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LOOK INSIDE

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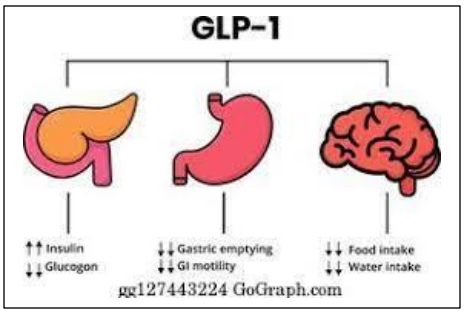
INSIDE THIS ISSUE



GLP-1 Agonists FDA-Approved for Weight Loss

Kim Broedel-Zaugg, RPh, MBA, PhD

Generally speaking, a GLP-1 is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.[1] Some of these medications have shown safety and efficacy in weight loss even in patient who do not present with diabetes mellitus. Tirzepatide (Mounjaro)[2] and semaglutide (Wegovy)[3] are two such medications. Further, Amgen is developing another such drug with the hopes of even greater weight loss.[4]

Only patients with a body mass index (BMI) of 30 or higher or a BMI between 27 and 30 with at least one co-morbidity (hypertension, dyslipidemia, cardiovascular disease, diabetes mellitus) associated with weight loss should be considered for treatment with one of these medications. Studies indicate that patients receiving tirzepatide lost between 15% and 20.9% of their body weight while those receiving a placebo lost between 2.4% and 3.1%.[2] Similar studies for semaglutide show a weight loss of about 15% for patients receiving medications compared to a loss of 2.4% in the placebo group.[3]

PROS of GLP-1 agonist use for weight loss

*effective for supporting weight loss in conjunction with diet and exercise
*can help suppress appetite and/or make the patient "feel full"
*once per week dosing schedule

CONS

*very expensive if not covered by insurance **(WV Medicaid does not currently cover any agent used for weight loss)**
*administered by injection
*may cause serious side effects[3]

GLP-1s carry a black box warning regarding the risk of thyroid C-cell tumors. Patients with a history of such disease should not use these medications.[5] Other risks and precautions include pancreatitis, hypersensitivity, kidney disease, and severe gastrointestinal disease.[1,6] Mild side effects include GI upset and redness or pain at injection site.

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DOSING

Tirzepatide (Mounjaro):
2.5 mg subcutaneously weekly for 4 weeks;
5 mg subcutaneously weekly for 4 weeks;
May increase in 2.5 mg increments every 4 weeks if needed for glycemic control with a maximum dose of 15 mg weekly[2]

Semaglutide (Wegovy):
0.25 mg subcutaneously weekly for 4 weeks;
0.5 mg subcutaneously weekly for 4 weeks:
1 mg subcutaneously weekly for 4 weeks;
1.7 mg subcutaneously weekly for 4 weeks;
2.4 mg subcutaneously weekly thereafter. Maximum dose of 2.4 mg weekly[3]

1. GLP-1 agonists: Diabetes drugs and weight loss - Mayo Clinic
2. Type 2 Diabetes Treatment to Lower A1C | Mounjaro™ (tirzepatide)
3. Weight-Loss Prescription Medication | Wegovy™ (semaglutide) Injection 2.4 mg
4. Amgen's AMG-133 shows potential in competing with GLP-1RA obesity therapies - Pharmaceutical Technology (pharmaceutical-technology.com)
5. InsulinPC-Combos-2020.pdf (diabetesed.net)

DSCSA and the Providers Office

Tyler B. Clay, PharmD, BCPS

In the early two thousands, as the number of incidences of illegitimate drugs entering the marketplace increased, several states were beginning to look at legislation to tighten the supply chain. At that time, the system ran almost entirely on trust without any verification and states realized traceability was needed, however each state having a different system to track medications posed obvious problems and would ultimately be unimplementable. From that came the Drug Supply Chain Security Act (DSCSA), a federal law that passed in 2013 which amended the Federal Food, Drug, and Cosmetic Act to grant the FDA more authority to regulate and monitor pharmaceutical compounding.

The DSCSA legislation was introduced with a 10-year implementation process with the final phase going into effect in November 2023. Phase I began in 2015 requiring dispensers to do lot level tracing. Phase II launched in 2018 requiring item level serialization to be initiated by manufactures. Phase III started in 2020 and mandated dispensers only buy serialized product, and finally Phase IV will be implemented on November 27th 2023 which will usher in requirements of item level tracing as well as mandating an electronic, interoperable tracing system. Although the bulk of the regulation compliance will be placed on pharmacies including providing traceability of medications to patients upon request, participation in product tracing for all transactions when required, as well as verification of suspect product, there are some elements that will apply for other sources of medication dispensing such as physicians' offices.

The inclusion of physicians' offices stemmed from the increasing number of case reports of patient harm as a result of medical practices purchasing medications from unlicensed wholesalers. Between 2012 and 2017 the FDA issued over 3,000 warning letters to providers offices that they must stop buying medications from these distribution outlets. Between 2005 and mid-2018, 59 doctors were prosecuted for crimes related to purchasing of non-FDA approved medications and illegal importation practices. From these cases, 57 providers were fined a combined total of $37.5 million dollars and 16 providers received prison sentences. Beginning in November 2023, providers will have two main compliance requirements for DSCSA.

First, medications may only be purchased from authorized trading partners that have valid licensure and keep corresponding records. Although purchasing of medications from unlicensed vendors has never been legal, there are additional requirements for documentation and record keeping that must be followed. Providers should visit the West Virginia Board of Pharmacy website to ensure any vendor used to obtain medications is WV licensed. Providers outside of West Virginia may visit the FDA's website to find a list of U.S. state agencies responsible for licensing wholesaler prescription drug distributers in each state. The link to each of these webpages can be found at the end of the article.
The second element of compliance relates to medication labeling. Beginning in November 2023, only products that have all required identifiers may be obtained unless exempt or grandfathered. There are four required identifiers. Most practitioners are already familiar with two of them which are lot numbers and expiration dates, however there are two additional identifiers which must be included on all units of sale which are a Serial Number and well as a Global Trade Item Number or GTIN. The serial number is the number that is used to follow the transaction history of a medication beginning with the manufacturer. This tracing may be done via a T3 report which must be supplied by all wholesalers. The GTIN is a unique and internationally recognized identifier for a product which is used to link corresponding products across databases. It should be noted that several products are exempt from these requirements.

Exempt products include:

- Blood and Blood components intended for transfusion
- Radioactive drugs and radioactive biological products
- Medications used for imaging
- Dialysis solution, fluids, electrolytes, and sterile water
- Medical gasses
- Homeopathic medications
- Medications compounded by 503A or 503B facilities

Although most practices are likely already compliant with these requirements, providers and office managers should be aware of the corresponding documentation. Offices should be prepared to readily present their documentation history should they be subject to regulatory audits as well as knowing the warning signs of counterfeit drugs that may prompt an investigation into their validity.

Referenced Links

1) https://www.wvbop.com/public/verify/index.asp

2) https://www.fda.gov/drugs/drug-supply-chain-integrity/verify-wholesale-drug-distributor-licenses

SGLT2 Inhibitors in Kidney Disease

Robert B. Stanton

A new major clinical trial, EMPA-KIDNEY, showed that empagliflozin (Jardiance) had a beneficial outcome in patients with kidney disease who did not have concurrent diabetes or heart failure. These results add to the results of the DAPA-CKD trial where dapagliflozin (Farxiga) in patients with and without Type 2 Diabetes Mellitus (patients with Type 1 Diabetes Mellitus were excluded from the trial) were evaluated. However, patients with underlying cardiovascular diseases were not excluded from the DAPA-CKD trial. The FDA approved dapagliflozin in 2021 for chronic kidney disease. The EMPA-Kidney trial looked at patients with underlying renal disease and excluded those patients with diabetes or heart failure giving a clearer picture of the effect of SGLT2 Inhibitors on renal disease alone. The weight of these two major clinical trials, along with the original CREDANCE trial for patients with diabetes and renal impairment, provides evidence that SGLT2 Inhibitors reduce mortality in patients with renal disease, including those patients with or without Type 2 Diabetes Mellitus and/or without Heart Failure. Both empagliflozin and dapagliflozin have FDA-approved indications for heart failure as well.

References

1. The EMPA-KIDNEY Collaborative Group. *Empagliflozin in Patients with Chronic Kidney Disease*. N Engl J Med. Published online November 4, 2022 Empagliflozin in Patients with Chronic Kidney Disease | NEJM
2. Heerspink HJL, Stefansson BV, Correa-Rotter R, and others. *Dapagliflozin in Patients with Chronic Kidney Disease.* N Engl J Med. October 8, 2020 https://www.nejm.org/doi/pdf/10.1056/NEJMoa2024816

Suicide Prevention Awareness and 988

Tiffany Davis, PharmD, R.PH.,TTS

In 2020, intentional self-harm was the 12th leading causes of death in the United States.[1] Even more concerning is the provisional data from the CDC's National Center on Health Statistics showing that both the number and rate of US suicide increased by 4% between 2020 and 2021.[2]

The fact that suicide is the 10th leading cause of death in West Virginia[3] gives credit to the National Alliance on Mental Illness (NAMI) report that "West Virginians struggle to get the help they need."[5] The statistics are staggering. West Virginia was ranked 10th among the states regarding rate/number of suicides (2020 ranking), a major jump from the 2019 16th ranking. Prior to 2019, WV had been in the 7th place position for several years. Suicide is an issue for which everyone should be concerned.

What can we do to help?

- Know the warning signs and risk factors
- Know where to get help
    - Although the 10-digit national Suicide Prevention Lifeline (800-273-8255) will remain in place, a more easily remembered 3-digit number was enacted this past July, **988.** This change also formally marks the expansion of the "Lifeline" to include mental, emotional, and substance abuse crises in addition to suicide crises. [4]
    - If you or someone you know is experiencing a mental health crisis, NAMI suggests contacting the resources below to be connected with a free crisis counselor.
        - Chat: www.988lifeline.org
        - Call or text: 988
        - Text "NAMI" to 741-741

Get involved

- Consider offering QPR (Question, Persuade, Refer) or Mental Health First Aid training to help patients identify people in crisis.
  - https://qprinstitute.com/
  - https://www.mentalhealthfirstaid.org/
- Become a mental health advocate by emailing Congress to request more crisis response infrastructure funding or by working with state policymakers.

Suicide Warning Signs and Risk Factors

Adults:

- Alcohol and drug overuse
- Changes in sex drive, eating or sleeping habits
- Excessive worrying or fear
- Prolonged irritability or anger
- Avoiding friends and social activities
- Thinking/talking about suicide

Children

- Frequent aggression, temper tantrum, or defiance
- Frequent nightmares
- Excessive worry or anxiety (which may manifest as fighting to avoid school or bed)
- Changes in school performance

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2. Curtin SC, Garnett MF, Ahmad FB. Provisional numbers and rates of suicide by month and demographic characteristics: United States, 2021. Vital Statistics Rapid Release; no 24. September 2022. DOI: https://dx.doi. org/10.15620/cdc:120830
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4. https://nami.org/NAMI/media/NAMI-Media/PDFs/NAMI-FAQs-for-Nationwide-Availability-of-988.pdf (accessed 11.30.2022)
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