Virginia Medicaid DUR Quarterly Newsletter

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Introduction

In this issue of the quarterly Drug Utilization Review (DUR) newsletter we look at the new gene therapy drug approved for spinal muscular atrophy, the new esketamine drug approved for treatment resistant depression (TRD) and the American Diabetes Association living standards for diabetes.

HOT TOPIC: GENE THERAPY APPROVED FOR SPINAL MUSCULAR ATROPHY

The United States (US) Food and Drug Administration (FDA) approved onasemnogene abeparvovec-xioi (Zolgensma®) for the treatment of patients < 2 years of age with spinal muscular atrophy (SMA) who have bi-allelic mutations in the survival motor neuron 1 (SMN1) gene, which instructs production of a protein critical for motor neuron function. SMA is the leading genetic cause of infant mortality. The most common form, SMA type 1, occurs in about 1 in 10,000 newborns, leading to about 500 new cases per year in the US. Patients with SMA type 1 experience progressive motor function decline beginning shortly after birth. If left untreated, permanent ventilation or death often occurs by 2 years of age. Zolgensma is the only gene replacement therapy approved for SMA. It is administered as a 1-time intravenous (IV) infusion over 1 hour and is used as part of a multidisciplinary approach to treat SMA type 1. In December 2016, the SMN2- directed antisense oligonucleotide nusinersen (Spinraza®) became the first disease-modifying therapy to treat SMA (all types) in pediatrics and adults; maintenance therapy is given intrathecally every 4 months.

Zolgensma was granted Breakthrough Therapy and Orphan Drug designations as well as Priority Review. FDA-approval of Zolgensma is supported by the ongoing STR1VE trial (n=21) and the completed 2-year START trial (n=12, therapeutic

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DUR BOARD MEETINGS

September 12, 2019	June 11, 2020
December 12, 2019	September 10, 2020
March 12, 2020	December 10, 2020

P&T COMMITTEE MEETINGS
September 19, 2019

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cohort). Both studies enrolled patients with SMA type 1. Treatment with Zolgensma led to significant improvement in reaching developmental motor milestones, such as head control, sitting without support, and/or standing/walking without assistance compared to the natural history of the disease. A durable effect of nearly 4 years was reported in the START long-term follow-up. Zolgensma carries a Boxed warning for acute serious liver injury.

Avexis/Novartis set a wholesale acquisition cost (WAC) of $2.125 million for the 1-time Zolgensma dose, making it the world's most expensive drug. The Institute for Clinical and Economic Review (ICER) published a value-based price benchmark for Zolgensma of $1.2 million to $2.1 million to reach a cost-effectiveness threshold of $100,000 to $150,000 per life year gained (LYG). This amount assumes durable effectiveness and considers the positive results of the SPR1NT trial in presymptomatic patients (< 6 months of age). Safety and efficacy of repeat administration have not been studied, nor has use in patients with advanced SMA (complete limb paralysis or permanent ventilator dependence). While Spinraza use after Zolgensma therapy has been reported, clinical benefits and risks have not been established. Zolgensma is available as patient-specific kits through a specialty pharmacy distributor. The company is working closely with payers to create 5-year outcome-based agreements and novel pay-over-time options.

ESKETAMINE APPROVED FOR TREATMENT-RESISTANT DEPRESSION (TRD)

The FDA approved Janssen's esketamine nasal spray (Spravato™), in combination with an oral antidepressant, for the treatment of TRD in adults. The N-methyl D-aspartate (NMDA) receptor antagonist was granted Breakthrough Therapy and Priority Review. Esketamine is the s-enantiomer of the anesthetic agent ketamine. Product labeling carries Boxed Warnings regarding the risks of sedation, dissociation, abuse and misuse, as well as suicidality. Due to these risks, esketamine must be dispensed only to a certified medical office, where the patient self-administers the dose and is monitored by a healthcare professional for at least 2 hours. The patient should not drive or operate machinery until the following day. Each nasal spray device contains a total of 28 mg of esketamine, delivered as 2 sprays. Initial dosage is 56 mg twice per week for 4 weeks, then 56 mg or 84 mg once weekly for 4 weeks, and 56 mg or 84 mg every 1 or 2 weeks thereafter.

In clinical trials in patients with TRD, when given with oral antidepressant therapy, esketamine demonstrated superior improvement in depressive symptoms at day 28 compared to placebo. In a long-term study, patients treated with esketamine were 51% less likely to relapse than those who received placebo. Esketamine is a Schedule III controlled substance and is only available through a restricted Risk Evaluation and Mitigation Strategy (REMS) program.

ADA LIVING STANDARDS FOR DIABETES

The American Diabetes Association (ADA) has established their Standards of Medical Care in Diabetes as a "living" document where new pertinent information is incorporated as appropriate. Recently, data from the REDUCE-IT trial demonstrated a reduction in cardiovascular (CV) events with the lipid-regulating agent icosapent ethyl (Vascepa®). This data led to a recommendation to consider the lipid-regulating agent for select patients with diabetes and atherosclerotic CV disease (ASCVD) or other cardiac risk factors if the patient's low density lipoprotein cholesterol (LDL-C) is controlled with statin therapy but elevated triglycerides levels (135 to 499 mg/dL) persist. Furthermore, the DECLARE-TIMI 58 trial revealed that treatment with dapagliflozin (Farxiga®) resulted in reductions in hospitalization for heart failure (HF) and progression of chronic kidney disease (CKD) in patients with type 2 diabetes mellitus (T2DM). As a result, the ADA added dapagliflozin as an antidiabetic option in patients with HF or risk of CKD. Based on dapagliflozin labeling revisions for patients with diabetes and CKD, the approved use per estimated glomerular filtration rate (eGFR) has been revised from ≥ 60 mL/min/1.73 m^2 to ≥ 45 mL/min/1.73 m^2.

June DUR Board Summary

The Board reviewed 1 new medication - Inbrija™. The Board also reviewed 3 physician administered drugs – Intravenous Immune Globulins (IVIG), Mozobil® and Imlygic®. Approved service authorization criteria are listed at the end of this newsletter. Additionally, the Board reviewed the results of several utilization analyses: children with peanut allergies,

compounded prescriptions, adult and pediatric narcotic utilization, concurrent use of opioids and benzodiazepines, opioids use with risk factors and no naloxone and antipsychotic duplication.

The next DUR Board meeting is scheduled for September 12, 2019.

The minutes from the June 2019 meeting can be found at:
https://www.virginiamedicaidpharmacyservices.com/provider/drug-utilization-review/

New Clinical Service Authorizations

Brand Name	Generic Name	Indication
Physician Administered Drugs		
IV Immune Globulins	immunoglobulin	IVIG is FDA indicated for use in primary immunodeficiency where antibody production is absent or deficient.
Mozobil®	plerixafor	A hematopoietic stem cell mobilizer which is indicated in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize hematopoietic stem cells (HSCs) to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma and multiple myeloma.
Imlygic®	talimogene laherparepvec	Imlygic is a genetically modified oncolytic viral therapy indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery.

References:

https://www.fda.gov/

http://diabetes.org/

https://www.janssen.com/

https://www.avexis.com/

https://icer-review.org/