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Pharmacists Must Fight the Opioid Epidemic

WITH THE OPIOID EPIDEMIC raging out of control, pharmacists are essential warriors in the fight against this scourge. On the front lines of dispensing pain medications and providing drug-related counseling, pharmacists can help by preventing and treating opioid use disorder and overdoses.

The numbers paint a bleak picture. Drug overdose deaths increased by nearly 5% between 2018 and 2019 and have quadrupled since 1999, and more than 70% of the 70,630 deaths in 2019 involved an opioid, according to the CDC.¹

The situation has not improved. The CDC estimates that more than 107,000 drug overdose deaths occurred in the United States between December 2020 and December 2021.²

The CDC offers resources for pharmacists to use in fighting the opioid epidemic, including an information sheet with tips on starting conversations with patients, preventing abuse, and red flags such as altered or forged prescriptions, cash payments, early or inconsistent fills, and multiple prescribers.³ Other resources are available from the American Pharmacists Association, the US Drug Enforcement Administration, and the Substance Abuse and Mental Health Services Administration.

Pharmacy Times Health-System Edition™ will continue to bring pharmacists the latest news and resources to help them play a part in fighting this national crisis.

Meanwhile, in this issue, our Cover Feature looks at how to build a successful biosimilar adoption plan. Other articles focus on prescribing of controlled substances going electronic, treatment options for immune thrombocytopenia purpura, a look at the 2022-2023 influenza season, how to successfully establish 503B relationships, and best practices in prophylactic

Enjoy the rest of the summer, and thanks for reading.

REFERENCES

Mike Hennessy Jr
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Build a Successful Biosimilar Adoption Plan

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AT PRESS TIME, there were more than 18,000 reported cases of monkeypox in the United States and approximately 50,000 cases worldwide. Most US cases have been among bisexual, gay, and other men who have sex with men, which has raised concerns about marginalizing high-risk communities, stigmatizing this population, and falsely minimizing the risk to other groups. There are concerns of repeating errors that occurred in the early phases of the HIV epidemic when inadequate attention was paid to the public health risks because of similar marginalization of high-risk groups and an inadequate, slow response. Anyone can be infected with the monkeypox virus through close personal contact with an infected individual, so it must be treated as a public health concern for all.

In a guest essay published in the New York Times, Scott Gottlieb, MD, former FDA commissioner and a senior fellow at the American Enterprise Institute, warned that monkeypox is at risk of becoming the next national public health failure because of a lack of national infrastructure, inadequate testing capacity, and limited stockpiles of effective treatments and vaccines. Overall, there is the risk of failing to heed the lesson learned from prior outbreaks such as COVID-19 and HIV, he wrote.

In response to concerns and criticism about an inadequate response, the Biden administration declared monkeypox a national health emergency on August 4, 2022, which will result in greater resources being directed toward the public health management of this outbreak.

There are several significant differences from prior major outbreaks in that monkeypox is generally a self-limited process that is only rarely fatal and is primarily managed on an outpatient basis. Although self-limited, monkeypox can present with severe symptoms, including painful esophagitis and proctitis, necessitating hospitalization for adequate management. Unlike other recent viral outbreaks, there are FDA-approved treatments and vaccines for orthopoxvirus infections that have good cross-coverage for monkeypox. Unfortunately, the strategic reserves for these agents were primarily intended to manage a bioterrorism event involving smallpox and were woefully inadequate in supply to respond to the demand created by this outbreak. This has led to many concerns about the supply of vaccine for pre- and post-exposure prophylaxis for most high-risk individuals and criticism of how the vaccine is being distributed from an equity perspective.

The federal government has taken steps to increase the supply of the JYNNEOS vaccine and has authorized the use of the intradermal administration that increases the number of

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**Monkeypox Treatment: Unnecessary Complexity Can Lead to Inequity**

Predictably, Patients in Underserved Rural, Urban Communities Will Face Challenges Gaining Access to Approved Study Sites

**BY CURTIS E. HAAS, PHARMD, FCCP, PHARMACY TIMES HEALTH-SYSTEM EDITION™ EDITOR IN CHIEF**
doses available 5-fold because of a much lower dose requirement, though evidence of effectiveness of the low-dose intradermal vaccine is very limited. Despite not being FDA approved for monkeypox, the JYNNEOS vaccine is being made broadly available through public health departments and other providers, which is much different than how the FDA-approved antiviral tecovirimat (TPOXX) is being managed.

TPOXX is FDA approved for the treatment of smallpox in adults and children. There is limited clinical evidence that it can shorten the course and severity of other orthopoxvirus-associated infections, including monkeypox. Overall, the drug is safe, with a relatively benign adverse effect profile, and it is available as both an injectable product and an oral capsule. Treatment with TPOXX is recommended as a medical countermeasure in select patients with severe monkeypox, for individuals who are at elevated risk for developing a severe presentation, and for patients with aberrant monkeypox infections. TPOXX is only available through a CDC-managed expanded access protocol, sometimes referred to as a treatment investigational new drug (IND) protocol. This can be done using an emergent single-patient IND application with retroactive institutional review board (IRB) approval, or it can be approved in advance by an IRB as a multipatient expanded access protocol. This requires the investigating physician(s) to complete an FDA 1572, revise a consent form template for the site, obtain IRB approval, obtain informed consent from each patient, fill out case report forms that have been simplified in recent weeks, and manage the receipt and distribution of the drug following good clinical practice (GCP) standards. The drug distribution to clinic sites is then managed by individual jurisdictions, such as state health departments. This level of complexity is beyond the experience and capabilities of many clinicians who may be involved in the management of these patients, and therefore a patient will need to be referred to a provider listed on the FDA 1572 for a site with an approved expanded access protocol, representing a major barrier to treatment access and an elevated risk of inequity.

It is predictable that patients in underserved rural and urban communities will face challenges gaining access to approved study sites and therefore access to treatment. The drug being managed as "experimental" may also create distrust in underserved communities. It would greatly simplify the process to make the drug available to be prescribed off-label by any qualified physician, which is done every day for many other approved drugs, including the FDA-approved orthopoxvirus vaccines. Although there would be a loss of data collection, that should be offset by much greater and more equitable access to treatment during this declared public health emergency.

This is also a call to action for health system pharmacists, many of whom are familiar with the treatment IND protocol process and can facilitate the regulatory filing process for busy frontline physicians. The pharmacy can also bring the expertise needed for proper handling of investigational drugs under GCP standards and facilitate the timely completion of case report forms. In addition, the pharmacy could distribute the drug widely using overnight couriers for patients with more limited access to large health systems most often qualified to manage treatment IND protocols. Initial and follow-up patient visits can be completed using telehealth technology where available, and then the drug can be distributed from the pharmacy.

Working closely with other members of the patient care team, pharmacists experienced in clinical research processes can take the lead in assuring equitable access to treatment options for monkeypox.

**REFERENCES**

Study Shows Rates of Type 2 Diabetes in Children Increased During Pandemic

INVESTIGATORS AT JOHNS Hopkins Children’s Center in collaboration with the University of Colorado School of Medicine have documented steep rises in type 2 diabetes (T2D) rates among children during the COVID-19 pandemic.

In a report published in the Journal of Pediatrics, the investigators wrote that it is unclear whether the disease was a factor in the rise. However, cancellation of sports and the switch to virtual learning are environmental factors that likely increased this risk, they noted.

“During the COVID-19 lockdown, children were removed from normal day-to-day routines, like going to school, playing sports, and other hobbies,” Sheela Magge, MD, MSCE, co-first author of the paper, said in a statement. “Not only were they less physically active, [but] they were confined to their homes and spent a lot more time watching TV, playing video games, or with other electronic devices.”

Magge is director of the Division of Pediatric Endocrinology at Johns Hopkins Children’s Center and an associate professor of pediatrics at Johns Hopkins University School of Medicine in Baltimore, Maryland.

Investigators launched a nationwide review of medical records to assess the impact of the pandemic on children and T2D risk.

They compared the rates of new-onset T2D among individuals aged 8 to 21 years in the 2 years prior to the pandemic from March 1, 2018, to February 29, 2020, with the first year of the pandemic from March 1, 2020, to February 29, 2021. Investigators included 3113 pediatric individuals from 24 centers across the United States. The average number of new diagnoses per year in the 2 years prior to the pandemic increased from 825 to 1463 during the first year of the pandemic—a 77% increase.

During the first year of the pandemic, the records showed that more male individuals were diagnosed with T2D than female individuals, which was a reversal of percentages prepandemic. In addition, compared with rates in previous years, the number of diagnoses among Hispanic individuals nearly doubled during the first year of the pandemic, and the number of diagnoses among Black individuals did double. Cases decreased among White individuals.

Magge said the study showed that disparities among ethnic and racial minority populations and families with socioeconomic challenges deepened during this time.—Ashley Gallagher

Medical Cannabis for Chronic Pain Elevates Risk of Heart Rhythm Disorders

CANNABIS PRESCRIBED FOR CHRONIC pain is associated with an increased risk of heart rhythm disorders, according to results of a study presented at the European Society of Cardiology Congress 2022.

“Chronic pain is a rising problem. According to Danish health authorities, 29% of Danish adults over 16 years of age reported chronic pain in 2017, up from 19% in 2000,” Nina Nouhravesh, MD, of Gentofte University Hospital in Copenhagen, Denmark, said in a statement.

“Medical cannabis was approved in January 2018 on a trial basis in Denmark, meaning that physicians can prescribe it for chronic pain if all other measures, including opioids, have proven insufficient. Safety data are sparse; hence, this study investigated the cardiovascular [adverse] effects of medical cannabis and arrhythmias in particular, since heart rhythm disorders have previously been found in users of recreational cannabis,” she said.

In Denmark, medical cannabis can be prescribed in various formulations, including dronabinol, which is high in Δ-9-tetrahydrocannabinol (THC); cannabinoid, which has more THC than cannabidiol (CBD); and CBD.

The study investigators included approximately 1.6 million individuals in Denmark who were diagnosed with chronic pain between 2018 and 2021. Of those, 4931 individuals claimed at least 1 prescription of cannabis, with 46% prescribed cannabinoids, 29% prescribed dronabinol, and 25% prescribed CBD.

All individuals were matched by age, sex, and pain diagnosis to 5 individuals with chronic pain who functioned as controls. Investigators followed those taking cannabis products and their controls for 180 days and compared the individuals’ risks of new cardiovascular conditions.—Ashley Gallagher

FDA Authorizes Updated Moderna, Pfizer-BioNTech COVID-19 Vaccines as Booster Dose

THE FDA HAS amended the emergency use authorizations to authorize bivalent formulations of the Moderna and the Pfizer-BioNTech COVID-19 vaccines for use as a single booster dose at least 2 months following primary booster vaccination. The updated boosters include the original SARS-CoV-2 strain, as well as a strain from the BA.4 and BA.5 lineages of the Omicron variant.

The updated Moderna booster vaccine is authorized for use as a single booster dose in individuals 18 years and older. The updated Pfizer-BioNTech booster is authorized for use as a single booster dose in individuals 12 years and older.

“The COVID-19 vaccines, including boosters, continue to save countless lives and prevent the most serious outcomes of COVID-19,” FDA Commissioner Robert M. Califf, MD, said in a statement. “As we head into fall and begin to spend more time indoors, we strongly encourage anyone who is eligible to consider receiving a booster dose with a bivalent COVID-19 vaccine to provide better protection against currently circulating variants.”

Both bivalent vaccines include an mRNA component of the original strain to provide an immune response that is broadly protective against COVID-19, as well as an mRNA component to provide better protection against COVID-19 caused by the Omicron variant. According to the statement, the BA.4 and BA.5 lineages of the Omicron variant are causing most cases of COVID-19 in the United States and are predicted to circulate during the fall and winter.—Aislinn Antrim
INSIDE THE PRACTICE™

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Build a Successful Biosimilar Adoption Plan
Many Health Care Systems Use These Products to Provide Similar but Cheaper Clinical Outcomes
BY RYAN HAUMSCHILD, PHARMD, MS, MBA

BIOSIMILARS HAVE BECOME welcome market disruptors when it comes to chronic and life-threatening diseases, as they provide additional treatment options and wider access to therapy for patients facing difficult conditions.

Because of their biologic nature and being created in a living cell system, biosimilars (like all biologics) generally exhibit high molecular complexity, and as a result, a small amount of natural variability is inherent in them. Despite this heterogeneity, all biological medicines, including biosimilars, must maintain a consistent clinical performance and quality to be approved by the FDA. The molecular similarity achieved by biosimilars by comparison with their reference drugs meets the appropriate standards for FDA approval and use as primary agents in treatment.

Given the ever-rising cost of care in the United States, it is important for health care providers to bend the cost curve and create financial stewardship of health care dollars. With these goals in mind, many health care systems are turning to biosimilars to provide clinical outcomes that are similar to those provided by reference products but at a reduced cost.

The biosimilar pipeline continues to grow based on demand and innovation in the marketplace, and health systems will need to turn to these therapies to reduce health care spending. Finally, managed care organizations are also starting to prefer biosimilar agents based on the accumulated experience with their use.

Understanding the Situation
Based on the most recent reports available, biosimilar use is predicted to increase significantly over the next 5 years. Although there are some barriers to adoption based on concerns about potential immunogenicity issues, provider familiarity, and scope of clinical trials, it is our responsibility as pharmacy leaders to evaluate these products as appropriate for use.

It is also important to recognize that every health system or integrated delivery network will have unique barriers that may vary compared with peer institutions. For example, different barriers may be present from finance, information technology, patients, and providers. It is the responsibility of pharmacy leaders to evaluate these barriers and provide guidance for use, considering the financial benefits of these products.

In January, The American Journal of Managed Care® and the Center for Biosimilars® in partnership with Samsung Bioepis Co, Ltd, hosted an online open forum, “What’s the Hold-Up? Overcoming Barriers to the Use of Biosimilars.” During this event, biosimilar experts compared the state of the US biosimilar industry with where it should be in the future.

Panelists agreed that if incentives were aligned and competition increased, there would be a smoother adoption process. Success cases were shared, and I had the opportunity to discuss insights into Emory Healthcare’s data-driven approach.

ABOUT THE AUTHOR RYAN HAUMSCHILD, PHARMD, MS, MBA, is the director of pharmacy services at Emory Healthcare and Winship Cancer Institute in Atlanta, Georgia.
Winship Cancer Institute’s Plan
At the Winship Cancer Institute, we encountered some initial resistance to use when the first few biosimilars came on the market. To identify the best path forward, we performed finance and clinical reviews of the products and conducted a baseline survey.

The baseline survey allowed us to better understand all the barriers to use within our organization and to uncover who within our system might be the best physician champions. Through the survey results, it became clear that some barriers existed that we were already aware of, such as the information technology build and interchangeability, as well as other barriers we were less aware of, such as finance and patient education. Given the need to overcome all these hurdles, we took this opportunity to create a strategy around biosimilar use and formulate a plan.

One of our first actions was to create education around biosimilars specific to nurses, patients, pharmacists, and providers. By developing this education internally, we were able to include data-driven information and financial benefits specific to the institution. We also made sure to represent the data in a fair and balanced manner that spoke to the highly similar nature of the biosimilar medications as defined by the FDA. This education created a solid foundation of biosimilar understanding that we were able to build on as we took these agents to our pharmacy and therapeutics (P&T) committee.

Recognizing that biosimilars would be increasingly coming to the market, we knew it was important to create a universal approach that could reduce the time to P&T approval for all biosimilars. We created information that relates to efficacy and safety, financial stewardship, immunogenicity data, and product interchangeability, allowing the P&T committee to make a uniform decision around these agents and to move forward with approvals.

We were also granted the ability to bring forward shortened monographs for new biosimilar products, giving the pharmacy the ability to select products that were in the best interest of our institution, patients, and payers. This P&T policy was key to forging a sustainable path forward that would allow us to adopt agents in real time for the benefit of patients. Under this P&T-approved policy, we also found it important to create efficient electronic medical record (EMR) frameworks that can be conducted in a timely manner and follow standard work protocols. Although initially we were concerned that building a new biosimilar and adding it within our order set and pathways would be difficult logistically, we were able to build out each medication in its generic name format so that plans involving multiple biosimilars for any given reference product could be adopted efficiently and safely.

This approach also upheld our financial standards and our National Drug Code accumulation, allowing us to demonstrate financial strength. The EMR build-out and the financial charging were key components of our operational success with biosimilar implementation.

One of the last but most important components of our biosimilar strategy involved creating patient education, both directly in the clinic by physicians and in the infusion center by our pharmacy team members. For simplicity’s sake, we decided to create a comprehensive, standard educational approach that would apply to both settings.

This approach led to patients understanding more fully why they were being transitioned to a biosimilar, how these medications would still support their treatment and outcomes, and how biosimilar use would reduce health care spending. Engaging patients early in this process is important, and we have found it to be essential to a high-functioning pharmacy department.

Conclusion
Biosimilar adoption will continue to increase rapidly based on the proven clinical benefits of these molecules, complemented by their reduced expense. Understanding a specific organization and its unique barriers allows the implementation of an adoption plan tailored to an institution, which will drive biosimilar adoption most effectively. In particular, establishing a P&T-approved policy can provide an expedited process of biosimilar selection, and effective education about these agents can facilitate their acceptance by patients and providers. Health systems affected financially by the COVID-19 pandemic can leverage the reduced cost of biosimilars to generate savings while treating patients effectively. Recognizing the rise of biosimilars and the strong pipeline of such products should motivate health systems to create timely adoption strategies that allow them to stay relevant in the health care marketplace. Most importantly, the incentives to adopt biosimilars must change, so they can benefit health systems and payers and also so patients can benefit from cost savings. All stakeholders should be evaluated to realign incentives, with the patient at the center.
Prescribing Controlled Substances Goes Electronic
Eliminating Paper Prescriptions Allows for Greater Legibility, Security, Trackability for Pharmacists, Providers

BY ALBERTO COUSTASSE, DRPH, MD, MBA, MPH; KEN MAXIK, MBA, BSPHARM; AND CRAIG KIMBLE, PHARMD, MBA, MS, BCACP

With the Affordable Care Act in 2010 came interoperability and meaningful use requirements. Part of these requirements included the implementation of electronic medical records (EMRs), which was a crucial part of achieving these standards.1 With EMRs, prescribers began sending electronic prescriptions.2 EMRs can provide advanced decision support when writing prescriptions, and they include features such as auto populating the quantity prescribed, formulary information, therapeutic duplications, warnings about interactions, or other potential clinical or regulatory issues. This system results in enhanced patient care and a more streamlined dispensing process. In addition, electronic prescriptions for controlled substances (EPCS) has become more widely used as a tool to combat the opioid epidemic.3

Some critical goals of EPCS have been to eliminate paper prescriptions by allowing providers to prescribe electronically, making them digital, legible, more secure, and trackable for both pharmacists and providers.4 This also has made prescriptions more readily retrievable in electronic archives for audits or drug utilization reviews, which makes the handling of controlled substance prescriptions more efficient.

With ECPS, states began implementing prescription drug monitoring programs (PDMPs), which are electronic databases that track controlled substance prescriptions. Now PDMPs can support authorities’ and providers’ timely information about patient and prescribing behaviors that contribute to opioid abuse and facilitate a directed and resourceful response. PDMPs have allowed providers to review the patient’s history prior to authorizing a prescription. PDMPs have grown from 35 states in April 2011 to 49 states, the District of Columbia, and Guam in 2022.5,6 In addition, the Centers for Medicare & Medicaid Services implemented a mandate for electronic prescribing that started on January 1, 2022. This mandate required all controlled drugs covered by Medicare Part D to be dispensed through EPCS.7 Many local and state laws have been implemented to better track controlled substance prescriptions using e-prescribing technology and PDMPs.8 The National Association of Boards of Pharmacy system has facilitated the transfer of the PDMPs across state lines, and many states now have working interfaces to make multistate data retrieval easier.

To limit the likelihood of drug abuse and diversion, the Drug Enforcement Administration (DEA) has acknowledged the importance of ensuring that the rules regulating electronic prescriptions do not unintentionally enable abuse and diversion.9 As a result, the DEA’s Interim Final Rule on EPCS went into effect in June 2010, allowing for e-prescribing and laying out the rules for its use in the United States.10 Pharmacies, pharmacy system vendors, prescription system application vendors, and providers were all subject to the rules.

Results
EPCS aimed to reduce prescription opioid addiction, abuse, diversion, and death.10 Additionally, EPCS can improve efficacy, quality, and safety and ultimately help reduce workload in the dispensing phase.11 EPCS can also improve efficiency, quality, and safety. EPCS has enhanced patient management and reduced prescription fraud associated with paper prescriptions.12 EPCS has gained popularity because of its ability to detect and prevent opioid diversion by removing paper prescriptions and allowing cross-referencing of PDMP databases.13
With up to 9% of opioid paper prescriptions suspected of being forged or fraudulent, the widespread use of EPSC has substantially influenced opioid prescribing.\(^{14}\)

EPSC has reduced stealing prescription pads or printing them and writing illegitimate paper prescriptions, altering a legitimate prescription to obtain a higher dose or more dosage units (eg, changing a 10 to a 40), and altering a prescription record at the pharmacy to hide diversion from a pharmacy stock, according to the DEA.\(^{14}\)

The results of a case study conducted at Yale New Haven Health System between February 2017 and August 2017 showed that the median number of opioid pills prescribed per surgery was reduced from approximately 30 pills before the prescription default modification to approximately 20 pills following the change in the prescription default.\(^{3}\) Prescriptions issued for 30 pills were reduced from 39.7% before the EPCS to 12.9% after the EPCS adoption, whereas prescriptions written for 12 pills rose from 2.1% before EPCS to 24.6% after EPCS. The number of prescriptions written for 20 tablets increased significantly from 12.2% before EPCS to 19.6% after EPCS. After acquiring EPCS, the total opioid prescription was reduced by 34.41 morphine milligram equivalents.\(^{3}\)

In another study done at a dental facility in New York, over 3 months before the required PDMP and between December 1, 2013, and February 28, 2014, after PDMP implementation, the most prescribed opioid analgesics were codeine, hydrocodone, and oxycodone.\(^{15}\) Following the mandated PDMP’s introduction, there was a general trend toward fewer opioid prescriptions and more nonopioid analgesic prescriptions by the end of the trial, with the total number of opioid analgesics prescribed over 3 months dropping from 5096 to 1120 pills, a 78% decrease in absolute numbers.\(^{15}\)

Conclusion

EMRs, EPSCs, and PDMPs have become essential tools in health care. They have curbed prescription errors, facilitated monitoring prescribed controlled substances, increased safety, and reduced possible abuses. In addition, EMRs and EPSCs have provided a complete record of controlled substance prescriptions, monitoring both patients and physicians. These have been essential tools for law enforcement initiatives, public health agencies, and pharmacists to combat the opioid epidemic that has affected millions of Americans.\(^{1}\)

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Immune Thrombocytopenia Purpura Treatment Options Abound
Corticosteroids Are First-Line Therapy for Gaining Platelet Stability but Should Only Be Used Short Term

BY JOANNA LEWIS, PHARMD, MBA

Thrombocytopenia is a condition characterized by a low platelet count, which are specialized cells in the blood that play a critical role in clotting. When the platelet count falls below the desired range, it increases an individual’s risk of bleeding and bruising. Fatigue, hospitalization, impaired quality of life, and even death can occur when thrombocytopenia is severe.

A normal platelet count ranges between 150,000 and 400,000/mm$^3$ (150 to 400 $\times 10^9$/L). Thrombocytopenia is defined as a platelet count of less than 150,000/mm$^3$ (150 $\times 10^9$/L). If the platelet count is between 70,000 and 150,000/mm$^3$ (70 and 150 $\times 10^9$/L), thrombocytopenia is classified as mild. However, if the platelet count is less than 20,000/mm$^3$ (20 $\times 10^9$/L), it is severe and can complicate outcomes. The clinical significance of mild thrombocytopenia is minimal and usually does not interfere with clinical management. Patients are commonly asymptomatic when the count is above 50,000/mm$^3$ (50 $\times 10^9$/L), but they may experience spontaneous or life-threatening bleeding if the platelet count falls below 20,000/mm$^3$ (20 $\times 10^9$/L).

A wide range of conditions, including alcohol use disorder, autoimmune disorders, bone marrow diseases, cancer treatments, enlarged spleen, exposure to toxic chemicals, pregnancy, and viral infections, can cause thrombocytopenia. Medications can also cause thrombocytopenia, including anticoagulants such as heparin, certain chemotherapy agents, furosemide, linezolid, penicillin, nonsteroidal anti-inflammatories, quinidine, quinine, and valproic acid. In rare cases, thrombocytopenia is inherited. All cases of thrombocytopenia follow 1 of 3 mechanisms: accelerated destruction of platelets, decreased or ineffective production of platelets in the bone marrow, or splenic platelet sequestration.

Immune thrombocytopenia, also called immune thrombocytopenic purpura (ITP), is acquired when autoantibodies form against platelet antigens. The American Society of Hematology (ASH) defines ITP as isolated thrombocytopenia (platelet count < 100,000/mm$^3$) with normal white blood cells and normal hemoglobin in the setting of a generalized purpuric rash. ITP was previously known as idiopathic thrombocytopenic purpura. ITP without a secondary cause or underlying disorder is known as primary ITP. Secondary ITP is defined as ITP with an underlying cause or disorder, which can include drug-induced, systemic illness–induced, or viral infection.

ITP affects 2 to 5 per 100,000 individuals annually and is divided into 3 types. These types are determined by time since diagnosis, which is often a factor in treatment decisions. They include the following:

- Newly diagnosed or acute: diagnosis less than 3 months
- Persistent ITP, lasting 3 to 12 months after diagnosis
- Chronic ITP, lasting more than 12 months after diagnosis

ITP must be distinguished from other causes of thrombocytopenia, which may have similar presentations but require different management approaches. It is also vital to evaluate whether ITP is primary or secondary to the underlying condition.

Treatment Options
Although there is no established cure for ITP, platelet counts usually improve with treatment. The treatment for acute ITP...
usually starts with corticosteroids. Because of adverse effects, such as insomnia, mood changes, and weight gain, ASH recommends using steroids for no more than 6 weeks. If platelet counts do not improve with corticosteroids or if a patient presents with bleeding, intravenous immunoglobulin is an option to raise platelet counts quickly.5

There are several options for treatment of chronic or persistent ITP. Thrombopoietin receptor agonists (TPO-RAs) stimulate the body’s production of platelets by megakaryocytes in the bone marrow, which release proplatelets that mature into platelets. There are 3 recommended TPO-RAs, and ASH encourages the use of TPO-RAs before other treatments for chronic or persistent ITP.5,6,8

These include the following:

• Avatrombopag (Doptelet): a once-daily oral tablet with food for adults with chronic ITP who have had insufficient response to a previous treatment

• Eltrombopag (Promacta): a once-daily oral tablet or suspension approved for individuals aged 1 year and older

• Romiplostim (Nplate): a weekly injection approved for individuals aged 1 year and older

The kinase inhibitor fostamatinib disodium hexahydrate (Tavazise), blocks the action of spleen tyrosine kinase in macrophages to inhibit downstream signaling in ITP.5,8

It is approved for use in adults with chronic ITP who have not responded to previous treatment. Adverse effects include abnormal liver tests, diarrhea, headache, and hypertension, but one advantage is that this drug has the least risk of thrombosis of any licensed treatment of ITP.

Rituximab (Rituxan) is a monoclonal antibody that reduces IgG antibody production. Although rituximab is part of the ASH guidelines, it is not an FDA-approved treatment for chronic or persistent ITP.5,8 Approximately half of patients respond initially, but just 20% to 30% are cured in long-term outcome studies.

Splenectomy is another treatment option for some individuals with chronic or persistent ITP. However, there is no test to show whether a splenectomy will work, and there are always risks with surgical procedures. Most guidelines recommend deferral of splenectomy for a year from diagnosis to determine whether a patient will go into remission.5 However, splenectomy remains an option for patients who do not succeed using other forms of treatment or in underserved areas, where more expensive alternatives are not available.

A small percentage of patients do not respond to or tolerate first- or second-line treatments. For those patients, medications such as azathioprine, cyclophosphamide, cyclosporine, danazol, dapsone, mycophenolate mofetil, and vinca alkaloids may be viable options.9

Finally, the FDA granted the drug rilzabrutinib fast track designation for treatment of ITP in November 2020 after previously granting an orphan drug designation. Rilzabrutinib is an oral, reversible, covalent inhibitor of Bruton tyrosine kinase (BTK).10

LUNA 3, a recent multicenter phase 1/2 dose-finding study (NCT04562766) showed promising results in adults with heavily pretreated ITP.11

This new type of BTK inhibitor reduces macrophage activity and the production of antiplatelet antibodies but does not affect the function of platelets. So far, study results have shown that treatment with rilzabrutinib led to a lasting, rapid increase in platelet count.10

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THE CONTINUING BATTLE against COVID-19 has strained the health care system and workforce like never before. Hospitals are experiencing shortages of pharmacy technicians, with a majority reporting turnover rates of at least 21% in 2021, and nearly 1 in 10 noting they had lost 41% or more of their technicians, according to a recent survey from the American Society of Health-System Pharmacists.1 In addition to significant workforce challenges, pharmacists and providers continue to navigate ongoing shortages of medications and products that are vital to patient care. Amid this landscape, pharmacy leaders are increasingly turning to outsourced 503B compounding facilities to help address staffing shortfalls, improve efficiency and productivity, and mitigate the impact of continuing drug supply disruptions. However, 503Bs can play an important role in enhancing the pharmacy supply chain, hospitals must choose their 503B facilities wisely.

Here are 4 key questions pharmacy leaders should ask when deciding whether a 503B is right for them:

1. **Can I off-load work and rely on a 503B partner to deliver high-quality products on time?** With the strain on virtually all hospital staff members, moving certain work off the hospital campus can make sense for pharmacy leaders. 503B partners can quickly assist by off-loading routine compounded sterile product (CSP) volume at their off-site locations and working closely with hospital leadership to coordinate delivery to various facilities as needed. This removes some of the predictable hospital pharmacy clean-room workload, increasing efficiencies and freeing up staff to focus on the most pressing tasks.

2. **Do they offer the products I need at a competitive price?** A key benefit to 503B outsourcing facilities is that they produce medications found on the FDA’s drug shortage list. By working with active pharmaceutical ingredients and raw materials with a Current Good Manufacturing Practice (cGMP) standard, patients and providers have access to drugs that would otherwise be unavailable. Additionally, providers should seek a 503B supplier to assist them with only the truly laborious CSPs to produce, including controlled substances and narcotics, high-risk compounds, and infrequently used medications. 503Bs produce difficult-to-handle medications under a highly repeatable process, with a high degree of certainty and quality. The operational capacity and automation capabilities can drive efficiencies, lowering cost and waste while offering providers more ready-to-use products.

3. **Should I select more than one 503B partner?** If so, how many? Pharmacy leaders should review CSP needs and aim to select more than one 503B partner to meet their unique product and volume demands. This supply chain diversification strategy helps mitigate overreliance on any 1 supplier, should they encounter a disruption in service, and it allows for more competitive pricing, creating a healthier market.
As the partnership matures, pharmacy teams should conduct regular business reviews with 503B suppliers to review sales information and volume for assurance that both are meeting commitments and maintaining high service levels.

 Doing so protects providers from having all their eggs in 1 basket and helps advance patient care.

4. What is their compliance and inspection record with the FDA, among other regulatory bodies? Section 503B of the Drug Quality and Security Act aims to establish federal standards for product integrity, quality assurance testing, reporting, and safety when producing large volumes of CSPs. 503B suppliers must comply with cGMP requirements, pass FDA inspection according to a risk-based schedule, meet other certain conditions, report adverse events, and provide the FDA with specific information about the products they compound. When selecting a 503B partner, purchasers should consider obtaining drugs from FDA-registered compounders and look for a consistent record of satisfactory FDA inspections for assurance that facility operations meet applicable cGMP standards and that the compounded drugs are labeled with the required information.

Upon selection of a 503B partner, pharmacy leaders should consider the following:

• Ask staff members to share concerns and feedback directly and transparently with pharmacy leadership.
• Collaborate with the 503B partner on ongoing program monitoring and measurement.
• Commit to purchase certain volumes of needed drugs to help mitigate reflexive purchasing and manage demand.
• Look at product needs across the enterprise, including in physician clinics and other off-campus locations.
• Share product data with the new supplier about current and future utilization needs.

As the partnership matures, pharmacy teams should conduct regular business reviews with 503B suppliers to review sales information and volume for assurance that both are meeting commitments and maintaining high service levels. Pharmacy teams can also work with trusted 503B partners to refine medication lists or codevelop new product formulations for cost savings and the highest patient benefits.

Pharmacy leaders are looking for effective and, in some cases, alternative solutions to help optimize scarce resources and build long-term resiliency. With the tips outlined above, pharmacy teams are well positioned to establish and sustain successful relationships with 503B suppliers to support their goals.

**REFERENCES**


HE UNIVERSITY OF Rochester Specialty Pharmacy is an integrated health system specialty pharmacy (HSSP) that serves nearly 20 different clinical areas. Integrated HSSPs focus on services outside the traditional dispensing role in collaboration with the interdisciplinary health care team. These services include benefits investigation, financial assistance evaluation, medication education and monitoring related to adherence, adverse reactions, drug interactions, labs, and other disease- or medication-specific monitoring parameters.

Wilmot Cancer Institute is part of the University of Rochester Medical Center and serves approximately 3 million patients diagnosed with cancer across Central and Western New York. To support the outpatient population treated within Wilmot Cancer Institute and prescribed oral anticancer therapy, the University of Rochester Specialty Pharmacy has 7 board-certified clinical pharmacists dedicated to the oncology specialty area. Patients taking oral anticancer therapy are frequently in contact with their assigned clinical pharmacists and medication access specialists, who complete a financial assistance evaluation prior to starting therapy to mitigate out-of-pocket costs. Patients then meet with a clinical pharmacist prior to medication initiation, when a thorough medication reconciliation is completed to assess for interactions with OTC and prescribed medications. If a drug interaction exists with the anticipated anticancer therapeutic agent, the pharmacist communicates with the primary oncologist to make any necessary medication adjustments. In addition, patients are followed regularly by clinical pharmacists during in-office clinic visits and follow-up telephone calls, which are completed in tandem with monthly refill assessments.

**Study Introduction**

A retrospective chart review was conducted at the University of Rochester Specialty Pharmacy to evaluate the clinical impact of concomitant proton pump inhibitor (PPI) therapy in patients treated with acalabrutinib (Calquence). Acalabrutinib is an oral Bruton tyrosine kinase inhibitor that is FDA approved for treatment-naïve and relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and relapsed/refractory mantle cell lymphoma.\(^1\)\(^-\)\(^3\)

Acalabrutinib solubility decreases with increasing pH, therefore the coadministration of acalabrutinib with acid-reducing agents decreases plasma concentrations and may decrease efficacy. The acalabrutinib prescribing information recommends avoiding PPIs and separating antacids or H2-receptor antagonists.\(^4\)\(^,\)\(^5\)

In clinical practice, if a patient does not have a successful trial with a PPI, providers may revert to PPI therapy despite the interaction. Although trials have been completed to determine coadministration recommendations based on under-the-curve measures, data are limited to assess the clinical impact of concomitant acalabrutinib and PPI use. This study aimed to evaluate the clinical impact of concomitant PPI therapy in patients treated with acalabrutinib therapy.

**Methods**

Adults diagnosed with CLL/SLL on acalabrutinib therapy for at least 3 months and treated at the Wilmot Cancer Institute between October 31, 2017, and September 15, 2020,
were identified via electronic medical records (EMRs).

The primary outcome of this study was defined as response to acalabrutinib (clinical complete remission, complete response, partial response, or partial response with lymphocytosis) at 3 months after the initiation of therapy (+/- 1 month) in CLL in patients with concomitant PPI therapy vs no concomitant PPI therapy. It was anticipated that not all patients would have restaging bone marrow biopsies or imaging completed at 3 months. Therefore, patients meeting clinical and laboratory complete remission criteria were considered to have achieved a clinical complete remission. Participants were considered to have taken concomitant therapy if they had documented evidence of taking a PPI while on acalabrutinib for a minimum of 1 day.

Statistical Analysis
Descriptive statistics were used to report baseline demographics and the number of patients with clinical complete remission, complete response, partial response, partial response with lymphocytosis, and stable disease. Response rates were summarized as a percentage of the number of patients per clinical response group over the total number of patients taking acalabrutinib therapy. Fisher’s exact test was used to compare responses between patients ever taking concomitant acalabrutinib and PPI therapy throughout the study period vs those never taking concomitant therapy.

Results
A total of 65 participants met inclusion criteria. The median duration of follow-up was 12 months (range 3.2-26.9 months). Baseline demographics and disease characteristics were similar to those living with CLL in the general population (Online Table 1).

Prior to starting acalabrutinib, 23 of 65 (35.4%) patients were taking a PPI. At the start of acalabrutinib, 4 patients remained on a PPI and 19 (83%) were taken off PPI therapy (18 patients switched to alternative acid suppression therapy and 1 successfully discontinued all acid suppression therapy). When the response rate was assessed at 3 months, 7 patients were taking concomitant PPI therapy (as 3 patients resumed).

Fifty-five patients were included in the response assessment at 3 months. Of 7 patients taking a PPI, 57% had a complete clinical remission and 43% had a partial response with or without lymphocytosis. Of the 48 patients not taking a PPI, 25% had a complete clinical remission and 69% had a partial response with or without lymphocytosis (Online Table 2). There was no evidence of a significant association of PPI status, with best response at 3 months post acalabrutinib initiation ($P = .59$).

Discussion
The results of this study did not support a statistically significant difference in the clinical impact of concomitant acalabrutinib and PPI therapy based on response rates between groups (Online Table 2; $P = .59$). However, the results did highlight the critical role the clinical pharmacists have in identifying drug interactions prior to initiating a medication. Acid suppression therapy is available for patients to purchase OTC. Therefore, it does not always appear on a patient’s documented medication list within the EMR. Clinical pharmacists at the University of Rochester Specialty Pharmacy involved in the management of acalabrutinib complete a thorough counseling session with medication reconciliation prior to the initiation of acalabrutinib. In total, 19 of 23 (83%) patients who were taking a PPI prior to the start of acalabrutinib were switched to alternative antacid therapy to avoid this significant drug interaction. This high substitution rate can be attributed to a highly integrated clinical pharmacist having a discussion with the patient prior to the initiation of acalabrutinib. The clinical pharmacists at the University of Rochester Specialty Pharmacy use a thorough documentation process via an integrated flow sheet within the EMR. It was confirmed via this documentation that discussions with providers regarding the interaction did occur for the remaining 4 of 23 patients. These patients were not ultimately considered to be candidates for a switch in therapy because of either failing with a previous

Acalabrutinib is an oral Bruton tyrosine kinase inhibitor that is FDA approved for treatment-naïve and relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma and relapsed/refractory mantle cell lymphoma.
switch attempt or having a separate diagnosis that requires PPI therapy.

There were several limitations to this study. First, there was a small sample size exposed to concomitant therapy, as just 7 patients had been on both acalabrutinib and a PPI at least once when the primary outcome was measured at 3 months post acalabrutinib initiation. A larger sample size with more concomitant use of acalabrutinib and a PPI would allow for further evaluation of the clinical impact of this interaction. Additionally, this study was completed over a time period affected by the COVID-19 pandemic, when telemedicine visits frequently replaced in-person office visits. Therefore, patients with telemedicine visits at 3 months lacked objective laboratory and physical assessments to verify clinical response.

Finally, a large number of patients were taking additional therapies other than acalabrutinib to target their disease state, which could have affected response rates. Additionally, all had differing disease features, which put some at a higher risk than others for disease progression. Although these confounders may have affected response rates, the heterogeneity in the patient population included in this study is representative of the real-world population seen in clinical practice.

**Conclusion**

The high rate of acid suppression therapy substitution noted in this study highlights 1 benefit of the integrated HSSP model. These observations suggest specialty pharmacists’ continuous assessment, ongoing monitoring, and counseling services lead to mitigation of drug interactions and optimization of drug therapy in this patient population.

Given the large switch rate (83%) at baseline from a PPI to a different antacid therapy that was observed within this study, there were minimal data for patients who were concomitantly administering acalabrutinib and PPI therapy. Throughout the entire duration of follow-up, 84% of patients were able to remain off PPI therapy. Further investigation with a clinical trial that has a larger patient population taking concomitant acalabrutinib and PPI therapy is required to determine the impact of this interaction on clinical practice.

**REFERENCES**


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During a recent *Pharmacy Times*® clinical forum titled “Best Practices in the Prophylactic Treatment of Hemophilia A,” experts discussed pharmacists’ involvement in effective management of hemophilia A, focusing on patient-centered care, including disease burden and quality of life, as well as considerations for specialty pharmacies.

Leslie Ward, PharmD, BCPS, BCOP, clinical pharmacist in benign hematology at UVA Health System, moderated the panel.

**Treatment Landscape**

The panelists discussed starting infants on emicizumab initially. Physicians do this because it is “easier [to] access for the parents [and is] less [traumatic for] the patient, so they don’t start off with that fear of needles when they’re younger,” said Lisa Schrade, clinical pharmacist at Optum Infusion Pharmacies, adding that adherence tends to be much better as they get older.

One big problem for patients who start off with the shorter-acting recombinant products or plasma-derived products is adherence, according to Schrade.

Older individuals typically do not switch from infusion products, as they are most comfortable with them, said Ata Caudhary, director of the hemophilia program and regional director of operations at America Inc.

When it comes to counseling tips, the focus should be on adherence, but Schrade said storage is another significant factor. The panelists also highlighted the importance of teaching patients how to self-infuse medication when they switch treatment plans, especially if they previously took emicizumab.

All cases should be patient specific, the panelists said. “You can’t just use a trial to determine what kind of therapy is going to be appropriate for that 1 individual, because they’re not cookie cutter,” Schrade said.

**Patient-Centered Care**

The panelists also discussed patient-centered care, including disease burdens. “I think there’s still a fear of this stigma,” said Kim Epps, PharmD, CSP, vice president and general manager of bleeding disorders at BioMatrix Specialty Pharmacy. “They remember how they were treated and what they went through, and there’s a fear that that’s going to come back.”

Patients also often feel as if they are costing insurance companies too much money, and they are meeting their lifetime caps too soon, Caudhary said. The disease is draining on families and patients both physically and mentally, Schrade said. Psychosocial support is key for patients, Epps said, adding that her pharmacy conducts many education programs that help ensure social and health care needs are met.

Another critical issue is patient preference, the panelists said, pointing out that sometimes patients don’t want to change their medications.

**Specialty Pharmacy Considerations**

In addition, the panelists discussed considerations for specialty pharmacies, including best practices, highlighting that developing relationships between patients and pharmacists is vital. “They don’t want to just be a number,” Schrade said. “They don’t want to be a dollar sign; they’ve been through that, lived through it, [and] they need somebody who’s going to actually care about the concern of their health care.”

The panelists also said that having a good relationship with the physician is essential. Keeping in mind that some want to collaborate more than others, pharmacists should take note of and respect how much communication goes on between patients and physicians.

Furthermore, the panelists spoke about how patients with hemophilia A should become involved in their communities to learn more about the disease from other individuals who have it. There are also many educational programs hosted by care coordinators and nurses that are related to hemophilia A that can help address the needs of individuals with the disease.

Finally, Priti Doshi Shah, PharmD, pharmacist in charge, specialty pharmacist at American Service and Product, Inc, and other panelists discussed educating patients about medications, including why medication for hemophilia A should be individualized.

“Sometimes the dose has to be adjusted from month to month,” Schrade said. “If I see that every May the patient is burning through factor like crazy, I find out well, it’s because they’re going hiking up in the mountains when the weather starts turning better so we need to dose that appropriately so they’re not ending up an emergency room with stress fractures.”
2022-2023 Influenza Season Looks to Be Severe
Outpatient Treatment Is Primarily Based on Patient-Specific Factors, Whereas
Oseltamivir Remains the Therapy of Choice for Inpatient Settings

BY JOHN P. BOMKAMP, PHARMD, BCPS-AQ ID; AND AMER EL-GHALI, PHARMD

Despite a very mild influenza season the past 2 years, the 2022-2023 influenza season has the potential to cause significant stress to an already overburdened US health care system. For 2021-2022, the flu positivity rate was historically low at 4.5%. This was largely because of increased COVID-19 restrictions and flu testing that may have lowered the positivity rate. However, in many parts of the country, a surge late in the last flu season is expected to continue into next season.

Low antibody levels related to low exposure, poor exposure, and relaxed COVID-19 restrictions all played parts in the latest flu surge. Initial preliminary reports released in October 2021 showed that this year’s flu vaccines were not significantly effective at reducing illness due to influenza A (H3N2), with a 16% overall vaccine effectiveness rate. However, a June 2022 report from the CDC’s Advisory Committee on Immunization Practices (ACIP) showed effectiveness rates of 34% (95% CI, 19%-46%), which is in line with what is typically observed.

The CDC has selected new flu vaccines that were available in August 2022, with a major change in the selection of the H3N2 and influenza B components. Additionally, the FDA approved a change in the recommended age for the Flucelvax Quadrivalent between ages 6 months and 4 years. The ACIP also recommends that adults aged at least 65 years receive 1 of the following adjuvanted or high-dose vaccines:

- Quadrivalent adjuvanted inactivated influenza vaccine
- Quadrivalent high-dose inactivated influenza vaccine
- Quadrivalent recombinant influenza vaccine

Therapeutic Management of Influenza
Antiviral treatments of influenza A and B are listed in the Table. Oseltamivir, peramivir, and zanamivir are viral neuraminidase inhibitors, which prevent the release of viral particles from the plasma membrane of infected human cells. Baloxavir introduced a novel mechanism of action through inhibition of viral replication by inhibiting the polymerase acidic protein within the viral RNA polymerase. Antiviral treatment should be initiated as soon as possible, with the greatest benefit observed when started within 48 hours of symptom onset. Antiviral-specific considerations are outlined in the Table.
Outpatient Influenza Management
The primary benefit of influenza treatment in the outpatient setting is a reduction in fever and symptoms by 1 to 2 days.\(^9\,11\) In patients with risk factors for influenza complications, there is an added benefit of lowering the likelihood of hospitalization.\(^9\) The CDC recommends equally all the aforementioned antivirals for outpatient antiviral therapy.\(^10\) The results of recent literature suggest baloxavir may be linked to additional benefits, such as rates of influenza-related complications and reduced health care–related costs.\(^12,13\) Furthermore, baloxavir offers a treatment option when there is concern for neuraminidase inhibitor resistance. However, this is balanced with the risk of baloxavir treatment-emergent resistance.\(^11\) The treatment duration with oseltamivir and zanamivir is 5 days, whereas baloxavir and peramivir require only a single dose.\(^7,9\)

Inpatient Influenza Management
Oseltamivir remains the preferred agent for hospitalized patients, as data are limited for other treatment options. The results of observational studies have shown that oseltamivir may reduce the duration of hospitalization and mortality. Although the most significant benefit is seen when antiviral treatment is started within 48 hours of symptom onset, oseltamivir still has benefit when started within 4 to 5 days, and possibly up to 7 days, from symptom onset. Treatment duration is 5 days, although the duration may be extended to 10 days or longer in patients who are immunocompromised or those with severe lower respiratory tract disease.\(^9\) In patients with poor oral access or malabsorption, peramivir is a treatment option\(^10;\) however, peramivir was studied in hospitalized patients in a randomized trial and did not show a significant clinical benefit.\(^14\) But the CDC suggests peramivir should still be considered for hospitalized patients who are unable to take oral medications.\(^10\)

Conclusion
The upcoming influenza season may be more severe because of low circulating antibody levels and relaxed mask restrictions. Outpatient treatment is primarily based on patient-specific factors, whereas oseltamivir remains the treatment of choice for inpatient settings.

<table>
<thead>
<tr>
<th>Antiviral agent</th>
<th>Route of administration</th>
<th>Standard dose and duration</th>
<th>Clinical pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oseltamivir</td>
<td>Oral capsules and suspension</td>
<td>75 mg orally twice a day for 5 days</td>
<td>Renal dose adjustment required</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Suspension may be given via OG/NG feeding tubes</td>
</tr>
<tr>
<td>Baloxavir</td>
<td>Oral tablets</td>
<td>≥80 kg: 80 mg 1 dose orally &lt;80 kg: 40 mg 1 dose orally</td>
<td>Avoid with polyvalent cations (eg, Al(^3+), Ca(^2+), Mg(^2+), Zn(^2+)), because of chelation. No renal dose adjustment required</td>
</tr>
<tr>
<td>Zanamivir</td>
<td>Powder for inhalation</td>
<td>10 mg (2 inhalations) via DISKHALER twice a day for 5 days</td>
<td>Formulation should not be manipulated for nebulization for mechanical ventilation</td>
</tr>
<tr>
<td>Peramivir</td>
<td>IV solution</td>
<td>600 mg IV × 1 dose</td>
<td>Renal dose adjustment required</td>
</tr>
</tbody>
</table>

\(^4\) intravenous; NG, nasogastric; OG, orogastric.

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