEOS) for each beneficiary receiving chemotherapy. The participating practices were also eligible for retrospective performance-based payments (PBPs) that were measured by financial benchmarks and quality metrics.

The program, which ended in June of this year, included 126 practices and five payers. The latest evaluation report of the program, which came out in December 2021, covered six performance periods starting July 1, 2016, and ending July 1, 2019. The report showed that practices participating in the OCM spent an average of $298 less per episode than a comparison group of practices not participating in the model. The reduced spending was concentrated in the care of for impact on patients and the healthcare system at large.”

But Carole Tremonti, MBA, R.N., vice president of clinical strategy for Project Ronin, a healthcare analytics and software company in San Mateo, California, says OCM didn’t produce results as hoped for several reasons.

“The first is that it was a concept without a process or method to apply it. It left health systems to figure out how to make a complicated process work, without necessarily a means to do so,” she says. “Where that becomes even more complicated is that in the space of oncology, there are multiple players involved in the treatment of a patient, plus their primary care doctor, who is not necessarily in close connection with the medical oncologist, nor do they have access to the same medical record. At baseline that puts the whole process at a disadvantage.”

Tremonti also points to the problem of measurement. “All health systems and providers have challenges in measuring population-level data,” she argues, adding that “the EHR (electronic health
Some key findings of the latest evaluation report OCM

The report, which came out in December 2021, covers the first six performance periods of the Oncology Care Model (OCM), starting with the first one, which began on July 1, 2016, and ending with the sixth one, which ended on July 1, 2019.

The OCM’s effect on episodes of care came from small reductions in Part A (which covers hospital costs) and Part B (which covers the cost of physician-provided care, including drugs administered by physicians) payments.

Practices participating in OCM reduced Part B payments by $182 per episode relative to the practices in the comparison group, most of it stemming from lower spending on supportive drugs, such as medications to treat the nausea from chemotherapy. OCM had no effect on Part B payment for chemotherapy.

Practices participating in OCM had a reduction in Part A payments of $104 per episode. Still, OCM had no statistically significant impact on payments for any individual measure of acute care hospitalizations or post-acute care.

OCM had no effect on Part D payments.

Over five performance periods, the practices participating in OCM produced total per-episode payment reductions of $19.3 million. But that "gross payment reduction" was offset by the monthly enhanced oncology services (MEOS) payments of $464.9 million and $106.5 million in payments for performance.

The Oncology Care Model “showed that when specialty practices are engaged directly in an alternative payment model — as opposed to indirectly through a total population costs-of-care model — they start transforming their practice and improve patient outcomes. It also showed that upside-only models are never budget-neutral for a payer.”

— FRANCOIS DE BRANTES, SIGNIFY HEALTH
practices benefitted from the rich data provided by OCM. At TOI, we have used that data to continuously improve quality measures and would imagine other practices are doing the same.”

TOI saved Medicare approximately $4,000 per episode in the most recent performance period, according to Miller. “This is especially notable given the relatively small percentage of our patients that qualify for the program,” he says. “TOI is already implementing similar measures through the managed care and capitated contracts that make up the majority of our practice.”

Ashley Tait-Dinger, MBA, director of analytics, alternative payment models and finance for Florida Alliance for Healthcare Value, believes OCM was effective because it incorporated additional services and touch points that were not addressed under the traditional care model. How providers implement these services and how they are paid for are issues that need to be addressed, she says.

The successor

The final performance period of OCM ended on June 30, 2022. One of the options CMS’ Center for Medicare & Medicaid Innovation (CMMI) considered was simply sticking with OCM but making it a

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**On net, not a good deal for Medicare**

<table>
<thead>
<tr>
<th>Gross episode payment reductions</th>
<th>Gains</th>
<th>Losses</th>
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<tbody>
<tr>
<td>PP1</td>
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<tr>
<td>PP2</td>
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<tr>
<td>PP3</td>
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<tr>
<td>PP4</td>
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Medicare gross payment reductions totaled $194.33 million across PP1-PP5

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<tr>
<th>Monthly enhanced oncology service (MEOS) payments</th>
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<th>PP2</th>
<th>PP3</th>
<th>PP4</th>
<th>PP5</th>
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<td>$60.87 M</td>
</tr>
</tbody>
</table>

Medicare net losses totaled $377.1 million during the first five performance periods (July 1, 2016-Jan 1, 2019).

Source: Evaluation of Oncology Care Model, Performance Periods 1-6, December 2021.
Evaluating Current and Future Opportunities for HIV PrEP

Appropriate use of PrEP has been proven to significantly reduce the risk of getting HIV; however, only about 1 in 5 persons with an indication for PrEP is receiving it. Numerous factors contribute to both access and adherence to PrEP medications. Addressing educational needs, coverage policies, and therapeutic innovations may increase access to and uptake of PrEP to prevent HIV infection.

Throughout this Population Health Perspectives video series, our expert faculty will discuss the following:

**Population Health in PrEP:**
- Economic impact of HIV
- Challenges and unmet needs

**Patient-Centered Care:**
- Quality of care assessments
- Adherence support and patient education programs

**Patient Access:**
- Disparities and inequities in access
- Utilization management strategies and challenges

**Future Opportunities:**
- New and novel dosage forms
- Potential challenges and logistical concerns for PrEP therapies

**Faculty:**

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- **Douglas Krakower, MD**
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  Executive Director, HIV-Hepatitis Policy Institute, Washington, DC

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two-sided risk model, which means practices could face financial penalties if they don’t meet financial and quality benchmarks. “That created an immediate and very negative reaction from oncologists across the U.S.,” de Brantes says. “They objected to the downside risk given the design of the model, which included all costs of care for the beneficiary, not just the cancer costs, and also included chemotherapy costs. As such, the Oncology Care First (OCF), as it was called, was put on hold.”

The assumption of downside risk — when and how much — has been a major issue with other value-based pay arrangements, including accountable care organizations. On June 27, CMS announced the successor program, which it is calling the Enhancing Oncology Model (EOM). Despite the misgivings about downside risk, EOM includes downside risk right from the start, although there are two tracks.

In broad outlines, EOM is much like OCM. It will be voluntary not mandatory (some experts say voluntary programs won’t be effective in bringing about value-based care). EOM has same basic structure of six-month care episodes. Practices will still get MEOS payments for providing enhanced services, although as proposed they would $70 per month rather than $160, and be eligible for PBPs. However, there are also some important differences. EOM will cover Medicare patients undergoing chemotherapy for the most common types of cancer (lung, breast, multiple myeloma and so on). However, according to a commentary by Stephen Schleicher, M.D., MBA, chief medical officer of Tennessee Oncology, EOM excludes cancers treated with hormone-only therapies, such as low-risk breast cancer. Schleicher said that narrowing the cancer treatments that are covered may prevent some of the variability seen in OCM based on case mix.

EOM also includes some new requirements for electronic patient reported outcomes, patient-provided data about side effects and adherence that is supposed to improve care by creating a continual feedback loop of information. Schleicher said that addition was welcome but also sounded a note of caution about adding reporting burdens on practices.

In its fact sheet about EOM, CMS emphasized that providers participating in the payment model will need to screen patients for health-related social needs (HRSNs), such as lack of transportation to infusion appointments, that may contribute to disparities among cancer patients. The HRSN screening requirement is part of the Biden administration’s push to have CMS programs of all kinds factor in healthcare disparities and ways to address them.

CMS is accepting applications for EOM through the end of September 2022. The program, which as proposed will run for five years, is not scheduled to start till July 2023. Some provider groups said the yearlong gap between the end of OCM and beginning of EOM will be a hardship because practices will be shouldering costs without the model’s benefits.

Miller, speaking before EOM came out, predicted that health equity would be front and center: “I expect to see an increased emphasis on health equity, which would be a welcome addition and a natural progression to ensure these programs are working for all patients.”

John Griggs, senior manager of solutions consulting at Managed Markets Insight & Technology, said prior to the EOM announcement that clearer guidelines and continual education for all key stakeholders are needed. “This would allow for quicker adoption and stricter enforcement,” he said “And once implemented, clear metrics must be defined for tracking the success and reporting outcomes from the programs by both payers and oncologists.”

Keith Loria is a freelance medical writer in the Washington, D.C., area.
Diabetes medications find new life as weight-loss drugs

Novo Nordisk’s Saxenda (liraglutide) and Wegovy (semaglutide) are leading the way for a new crop of drugs that reduce appetite. But their cost-effectiveness is in question, and many payers are saying no to coverage — for now.  by JARED KALTWASSER

To understand David Skomo’s struggle to get to a healthy body weight, you need to go back decades. “Weight management for me has always been an issue I’ve dealt with, since probably early childhood,” he says.

Skomo, 50, the chief operating officer of pharmacy benefits manager WellDyne, was a bit overweight in middle school and high school but never obese. As he grew older, though, it became harder and harder to achieve a healthy weight.

It was not for lack of trying. He watched his diet. He exercised. And Skomo had some success, but as is so often the case with weight loss, the pounds had a way of coming back. “If you really work hard and diet and exercise, you lose weight,” he says. “But that also means having the willpower to not eat when your body’s telling you that’s the answer. That’s where it really becomes hard.”

But Skomo had never tried weight-loss drugs. “Some of the early products were not providing much benefit at all,” he says. “They were dangerous, they had addictive properties, and it was not something I wanted to get involved in.”

Yet Skomo read the positive results for Wegovy (semaglutide), which the FDA approved in June 2021, and was willing to give it a try. At the time, Skomo qualified for the drug because he had a body mass index (BMI) of 29 and hypertension. A pharmacist by training, Skomo said the fact that Wegovy had a different mechanism of action was a compelling reason for trying it. “I could see how this agent is much different than earlier generations of weight-loss medications, he says. Skomo talked it over with his wife, who is also a pharmacist, and she agreed. His only reservation was the potential for gastrointestinal side effects.

Nearly a year later, he has lost 18% of his body weight and has a BMI of 23. “I said to myself, if I could get around a 30-pound weight loss over time, I’d be thrilled,” he says. “And I’m up to about 35 pounds of weight loss now.”

Saxenda was first

Stories like Skomo’s are part of the reason a new class of weight-loss drugs are coming on strong. The notion that pharmaceuticals could stem the U.S. obesity epidemic is alluring, but drugs for weight loss have a checkered past of lack of long-term efficacy and, in some cases, lack of safety.

But now there is a cohort of new drugs with new mechanisms of action that could bring drug-aided weight loss into the medical mainstream, although their high prices could be an issue. First approved in 2014, Novo Nordisk’s Saxenda (liraglutide) was in the vanguard. Results from a clinical trial published in 2015 showed that nearly two-thirds of adult patients lost at least 5% of their body weight after 56 weeks of taking Saxenda. One-third of patients lost more than 10%.

Next came Wegovy, which is also made by Novo Nordisk. Then, in late April of this year, Eli Lilly made a splash, publicizing the results of a phase 3 trial of its weight-loss drug, Mounjaro (tirzepatide). The company said the drug helped people lose 22.5% of their body weight.

All three drugs were first approved by the FDA as diabetes medications before Novo Nordisk and Eli Lilly set out to get the agency’s OK to add indications that they can be used for weight management. The FDA approved Mounjaro as a type 2 diabetes medication in May. Eli Lilly is expected to seek a weight man-
A paradigm shift

Robert Kushner, M.D., one of the investigators involved in the phase 3 trial of Wegovy and a professor at Northwestern University Feinberg School of Medicine, tells Managed Healthcare Executive® that the drug represents the start of a second generation of obesity pharmacotherapy. “There has been a paradigm shift in obesity treatment that has paralleled our understanding of the underlying appetite dysregulation of the disease,” he says.

Saxenda was the first step in the new direction but requires daily administration, Kushner notes. It was a major step forward when Wegovy, and now Mounjaro, proved to be effective but require weekly rather than daily injections, notes Kushner.

According to Kushner, these new therapies are able to fix the underlying appetite dysregulation at the root of many patients’ weight problem. “By harnessing the appetite effects of naturally occurring gastrointestinal and pancreatic hormones we can biologically alter appetite dysregulation, he says.

All three drugs leverage glucagon-like peptide-1 (GLP-1), a natural hormone released in response to food intake that regulates appetite and caloric intake. By binding to the GLP-1 receptor and activating it, the drugs help patients feel fuller faster. In addition to targeting GLP-1, Mounjaro also targets glucose-dependent insulinotropic polypeptide (GIP), a hormone that regulates blood glucose. Clinical trial data suggest this dual approach can increase the weight-loss effects. However, all three drugs can lead to gastrointestinal side effects.

Kushner says with Wegovy, it is important for prescribers and patient to be in touch regularly to dose and dietary counseling. But Kushner stressed that the repurposed diabetes medications cross an efficacy threshold: “The 15%-plus weight loss is significant because it more closely matches patients’ expectations of a good weight-loss response and is associated with clinical improvements in blood pressure, blood glucose and sense of well-being.”

High prices

Evidence of efficacy and long-term benefits will be essential for these weight-loss drugs because the manufacturers have put high price tags on them. Payers will be scrutinizing them through the lens of cost-effectiveness, which is complicated with weight-loss drugs. How do all the cost savings associated with preventing the myriad conditions stemming from being overweight and obese get factored?

In 2019, a team of investigators reported the results of a cost-effectiveness analysis of six weight-loss drugs, including semaglutide (it hadn’t been branded as Wegovy yet) and Saxenda, along with a lifestyle intervention plan. The results, reported in the journal Obesity Science and Practice, showed that semaglutide was second only to Lomaira (phentermine) in effectiveness after one year. However, weight loss with Lomaira tapered off after a year, while semaglutide had weight-loss benefits for five. Still, the researchers, some of whom reported receiving consulting fees from Novo Nordisk, found that semaglutide was not cost-effective due to its high price.

But there are some caveats. The analysis was based on time horizons of one, three and five years, so it couldn’t take into account the long-term savings from having a healthy body weight. Also, the analysis was done before Novo Nordisk started to market semaglutide as Wegovy.

The researchers used an annual cost of $8,273 based on semaglutide’s price as a type 2 diabetes therapy (as a diabetes drug, semaglutide is sold under the brand name Ozempic). The price of Wegovy is higher: the monthly list price is $1,349, according to Novo Nordisk’s website, which works out to an annual price of $16,188.

Skomo says he is hopeful that the approval of additional medications will be better for patients, not only in terms of finding the right medication, but also in terms of easing the drugs’ entry into the marketplace.

“We’ll see some competition in the marketplace for formulary placement and that type of thing, which should help start to drive down some of the cost of medications as well,” he says. “So, I think it’s a win-win when we get more products in the marketplace.”

Skomo says WellDyne is recommending that clients add coverage for Wegovy, though he said most have not yet taken that advice. Kushner says cost is always an issue with medications, but he is frustrated by insurers that are either limiting or entirely exclude medications in this category. “The dilemma is that we have effective and safe medications for our patients that will help them be healthier, yet they cannot afford them,” he says. “Most certainly, coverage must be expanded, and the cost must come down.”

Jared Kaltwasser is a health and medical writer who resides in Iowa and a regular contributor to Managed Healthcare Executive®.
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