Pharmacy Focus:
Lenmeldy™ — New Gene Therapy for Metachromatic Leukodystrophy (MLD)

Key Takeaways Regarding Lenmeldy™

- Lenmeldy was approved by the FDA March 18, 2024; it had received Priority Review, Orphan Drug, Rare Pediatric Disease, and Regenerative Medicine Advanced Therapy (RMAT) designations.
- This was the first FDA-approved treatment option for children with pre-symptomatic late infantile, pre-symptomatic early juvenile or early symptomatic early juvenile Metachromatic Leukodystrophy.
- The projected cost of Lenmeldy is $4.25 million plus hospitalization costs.

Metachromatic Leukodystrophy (MLD) Disease Overview[1-4]

Metachromatic Leukodystrophy (MLD) is a rare, fatal, recessive genetic disorder caused by a mutation in the arylsulfatase-A (ARSA) gene in which the ARSA enzyme is not produced as needed. Without the ARSA enzyme, fats accumulate in the brain, nervous system and other parts of the body causing loss of motor function (i.e., walking difficulties), gradual cognitive decline and eventual death. It is estimated that about 50 percent of children with the most aggressive form of MLD will pass away within five years of disease onset.

MLD is comprised of three major subtypes divided by the age of disease onset: late infantile onset (six months to two years of age), juvenile onset (three to 16 years of age), and adult onset (16 years or older). Exact prevalence is unknown, but MLD is estimated to affect one in every 100,000 births with males and females both affected. Some symptoms that may occur but will depend on the subtype include seizures, difficulty talking, changes in personality and behavioral changes. The last stage of the disease can progress to include symptoms of blindness, unresponsiveness and the inability to speak or move.

Currently, there is no universal newborn screening for MLD in the United States. Symptoms such as walking difficulties/motor delays in children or speech/behavior changes in adults can alert to a possible diagnosis of MLD. An exact diagnosis of MLD is proven by genetic testing and biochemical assays to analyze ARSA enzyme activity. An MRI also will show myelin loss in the individual's brain confirming the diagnosis.

Current Treatment Options[1-4]

Currently, there is no cure for MLD. Supportive care is the general standard of care for MLD and will become more intensive as the disease progresses, ranging from physical therapy to ventilators. Allogeneic hematopoietic cell transplantation (HSCT) is a potential option for those having no or very early MLD symptoms, as it may stop disease progression through the introduction of healthy donor cells that can produce the deficient enzyme. Treatment with HSCT, however, comes with many risks and potential complications with each step of the process – from the severe side effects related to the chemotherapy conditioning regimens to graft-versus-host disease following transplantation.

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Lenmeldy™ Overview[5-9]

Lenmeldy (atidarsagene autotemcel) was approved on March 18, 2024, and is the first FDA-approved gene therapy treatment for pre-symptomatic late infantile, pre-symptomatic early juvenile or early symptomatic early juvenile Metachromatic Leukodystrophy (MLD). Prior to approval in the United States, Lenmeldy was approved by the European Commission in 2020 with the name of Libmeldy. It is important to note that most symptomatic patients are unlikely to be considered eligible for Lenmeldy due to the rapid progression of the disease.

Lenmeldy is an autologous hematopoietic stem cell-based gene therapy, meaning the patient's own stem cells are collected, genetically modified to include functional copies of the missing gene, and then infused back into the patient. Prior to infusion of the genetically modified cells, patients undergo myeloablative conditioning (intensive chemotherapy) to rid the body of cells with the gene mutation and allow for the new cells to take over.

Many of the adverse effects reported were from the busulfan conditioning or disease progression rather than the treatment itself and included fever, infections, low white blood cell count, enlarged liver and gastrointestinal infections. Other warnings/precautions for Lenmeldy include blood clotting (thrombosis) events, swelling of the brain (encephalitis), serious infections and a potential risk of blood cancers (although no cases have been reported in those treated with Lenmeldy thus far).

Approval for Lenmeldy was based on two single-arm, non-randomized, open-label, phase I/II trials and expanded European access trials where 37 children with a diagnosis of pre-symptomatic or early symptomatic early onset MLD were treated with Lenmeldy. Compared to a 58 percent survival rate in untreated children, all children in the study were still alive at six years of age, and 71 percent were able to remain ambulatory without help at five years of age. These results demonstrate that Lenmeldy helps to significantly extend overall survival, as well as preserving motor function and cognitive skills past the usual age of severe cognitive and motor impairments in untreated children.

The cost of Lenmeldy is projected to be $4.25 million in the United States for the drug acquisition cost alone. Due to the intensive chemotherapy required to receive this treatment, ancillary costs are also likely to be associated with hospitalization and acute care under the medical benefits.

Cost Containment Considerations

As part of its HMConnects™ cost containment program, HM Insurance Group (HM) works to support cost management opportunities around the use of gene and cell therapies and other high-cost pharmaceutical treatment options that can impact our clients' bottom line. The Pharmacy Operations (RxOps) team watches the market – and our book of business – to anticipate how current and future advancements will impact financial risk levels for HM's client base. Standard practices include reviewing, auditing and collaborating on the content of current policies, monitoring trends and implementing appropriate cost savings techniques. Additional practices include the prevention of stockpiling, working to ensure prescriptions are filled via in network pharmacies and assessing to determine if patients are properly dosed based on weight and lab values when appropriate. All these services are provided to HM's clients at no additional cost to them.

Pharmacy Focus provides valuable information about pharmaceutical industry developments and their associated costs that can impact the growing claims trend in the self-funded insurance market. Be aware of influences and gain insight into approaches that may help to contain costs. Please share topic suggestions or feedback with **HMPharmacyServices@hmig.com**.

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