FDA Approves First Gene Therapy to Treat Adults with Metastatic Synovial Sarcoma

Today, the U.S. Food and Drug Administration approved Tecelra (afamitresgene autoleucel), a gene therapy indicated for the treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy, are HLA antigen(s) A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive, and whose tumor expresses the MAGE-A4 antigen as determined by FDA authorized companion diagnostic devices.

Synovial sarcoma is a rare form of cancer in which malignant cells develop and form a tumor in soft tissues of the body. This type of cancer can occur in many parts of the body, most commonly developing in the extremities. The cancerous cells may also spread to other parts of the body. Each year, synovial sarcoma impacts about 1,000 people in the U.S. and most often occurs in adult males in their 30s or younger. Treatment typically involves surgery to remove the tumor and may also include radiotherapy and/or chemotherapy if the tumor is larger, returns after being removed or has spread beyond its original location.

"Potentially life-threatening cancers such as synovial sarcoma continue to have a devastating impact on individuals, especially those for whom standard treatments have limited efficacy due to tumor growth and progression," said Peter Marks, M.D., Ph.D., director of the FDA's Center for Biologics Evaluation and Research (CBER). "The approval of this state-of-the-art immunotherapy technology provides a critical new option for a patient population in need and demonstrates the FDA's dedication to the advancement of beneficial cancer treatments."

Tecelra is also the first FDA-approved T cell receptor (TCR) gene therapy. The product is an autologous T cell immunotherapy composed of a patient's own T cells. T cells in Tecelra are modified to express a TCR that targets MAGE-A4, an antigen (substance that normally triggers your immune system) expressed by cancer cells in synovial sarcoma. The product is administered as a single intravenous dose.

Tecelra was approved using the Accelerated Approval pathway, under which the FDA may approve drugs for serious or life-threatening diseases or conditions where there is an unmet medical need and the drug is shown to have an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit to patients (improving how patients feel or function, or whether they survive longer). This pathway can allow earlier approval while the company conducts further trials to verify the predicted clinical benefit. A confirmatory trial is ongoing to verify Tecelra's clinical benefit.

"Adults with metastatic synovial sarcoma, a life-threatening form of cancer, often face limited treatment options in addition to the risk of cancer spread or recurrence," said Nicole Verdun, M.D., director of the Office of Therapeutic Products in CBER. "Today's approval represents a significant milestone in the development of an innovative, safe and effective therapy for patients with this rare but potentially fatal disease."

The safety and effectiveness of Tecelra was evaluated in a multicenter, open-label clinical trial including patients with inoperable and metastatic synovial sarcoma who had received prior systemic therapy and whose tumor expressed the MAGE-A4 tumor antigen. Effectiveness was evaluated based on overall response rate and the duration of response to treatment with Tecelra. Among the 44 patients in the trial who received Tecelra, the overall response rate was 43.2% and the median duration of response was six months.

The most common adverse reactions associated with Tecelra included nausea, vomiting, fatigue, infections, fever, constipation, dyspnea (shortness of breath), abdominal pain, non-cardiac chest pain, decreased appetite, tachycardia (abnormally fast heart rate), back pain, hypotension, diarrhea and edema (swelling due to buildup of fluid in body tissues).

Patients treated with Tecelra may experience cytokine release syndrome (CRS), which is a dangerous type of aggressive immune system response, including potentially life-threatening reactions. CRS was observed following administration of Tecelra during clinical trials. A Boxed Warning is included in the label containing information about this risk.

Patients may also exhibit Immune Effector Cell-associated Neurotoxicity Syndrome (ICANS), an immune system-related syndrome that can occur following some immunotherapies, infections, secondary malignancies, or hypersensitivity reactions, and severe cytopenia (an abnormally low level of blood cells) for several weeks following lymphodepleting chemotherapy and Tecelra infusion. Patients receiving this product should be monitored for signs and symptoms of infection and are advised

not to drive or engage in hazardous occupations or activities for at least four weeks after receiving Tecelra.

The FDA granted Tecelra Orphan Drug, Regenerative Medicine Advanced Therapy and Priority Review designations for this indication.

This application was reviewed using a coordinated, cross-agency approach, including CBER, the FDA's Oncology Center of Excellence and the Center for Devices and Radiological Health.

The FDA granted the approval of Tecelra to Adaptimmune, LLC.

FDA News released Aug 2, 2024. www.fda.gov.

FDA Approves First Nalmefene Hydrochloride Auto-Injector to Reverse Opioid Overdose

Agency Continues to Support Development of Overdose Reversal Drugs including Naloxone and Nalmefene

Today, the U.S. Food and Drug Administration approved approved Zurnai, the first nalmefene hydrochloride auto-injector for the emergency treatment of known or suspected opioid overdose in adults and pediatric patients 12 years of age and older. The agency approved the first nasal spray formulation of nalmefene in May 2023.

Drug overdose persists as a major public health issue in the U.S., with more than 107,000 reported fatal overdoses occurring in 2023, primarily driven by synthetic opioids like illicit fentanyl. Nalmefene and naloxone are two available options to reverse opioid overdose. The FDA has worked to increase availability and accessibility of both options to encourage harm reduction and reduce overdose death.

"The FDA remains focused on broadening access to opioid overdose reversal agents, including naloxone and nalmefene. Today's approval adds a new nalmefene product and route of administration to support greater options for opioid overdose reversal," said FDA Commissioner Robert M. Califf, M.D. "Since launching the FDA Overdose Prevention Framework in 2022, the agency continues to build upon efforts that address the overdose crisis currently impacting the nation."

Nalmefene is an opioid receptor antagonist which is used to treat acute opioid overdose. If nalmefene is administered quickly, it can reverse the effects of opioid overdose, including respiratory depression, sedation and low blood pressure (hypotension). The newly approved product delivers 1.5 milligrams (mg) of nalmefene under the skin (subcutaneous) or into muscle (intramuscular). Zurnai is a single-dose, pre-filled auto-injector and is available only by prescription.

The approval of Zurnai is supported by safety and pharmacokinetic studies, as well as a study in healthy individuals who use opioids recreationally, to assess how quickly the product works. The most common adverse reactions are feeling hot, dizziness, nausea, headache, chills, vomiting, feeling pain from actions that aren't typically painful such as lightly touching your skin (allodynia), palpitations, ringing or buzzing in the ear (tinnitus), ear discomfort, feeling abnormal, burning sensation, hot flush and irritability.

The use of nalmefene hydrochloride in patients who are opioid-dependent may result in opioid withdrawal characterized by the following signs and symptoms: body aches, diarrhea, fast heart rate (tachycardia), fever, runny nose, sneezing, goosebumps (piloerection), sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, shivering or trembling, abdominal cramps, weakness and increased blood pressure.

The FDA granted this application Fast Track and Priority Review designations, which expedite the development and review of drugs that have the potential to provide a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious condition.

The FDA granted approval of Zurnai to Purdue Pharma L.P.

FDA News released Aug 7, 2024. www.fda.gov.

FDA Approves First Nasal Spray for Treatment of Anaphylaxis

Today, the U.S. Food and Drug Administration approved neffy (epinephrine nasal spray) for the emergency treatment of allergic reactions (Type I), including those that are life-threatening (anaphylaxis), in adult and pediatric patients who weigh at least 30 kilograms (about 66 pounds).

"Today's approval provides the first epinephrine product for the treatment of anaphylaxis that is not administered by injection. Anaphylaxis is life-threatening and some people, particularly children, may delay or avoid treatment due to fear of injections," said Kelly Stone, MD, PhD, Associate Director of the Division of Pulmonology, Allergy and Critical Care in the FDA's Center for Drug Evaluation and Research. "The availability of epinephrine nasal spray may reduce barriers to rapid treatment of anaphylaxis. As a result, neffy provides an important treatment option and addresses an unmet need."

Allergic reactions happen when a person's immune system reacts abnormally to a substance that normally does not cause symptoms. Anaphylaxis is a severe, life-threatening allergic reaction that typically involves multiple parts of the body and is considered a medical emergency. Common allergens that can induce anaphylaxis include certain foods, medications and insect stings. Symptoms usually occur within minutes of exposure and include, but are not limited to, hives, swelling, itching, vomiting, difficulty breathing and loss of consciousness. Epinephrine is the only life-saving treatment for anaphylaxis and has previously only been available for patients as an injection.

Neffy's approval is based on four studies in 175 healthy adults, without anaphylaxis, that measured the epinephrine concentrations in the blood following administration of neffy or approved epinephrine injection products. Results from these studies showed comparable epinephrine blood concentrations between neffy and approved epinephrine injection products. Neffy also demonstrated similar increases in blood pressure and heart rate as epinephrine injection products, two critical effects of epinephrine in the treatment of anaphylaxis. A study of neffy in children weighing more than 66 pounds showed that epinephrine concentrations in children were similar to adults who received neffy.

Neffy is a single dose nasal spray administered into one nostril. As with epinephrine injection products, a second dose (using a new nasal spray to administer neffy in the same nostril) may be given if there is no improvement in symptoms or symptoms worsen. Patients may need to seek emergency medical assistance for close monitoring of the anaphylactic episode and in the event further treatment is required.

Neffy comes with a warning that certain nasal conditions, such as nasal polyps or a history of nasal surgery, may affect absorption of neffy, and patients with these conditions should consult with a health care professional to consider use of an injectable epinephrine product. Neffy also comes with warnings and precautions about use of epinephrine by people with certain coexisting conditions and allergic reactions associated with sulfite.

The most common side effects of neffy include throat irritation, tingling nose (intranasal paresthesia), headache, nasal discomfort, feeling jittery, tingling sensation (paresthesia), fatigue, tremor, runny nose (rhinorrhea), itchiness inside the nose (nasal pruritus), sneezing, abdominal pain, gum (gingival) pain, numbness in the mouth (hypoesthesia oral), nasal congestion, dizziness, nausea and vomiting.

The FDA granted neffy Fast Track designation for this application.

The FDA granted the approval of neffy to ARS Pharmaceuticals.

FDA News released Aug 9, 2024. www.fda.gov.

Source: FDA