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Gene Therapy Medication Update

Cellular and gene therapy-related research and development in the United States continues to grow at a fast rate, with a number of products advancing in clinical development. The Center for Biologics Evaluation and Research (CBER) regulates cellular therapy products, human gene therapy products and certain devices related to cell and gene therapy. CBER uses both the Public Health Service Act and the Federal Food, Drug and Cosmetic Act as enabling statutes for oversight of these medications.

Human gene therapy seeks to modify or manipulate the expression of a gene or to alter the biologic properties of living cells for therapeutic use. Gene therapy is a technique that modifies a person's genes to treat or cure disease. Gene therapies can work by several different mechanisms: replacing a disease-causing gene with a healthy copy of the gene, inactivating a disease-causing gene that is not functioning properly or introducing a new or modified gene into the body to help treat a disease. Gene therapy products are currently being studied to treat diseases including cancer, genetic diseases and infectious disease.

The following gene therapy products are available for use in the United States:

- Imlygic (talimogene laherparepvec) – indicated for the local treatment of unresectable cutaneous, subcutaneous and nodal lesions in patients with recurrent melanoma after initial surgery. This agent uses a modified herpes simplex virus to induce tumor lysis and deliver localized expression of granulocyte colony-stimulating factor (GM-CSF) to injected lesions. The National Comprehensive Cancer Network (NCCN) guidelines recommend this agent as a category 1 recommendation for treatment of Stage III-IV melanoma. It has also been studied for treatment of advanced, unresectable melanoma in combination with ipilimumab.

- Kymriah (tisagenlecleucel) – indicated for patients up to age 25 with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse. It is also indicated for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic chemotherapy including diffused large B-cell lymphoma (DLBCL), high grade B-cell lymphoma and DLBCL arising from follicular lymphoma. For ALL, the NCCN guidelines recommend this agent as a clinical option for patients less than 26 and with refractory disease or two more relapsed and failures of two tyrosine kinase inhibitors (TKIs) such as imatinib, nilotinib, dasatinib and ponatinib. For relapsed B-cell lymphoma, this agent is recommended as a clinical option. However, high-dose chemotherapy with autologous stem cell rescue is considered the preferred treatment modality.

- Laviv (Azficel-t) – indicated for improvement of the appearance of moderate to severe nasolabial fold wrinkles in adults.

- Luxturna (voretigene neparvovec-rzyl) – an adeno-associated virus vector-based gene therapy indicated for the treatment of patients with confirmed biallelic RPE65 mutation-associated retinal dystrophy.

- Provenge (sipuleucel-T) – indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer. The NCCN guidelines recommend this agent as a category 1 recommendation for castration resistant prostate cancer after progression of the disease following treatment with apalutamide (Erleada) or enzalutamide (Xtandi).

- Yescarta (axicabtagene ciloleucel) – CD19-directed genetically modified autologous T-cell immunotherapy indicates for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy. The NCCN guidelines only recommend this treatment after two or more prior chemoimmunotherapy regimens.

- Zolgensma (onasemnogene abeparvovec-xioi) – indicated for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy (SMA) with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene. Mutations in the SMN1 gene lead to survival motor neuron (SMN) protein deficiency that causes motor neuron loss in the brainstem and spinal cord, leading to weakness and muscle atrophy. Zolgensma is designed to deliver a normal copy of the gene encoding the SMN protein in patients with SMA. This currently is only FDA approved for a one-time administration. Safety and efficacy of repeat administration has not been evaluated. Use in patients with advanced SMA (complete paralysis limbs, ventilator-dependent) has not been evaluated.

These therapies are considered specialty medications, but it may not be appropriate to dispense under the pharmacy benefit. If you would like to discuss these medications, please contact your Clinical Account Executive or Account Manager. This list is subject to change so CastiaRx will continue to monitor the medications approved in this class.

References

1. What is gene therapy? Cellular and Gene Therapy Products. U.S. Food and Drug Administration (FDA). https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy. Updated July 25, 2018. Accessed July 19, 2019.
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3. National Comprehensive Cancer Network. NCCN Guidelines: Acute Lymphoblastic Leukemia. https://www.nccn.org/professionals/physician_gls/pdf/all_blocks.pdf. Accessed July 19, 2019.
4. National Comprehensive Cancer Network. NCCN Guidelines: B Cell Lymphoma. https://www.nccn.org/professionals/physician_gls/pdf/b-cell_blocks.pdf. Accessed July 19, 2019.
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