In This Issue

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Can Semaglutide Revolutionize Weight-Loss?

By: Gilnou Pamphile, Pharm.D., MS

Background: Obesity is a growing global health concern, and it has significant implications for both physical and mental health.[1] The World Health Organization states that obesity has nearly tripled since 1975.[2] While only about 1% of the children and adolescents aged 5 to 19 were obese in 1975, more than 124 million in that age range were considered obese in 2016.[2] Obesity has been associated with several health issues including type 2 diabetes, cardiovascular disease, hypertension, depression, and anxiety.[3-5] Addressing obesity requires a comprehensive approach involving lifestyle modifications, such as adopting a balanced diet, increasing physical activity, and incorporating behavioral changes. Semaglutide (Wegovy®;Novo Nordisk), is approved by the Food and Drug Administration (FDA) as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in the following patients: adults with an initial body mass index (BMI) of ≥30 kg/m^2 (obesity) or ≥27 kg/m^2 (overweight) with the presence of at least one weight-related comorbid conditions (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia) and children ≥ 12 years old with an initial BMI ≥95 percentile for their age and sex (obesity).[6]

Mechanism of Action: Semaglutide functions as a selective glucagon-like peptide-1 (GLP-1) receptor agonist increasing insulin production in response to elevated blood glucose levels.[6,7] It also slows gastric emptying prolonging the feeling of fullness after eating and thus works as an appetite suppressant by targeting areas of the brain responsible for hunger and cravings.

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Elfabrio™ for Fabry Disease

By: Rachel Dittrich, Pharm.D.

What is Fabry Disease? Fabry Disease (FD) is a rare, progressive, X-linked lysosomal storage disorder caused by a partial or complete deficiency of the alpha-galactosidase A (AGAL) enzyme due to mutations in the AGAL gene.[1] This enzyme deficiency causes an accumulation of glycosphingolipids mainly globotriaosylceramide (Gb3) in the various organs and tissues often leading to multisystem abnormalities such as renal insufficiency, cardiomyopathy, recurrent strokes, gastrointestinal pain, as well as "Fabry Crises", commonly consisting of fever and neuropathic pain.[1] The National Fabry Disease Foundation estimates that over 7,000 patients are affected by FD in the United States.[2]

What agents are currently available to treat Fabry Disease? Current FD treatment options approved in the United States include recombinant enzyme replacement therapy (ERT) and chaperone therapy.[2] In 2003, agalsidase beta (Fabrazyme®; Sanofi Genzyme) was the

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Clinical Trials The safety and efficacy of semaglutide were studied separately in adults (STEP1) and adolescents (STEP TEENS) through two randomized, double-blind, placebo-controlled trials.[4,5] In both studies, the patients were administered either semaglutide or placebo injections once a week for 68 weeks and monitored for an additional 7 weeks. The dosage of semaglutide in both trials started at 0.25 mg and gradually increased to the target dose of 2.4 mg over 16 weeks. The co-primary endpoints for the STEP1 trial were the percentage change in body weight from baseline to week 68 and the achievement of a reduction of ≥ 5% of body weight from the baseline to week 68. The primary endpoint for the STEP TEENS trial was the percentage change in BMI from baseline to week 68. STEP1 randomized a total of 1961 participants to receive semaglutide (n=1306) or placebo (n=655).[4] Participants were mainly female (74.1%) and white (75.1%) with a mean age of 46 years. The semaglutide treatment group had an estimated mean weight change at week 68 of -14.9% compared to -2.4% in the placebo group (estimated treatment difference, -12.4 percentage points; 95% CI, -13.4 to -11.5; p<0.001). More patients in the treatment group than the placebo group achieved weight reductions of 5% or more (86.4% versus 31.5%, respectively). The STEP TEENS trial randomized 201 participants to receive semaglutide (n=134) or placebo (n=67).[5] Participants were mainly female (62%) and white (79%) with a mean age of 15.4 years. The mean estimated percentage change in BMI from baseline to week 68 was -16.1% for the semaglutide treatment group compared to 0.6% for the placebo group (estimated difference, -16.7 percentage points; 95% CI, -20.3 to -13.2; p<0.001). Adverse events reported in the two studies were similar with gastrointestinal (GI) disorders such as nausea, diarrhea, vomiting and constipation being the most common. Ultimately, both trials concluded that semaglutide 2.4 mg once weekly injection plus lifestyle interventions was associated with a clinically relevant and greater reduction in BMI when compared to lifestyle interventions alone.[4,5]

Dosing and Administration: The dosage initiation and escalation schedule of Wegovy® for weight loss in adult and pediatric patients is listed in Table 1. Patients who cannot tolerate the 2.4 mg once-weekly dose, can be decreased to 1.7 mg for a maximum of 4 weeks.[6] The 2.4 mg dose should be reinitiated after the 4-week period and if the patient cannot tolerate the dose, the medication must be discontinued.

Table 1. Wegovy® Dosing Schedule[6]

Weeks	Weekly Dose	
1 through 4	0.25 mg/ 0.5 mL	Dose escalation
5 through 8	0.5 mg/ 0.5 ml	
9 through 12	1 mg/ 0.5 mL	
13 through 16	1.7 mg/ 0.75 mL	
17 and onward	2.4 mg/ 0.75 mL	Maintenance weekly dose

Pharmacist's Considerations: Patients should be counseled on all potential side effects and risks associated with semaglutide such as GI disorders, thyroid C-cell tumors, acute kidney injury, and suicidal ideation.[6,7] Additionally, all patients taking semaglutide for weight loss should be encouraged to incorporate dietary and physical lifestyle changes. Due to the risk of weight regain, patients should be informed that this therapy may be life-long to maintain weight loss.[7,8] The average wholesale price of Wegovy® is $404.71 per injectable pen totaling $1,618.84 for a month's supply.[9] Ozempic®, a semaglutide medication FDA-approved as a type 2 diabetes treatment, is being used off-label for weight loss.[7] The popularity of Ozempic® and Wegovy® has led to shortages of these medications.[10] Therefore, healthcare providers should consider the other four agents approved for long-term weight management as options for their patients: liraglutide, orlistat, naltrexone plus bupropion, and phentermine plus topiramate.[11-14] Moreover, the FDA is now investigating the use of tirzepatide (Mounjaro®; Eli Lilly), a GLP-1 receptor agonist combined with glucose-dependent insulinotropic peptide, for obesity treatment, as it mimics natural hormones within the body to suppress hunger.[7]

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first ERT on the market.[3] Approximately 83% of patients who receive Fabrazyme® develop anti-drug antibodies reducing its efficacy and leading to further estimated glomerular filtration rate (eGFR) reductions and ongoing cardiac hypertrophy. Before Fabrazyme®, patients received migalastat (Galafold®; Amicus Therapeutics), a chaperone therapy that is only effective in patients with specific mutations.[4] Pegunigalsidase alfa-iwxj (Elfabrio™; Chiesi USA) was created to provide a safe and tolerable therapy for all patients diagnosed with FD, regardless of specific mutations.[2,5] In May 2023, Elfabrio™ was approved by the Food and Drug Administration (FDA) for the treatment of adults with confirmed FD.[5]

What is the mechanism of action of Elfabrio™?
Elfabrio™ provides an exogenous source of AGAL that is internalized and transported into lysosomes to exert enzymatic activity and reduce the accumulation of Gb3.[5]

What clinical trial led to the FDA approval of Elfabrio™? The BALANCE trial was a randomized, double-blind, 2-year, phase III study to examine the safety and efficacy of pegunigalsidase alfa compared to agalsidase beta.[2,6] This study included 78 adults with FD and impaired kidney function who received treatment with agalsidase beta for at least 1 year before enrollment. Participants were randomized to receive at least one dose of pegunigalsidase alfa (n=52) or agalsidase beta (n=25). Both therapies were administered as an intravenous (IV) infusion dose of 1 mg/kg every 2 weeks for up to 104 weeks. The primary endpoint was to determine non-inferiority between the two treatment groups in the median annualized estimated eGFR over a 104-week period. The annualized rate of change in eGFR assessed over 104 weeks was -2.4 mL/min/1.73 m^2/year in the pegunigalsidase alfa group and -2.3 mL/min/1.73 m^2/year in the agalsidase beta group with a difference of -0.1 (95% CI:-2.3 to 2.1). This result met non-inferiority requirements. The rate of infusion-related reactions (IRRs) per 100 infusions was significantly lower in the pegunigalsidase alfa group compared to the agalsidase beta group (0.5 events per 100 infusions versus 3.9 events per 100 infusions, respectively; p<0.0001). In the pegunigalsidase alpha group, the percentage of anti-drug antibodies declined from 35% at baseline to 23% at 2 years compared to a reduction of 32% at baseline to 26% in the agalsidase beta group. The authors concluded that pegunigalsidase alfa demonstrated noninferior efficacy to agalsidase beta based on the rate of eGFR decline over 2 years with a lower rate of treatment-emergent adverse events including IRRs.

What are the common side effects of Elfabrio™?
The most common adverse effects (>15%) of Elfabrio™ are IRRs, nasopharyngitis, headache, diarrhea, fatigue, nausea, back pain, pain in extremities, and sinusitis.[5]

What are the dosing and administration of Elfabrio™? Elfabrio™ is administered as an IV infusion every 2 weeks at a 1 mg/kg dose based on actual body weight.[2,5] It should be infused via a dedicated line utilizing a low protein-binding 0.2-micron in-line filter. Afterwards, the line should be flushed with normal saline at the same infusion rate as the drug. Before administration, it is recommended to pre-medicate both ERT-naïve and experienced patients with antihistamines, antipyretics, and/or corticosteroids. Infusion rates for ERT-experienced patients are based on actual body weight and are listed in the package insert. Patients receiving Elfabrio™ have experienced hypersensitivity reactions, including anaphylaxis, which has lead to a Black Box Warning stating that appropriate medical support measures, including cardiopulmonary resuscitation equipment, should be readily available during administration. If hypersensitivity should occur the drug must be immediately discontinued and appropriate medical treatment initiated.

How does Elfabrio™ differ from Fabrazyme®?
Unlike Fabrazyme®, Elfabrio™ is not currently FDA-approved for pediatric patients.[2,3,5] However, ongoing trials are evaluating its use in pediatric patients as well as extending its dosing interval from 2 to 4 weeks.[2]

What is the cost and availability of Elfabrio™? Elfabrio™ is packaged as a 20 mg/10 mL vial (NDC: 10122-0160-02) at $496.21 per mL.[2,5] The annual cost of therapy for a 100 kg patient is approximately $600,000.[2] There is a patient assistance program available through the manufacturer's website.[5]

What is the formulary status of Elfabrio™? Elfabrio™ was added to the Adult CCHS Formulary restricted to the Department of Hematology and Oncology for outpatient use only.

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Additions to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Alfibercept (Eylea® HD) Intravitreal Injection	VEGF Inhibitor	nAMD DME DR	Restricted to the Department of Ophthalmology for outpatient use only
Cipaglucosidase alfa (Pombiliti™) Intravenous Injection and Miglustat (Opfolda™) capsule	Enzyme and Enzyme Stabilizer	Late Onset Pompe Disease	Restricted to the Department of Hematology/ Oncology for outpatient use only
Dostarlimab-gxly (Jemperli®) Intravenous Injection	PD-1 Inhibitor	Primary Advanced or Recurrent Endometrial Cancer	Restricted to the Department of Gynecology/ Oncology and the Department of Hematology/ Oncology for the treatment of endometrial cancer in the outpatient setting
Liposomal Daunorubicin and Cytarabine (Vyxeos®) Intravenous Injection	Antineoplastic Agent	t-AML AML-MRC	Restricted to the Department of Hematology/ Oncology for outpatient use only. Patients will be reviewed for Vyxeos® by the Leukemia Tumor Board
Rozanolixizumab-noli (Rystiggo®) Subcutaneous Injection	Monoclonal Antibody	gMG	Restricted to the Department of Neurology for outpatient use only in patients with refractory gMG positive for AChR or MuSK antibodies

VEGF=Vascular endothelial growth factor nAMD=Neovascular age-related macular degeneration DME=Diabetic macular edema
DR=Diabetic retinopathy PD-1=Programmed death receptor-1 t-AML=Therapy-related acute myeloid leukemia
AML-MRC= Acute myeloid leukemia with myelodysplasia-related changes gMG=Generalized myasthenia gravis
AChR=Acetylcholine receptor MuSK-=Muscle-specific tyrosine kinase

Additions to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Sulbactam-Durlobactam (Xacduro®) Intravenous Injection	Antibiotic	HAP VAP VP	Restricted to the Department of Infectious Diseases for the treatment of a known or history of carbapenem-resistant Acinetobacter that is resistant to other recommended therapies, including OXA-producing Acinetobacter-identified by genotypic testing, or after failure of other susceptible agents Sulbactam-durlobactam will be added to the antimicrobial list for the Medication Dose Optimization and Monitoring Standard Operating Procedure.
Upadacitinib (Rinvoq®) Tablet	JAK Inhibitor	UC CD	Restricted to the Department of Gastroenterology for initiation of therapy in patients with moderate to severe UC or CD; however, continuation of therapy from home is not restricted

HAP=Hospital-acquired bacterial pneumonia VAP=Ventilator-associated bacterial pneumonia VP=Ventilator pneumonia
JAK=Janus kinase UC=Ulcerative colitis CD=Crohn's disease

Denial to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Comments**
Vilobelimab (Gohibic™) Intravenous Injection	Monoclonal Antibody	Treatment of COVID-19 Infections	Vilobelimab was not added since the Infectious Diseases Society of America has not commented on its use for the treatment of COVID-19 infections and the National Institutes of Health guidelines state that there is insufficient evidence to recommend it.

COVID-19=Coronavirus disease 2019

Changes in Restrictions to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Albumin 5% Intravenous Injection	Blood Product	Plasma Volume Expander	Modified restrictions to include: Use by Dr. Adriano Tonelli for patients with autonomic dysfunction and/or preload insufficiency refractory to traditional therapies. Patients would only be offered this treatment if they experience significant improvement in symptoms and longer duration of effect than with crystalloids
Lanreotide (Somatuline® Depot) Subcutaneous Injection	Somatostatin Analog	Gastroenteropancreatic Neuroendocrine Tumors	Modified restrictions to include: Use by Dr. Michelle Kim from the Department of Gastroenterology in the outpatient setting
Meperidine (Demerol®) Injection	Opioid	Pain Management Hypothermia Rigors Post-operative Shivering	Added restrictions for use in surgical and perioperative areas or use for shivering or rigors

Product Standardizations of the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Acetylcholinesterase Inhibitor Therapeutic Interchange	Acetylcholinesterase Inhibitor	Alzheimer's Dementia Parkinson's Disease	A therapeutic interchange involving conversion of donepezil ODT to IR tablets and galantamine ER and oral solution to IR tablets was approved. Details are in Lexicomp. Rivastigmine will not be part of the therapeutic interchange.
Amoxicillin-Clavulanate Therapeutic Interchange	Antibiotic	Various Infections	A therapeutic interchange based on renal function for amoxicillin-clavulanate XR to amoxicillin-clavulanate IR was approved. Details are in Lexicomp.
Mesalamine Extended-Release Products	5-Aminosalicylic Acid Derivatives	Ulcerative Colitis	A therapeutic interchange for mesalamine extended-release products to balsalazide was approved. Details are in Lexicomp.

ODT=Oral disintegrating tablet IR=Immediate-release ER=Extended-release XR=Extended-release

Removals from the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Comments**
Amoxicillin-clavulanate 1000 mg/62.5 mg (Augmentin® XR) Tablets	Antibiotic	Various Infections	Please refer to the Adult Product Standardization section for further details
Galantamine ER Tablets and Oral Solution	Acetylcholinesterase Inhibitor	Alzheimer's Dementia Parkinson's Disease	Please refer to the Adult Product Standardization section for further details

XR=Extended-release ER=Extended-release

Process Changes to the Adult CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Comments**
Anticoagulants and Antibiotics	Anticoagulant Antibiotic	Various Indications	The following medications were added to the Medication Dose Optimization and Monitoring SOP: 1. Apixaban* 2. Dabigatran* 3. Enoxaparin* 4. Rivaroxaban* 5. Sulbactam-durlobactam Antimicrobial prophylaxis dosing was also added to this SOP. Details are in PPM.
Antiretroviral Therapy Injectable	Antiretroviral	Treatment and Prevention of HIV Infection	An Adult (18+) Infectious Diseases Injectable Antiretroviral Services SOP for a Pharmacist Consult Agreement was established. Details are in PPM.
Hepatitis C Medications	Antiviral Agents	Treatment of Hepatitis C	A Pharmacy Consult Agreement for Hepatitis C medications was established. Details are in PPM.
RSVpreF Vaccine (Abrysvo®)	Vaccine	Prevention of RSV Infection in Infants	The CCHS will endorse the practice of providing RSVpreF vaccine to pregnant women between 32 and 36 weeks gestational age to prevent RSV infection in the infant.

*Dose Optimization and Monitoring have not yet been implemented for this medication
PPM=Policy and Procedure Manager HIV=Human immunodeficiency virus SOP=Standard of practice RSV=Respiratory syncytial virus

Changes in Restrictions to the Pediatric CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Restrictions/Comments**
Immune Globulin (Gammagard®) Intravenous Injection	Blood Product Derivative	DSRD	Modified restrictions to include possible or probable DSRD based on evaluation and recommendation by Pediatric Neurology
Ivabradine (Corlanor®) Tablet and Oral Solution	Cardiovascular Agent	Stable Symptomatic Heart Failure due to DCM	Modified restrictions to state: Initiation of ivabradine is restricted to the Department of Pediatric Cardiology, Department of Pediatric Heart Failure/Transplant, and Department of Pediatric Intensive Care. Continuation of therapy from home is not restricted.
Midazolam Intranasal Syringe	Benzodiazepine	Procedural Sedation Treatment of Seizures	Modified restrictions to include patients of all ages.

DSRD=Down syndrome regression disorder DCM=Dilated cardiomyopathy

Process Change for the Pediatric CCHS Formulary			
Drug	**Pharmacologic Class**	**Formulary Use**	**Comments**
Antibiotics	Antibiotic	Various Indications	Medication Dose Optimization and Monitoring SOP additions: 1. The addition of prophylactic antimicrobial dosing was added to the Antimicrobial Dosing Guidelines for pediatric patients ≥1 years of age 2. Please refer to the Adult Process Changes for more details.

SOP=Standard of practice