Pharmacy in the News:

**Johnson & Johnson, AstraZeneca COVID-19 Vaccines Share Concerns About Rare Blood Clots**

- FDA and CDC have paused the use of the Johnson & Johnson (Janssen) COVID-19 vaccine due to reports of cerebral venous sinus thrombosis (CVST).
- The AstraZeneca vaccine also had similar concerns in Europe.
- Research is currently ongoing to investigate the correlation between the Johnson & Johnson vaccine and CVST.

**Study: COVID-19 Patients on Intravenous Immunoglobulin Have Reduced Hospital Stays, Test Negative Earlier**

- A phase 2 study by the Journal of Infectious Diseases evaluated the safety and efficacy of intravenous immunoglobulin (IVIG) for the treatment of COVID-19 patients with moderate pneumonia.
- The study was an open-label, multicenter, comparative, randomized study enrolling 100 eligible patients receiving either IVIG + standard of care (SOC) or SOC alone.
- Results showed a significantly shorter hospital stay in the IVIG group compared with SOC alone (7.7 vs 17.5 days; \( p = 0.0001 \)). Duration for normalization of oxygen saturation, body temperature, and mechanical ventilation were significantly shorter in the IVIG group compared with SOC. The percent of mechanically ventilated patients were similar between the two groups.
- The study concluded that IVIG was safe and effective as an adjuvant in treating COVID-19.

**Assessing Germline, Somatic Genetic Testing for Prostate Cancer**

- Germline mutations occur in 11.8% to 16.2% of patients with metastatic prostate cancer compared to 4.6% in localized prostate cancer, and 2% to 3% in the general population.
- Common gene mutations include \( BRCA2, ATM, \) and \( CHEK2 \). Other mutations include mismatched repair mutations MSH2 and MSH6.
- Approximately 89% of patients with metastatic castration-resistant prostate cancer have actionable mutations for both germline and somatic mutations.
- Currently, 3 guidelines provide recommendations for obtaining germline testing: the National Comprehensive Cancer Network guidelines, the Philadelphia Prostate Cancer Consensus (PPCC), and the European Advance Prostate Cancer Consensus.
- All three guidelines recommend patients who have metastatic prostate cancer to have germline testing and somatic tumor testing done.
Recently Approved Generics:

- Northera (droxidopa) 100 mg, 200 mg, and 300 mg capsules – 02/18/2021
- Otezla (apremilast) 10 mg, 20 mg, and 30 mg tablets – 02/18/2021
- Linzess (linaclotide) 145 mcg and 290 mcg capsules – 02/09/2021
- Qudexy XR (topiramate ER) 25 mg, 50 mg, 100 mg, 150 mg, and 200 mg capsules – 02/01/2021
- Zyclara (imiquimod) 3.75% cream – 01/26/2021
- Feraheme (ferumoxytol) 510 mg iron/17 mL (30 mg/mL) single-dose vials – 01/15/2021

Newly Approved Drugs

**Zegalone (dasiglucagon)**, Zealand Pharma; 03/22/2021

*Indication:* Severe hypoglycemia

*MOA:* Glucagon receptor agonist, which increases blood glucose concentration by activation hepatic glucagon receptors

*Dosage:* 0.6 mg administered by subcutaneous injection into the lower abdomen, buttocks, thigh, or outer upper arm

**Nulibry (fosdenopterin),** Origin Biosciences; 02/26/2021

*Indication:* Molybdenum cofactor deficiency (MoCD) Type A

*MOA:* Substrate replacement therapy provides an exogenous source of cPMP, which is converted to molybdopterin then to molybdenum cofactor, which activates molybdenum-dependent enzymes, including one that reduces levels of neurotoxic sulfites

*Dosage:* Patients 1 year/older: 0.9 mg/kg (as actual body weight) administered as an intravenous infusion once daily. For patients < 1 year old, see the prescribing information

**Lupkynis (voclosporin),** Regeneron Pharmaceuticals; 01/22/2021

*Indication:* Lupus nephritis

*MOA:* Lymphocyte activation involves an intracellular calcium increase that binds to the calcineurin regulatory site and activates calcmodulin binding catalytic subunit and through dephosphorylation activates the transcription factor, Nuclear Factor of Activated T-Cell Cytoplasmic (NFATc). The immunosuppressant activity results in inhibition of lymphocyte proliferations, T-cell cytokine production, and expression of T-cell activation surface antigens

*Dosage:* 23.7 mg orally twice daily

**Azstarys (serdexmethylphenidate and dexamethylphenidate),** Corium Inc.; 03/02/2021

*Indication:* Attention deficit hyperactivity disorder (ADHD)

*MOA:* Prodrug of dexamethylphenidate. Dexamethylphenidate HCl is a central nervous system (CNS) stimulant

*Dosage:* Patients 6-12 and 13-17 years: Recommended starting dosage is 39.2/7.8 mg orally once daily in the morning. Each age group has a different titration schedule

**Verguvo (vericiguat),** Merck; 01/19/2021

*Indication:* Heart failure (HF)

*MOA:* Stimulator of soluble guanylate cyclase (sGC), an important enzyme in the nitric oxide (NO) signaling pathway. When NO binds to sGC, the enzyme catalyzes the synthesis of intracellular cyclic guanosine monophosphate (cGMP), a second messenger that plays a role in the regulation of vascular tone, cardiac contractility, and cardiac remodeling

*Dosage:* Initial dose of 2.5 mg orally once daily with food

**Tepmetko (tepotinib),** EMD Serono Inc.: 02/03/2021

*Indication:* Non-small cell lung cancer (NSCLC)

*MOA:* Kinase inhibitor that targets MET, including variants with exon 14 skipping alterations. Inhibits hepatocyte growth factor (HGF)-dependent and -independent MET phosphorylation and MET-dependent downstream signaling pathways

*Dosage:* 450 mg orally once daily with food
Apps of the Month

Speechify (text-to-speech app)

- A few lower quality free options to choose from for voices as well as high quality paid voices
- Take pictures of text, paste web links, import files, or paste text directly to have it read to you
- Ability to take multiple pictures of text that link together to form a “book” that will be read without breaks
- Variety of reading speeds for any level listener
- Can help with multi-tasking or dyslexia

App Store rating: 4.7/5 stars with 46k raters

Medisafe (personal medication adherence app)

- Ability to personalize medication reminders set to any time of the day
- Medication list function with day-by-day calendar to keep track of non-daily dosed drugs (think methotrexate)
- Doctor information and appointment tracking
- Weekly adherence reports
- Diary section for note-taking of symptoms to report to the physician
- Patient-centered videos with information on each drug on their medication list (side effects, things to watch for, and more)

App Store rating: 4.7/5 stars with 52k raters

Writing Tip #1
Avoid nominalizations, which are verbs turned into nouns. Example: “Measurement of” is better as “was measured by.”

Writing Tip #2
Avoid use of “respectively.” This word forces the reader to go back and think through what was written, so it is unintuitive for readers.
Drug Information Question of the Month

**Question:**

“What evidence exists for the contribution of semaglutide (Ozempic) to the development of diabetic retinopathy (DR)?”

**Response:**

According to prescribing information for semaglutide, a clinical trial had reported diabetic retinopathy (DR) as a possible complication with the medication. Patients with a history of DR should be closely monitored for progression of DR while on semaglutide.\(^1\) The ADA 2021 guidelines recommend that patients with type 2 diabetes mellitus obtain an initial dilated and comprehensive eye exam at the time of diagnosis. If glycemia is well controlled and there is no evidence of retinopathy after one or more annual exams, then patients may be screened every 1 to 2 years. If evidence for retinopathy is present, then annual comprehensive eye exams are warranted.\(^2\)

In the SUSTAIN 6 trial, 3297 patients were followed for 2 years and received either once-weekly injections of semaglutide (0.5 mg or 1.0 mg) or placebo. They defined DR complications as having a vitreous hemorrhage, onset of diabetes-related blindness, and need for treatment with an intravitreal agent or retinal photocoagulation. DR complications occurred in 50 (3%) participants in the semaglutide group vs 29 (1.8%) participants in the placebo group which was statistically significant (HR, 1.76; 95% CI, 1.11 to 2.78).\(^3\) The NNH was calculated to be 83 meaning that 83 people would need to be treated with semaglutide before an additional DR complication would be examined. In the semaglutide group, 42 (84%) participants with DR complications had DR at baseline vs 24 (82.8%) participants in the placebo group with DR complications had DR at baseline.\(^3\)

A meta-analysis conducted by Vilsbroll et al, analyzed all of the SUSTAIN trials (1 to 6) as well as 2 Japanese trials to assess semaglutide and the risk for DR. In the short-term, rapid glucose lowering has been associated with worsening of retinopathy in diabetic patients.\(^3,4,5\) This is counterbalanced by the long-term effects of reduction in DR with improved glucose control. In the SUSTAIN 1 to 5 and Japanese trials, they excluded participants with known proliferative retinopathy or maculopathy whereas the SUSTAIN 6 trial had no exclusions in regard to pre-existing retinopathy. In the SUSTAIN 1 to 5 and Japanese trials, all events were mild or moderate with no serious adverse effects with regard to DR. A time-to-event analysis of all the trials showed no statistical difference in participants who did not have DR at baseline (HR 1.33; 95% CI, 0.36 to 4.95). The authors then separated participants who did have DR at baseline into two groups: those who were on insulin and those who were not. Of those who were on insulin, a statistical difference in time-to-event was found (HR 1.96; 95% CI, 1.15 to 3.33). In those who were not on insulin, no statistical difference in time-to-event was found (HR 0.48; 95% CI, 0.08 to 2.90). This further confirms the worsening of DR due to more aggressive treatments in rapid glucose lowering.\(^4\)

In another meta-analysis comparing GLP-1 RAs with microvascular outcomes by Avgerinos et al, 60 studies were analyzed including over 60,000 participants. Eligible studies were RCTs comparing GLP-1 RAs (liraglutide, exenatide, lixisenatide, dulaglutide, and semaglutide) with another antidiabetic agent or placebo in adults with T2DM for a treatment duration of at least 12 weeks. Of the 60 studies, 8 trials studied the effects of semaglutide. The authors found that there were no association between the use of GLP-1 RAs and the incidence of DR when compared to placebo (OR 1.01; 95% CI 0.89 to 1.16; I\(^2\) = 0%). The GLP-1 RAs were also not associated with an increase in retinal detachment, macular oedema, or retinal hemorrhage. They were, however, associated with a higher incidence of vitreous hemorrhage when compared to placebo (OR, 1.93;
95% CI, 1.09 to 3.42; I² = 0%) which the authors accredited to incidence of diabetic retinopathy, under-reporting of outcomes, and high risk of bias and inconsistency. With these findings, the authors concluded that GLP-1 RAs are safe in terms of their effect on DR.\(^5\)

Currently, Novo Nordisk is sponsoring a phase 3 clinical trial that hopes to enroll 1500 participants and follow them for 5 years. The study start date was May 8, 2019 and the last posted update was January 14, 2021. The trial will be assessing the progression of DR with the use of semaglutide when compared to placebo, and completion of the study is estimated to be by July 13, 2026.\(^6\)

In conclusion, there have been some mixed data regarding the use of semaglutide and the progression of DR. However, when accounting for confounding variables (concurrent insulin use and previous history of retinopathy), the progression of DR complications is better explained. The use of semaglutide in patients with DR and concurrently using insulin resulted in a statistically significant increase in DR complications. However, the use of semaglutide in participants without DR at baseline resulted in no statistically significant difference when compared to placebo. Similarly, the use of semaglutide in participants who had DR at baseline but was not being treated with insulin resulted in no statistically significant difference when compared to placebo.

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References:

2. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes—2021 American Diabetes Association Diabetes Care Jan 2021, 44 (Supplement 1) S151-S167; DOI: 10.2337/dc21-S011
Racial Disparities in Health Care

Introduction

Racial disparities in healthcare have been present for decades. These can often lead to decreased quality of life, differences in therapy, and increased mortality among individuals of different races. Influences and factors for these differences in care have been identified. Various guidelines, studies, and articles have started to place importance around these differences. As health care providers, pharmacists should stay current on this topic and continue to research and study literature to optimize patient outcomes.\(^1\)\(^2\) Below are brief summaries of three common health conditions that highlight the racial disparities currently present with these conditions as well as an overview of the identified gaps in care with recommendations for mitigation of adverse effects related to these gaps. Locations to find more information are additionally cited below for the interested reader.

Guideline Evidence – Gaps in Care and Recommendations for Addressing Them

The Pain Management Best Practices Guideline has an entire section dedicated to special populations with healthcare disparities in racial and ethnic populations including Hispanics/Latinos, African Americans, American Indians, and Alaska Natives.

Gap 1: Socioeconomic and cultural barriers may hinder patient access to effective care. Evidence exists of racial and ethnic disparities in pain treatment and outcomes in the United States, yet few interventions have been designed to address these disparities. Lower quality pain care may be related to many factors, including lack of insurance, barriers to accessing health care, discrimination, lack of a PCP, lack of childcare, lower likelihood to be screened or receive treatment, and environmental barriers that impede self-management.\(^3\)

Recommendation 1: Development of intervention programs informed by the biopsychosocial model to focus on reduced racial and ethnic disparities in pain management.

Gap 2: Research shows that ethnic minorities may potentially have greater pain sensitivities and are at higher risk for chronic pain, but they remain underserved.

Recommendation 2: Develop biopsychosocial interventions for pain that are culturally enhanced and scalable.\(^3\)

Pregnancy:

Maternal mortality has been on the rise in the United States. Most notable rise occur in non-Hispanic Black women. Prenatal care to engage patients in early pregnancy and providing psychosocial, cultural, and educational support may help improve pregnancy outcomes. Of note, 10% of Black women received late or no prenatal care compared to 4% of White women in 2014. They are also less likely to be assessed timely and have affordable care.\(^4\)

Obesity:

Obesity has been a major problem in the United States. The prevalence of adult obesity is reported to be 36.9% in Black men, 54.8% in Black women, 14.8% in White men, and 38.0% in White women. Research shows Black Americans are less likely than White Americans to obtain treatment for weight loss such as bariatric surgery. Black Americans are less likely to be diagnosed with obesity, and therefore not referred to these surgical centers. Many Black American men may also perceive excess
weight as a societal norm and refuse to seek treatment. It is important to quickly diagnosis obesity and educate patients to seek lifestyle modifications and pharmacotherapy when appropriate.\(^5\)

**Acute Myocardial Infarction (AMI):**

AMI is a leading cause of morbidity and mortality in the United States. Recent findings show non-White individuals receive less guideline directed care and experience more adverse outcomes compared to White individuals. Non-White individuals were less likely to undergo coronary angiography, angioplasty, and coronary artery bypass surgery when compared to White individuals. Additionally, Black American patients were less likely to receive newer therapies such as glycoprotein IIb/IIIa inhibitors, P2Y12 inhibitors, and statins.\(^6\)

**The Role of Pharmacists**

We can play a role in identifying barriers as well as resources to overcome disparities in the healthcare field. For cost-related barriers, we can help search for assistance programs or call prescribers for a cost-effective alternative. For medical hesitancy, we can provide education and guidance to make an impact on patient health. Numerous resources such as those described below are available to assist in these efforts; however, the first step is to identify these barriers.

**Informational Resources**

- Center for Disease Control and Prevention (CDC)
  - The CDC discusses how and why racial and ethnic disparities exist while focusing on how these disparities relate to the current COVID-19 pandemic.
  - The CDC also has information regarding exposures and deaths from COVID-19 related to disparities as well as information on promoting fair access to health.
- American Psychology Association (APA)
  - The APA gives information regarding disparities from a psychology standpoint and goes much further into the detail of explaining why disparities exist from this psychology standpoint.
  - [https://www.apa.org/topics/racism-bias-discrimination](https://www.apa.org/topics/racism-bias-discrimination)

**References:**