Jefferson Health Plans

DR.014.B Gene Therapy:

Etranacogene dezaparvovec-drlb (Hemgenix®), Viltolarsen (Viltepso®), Nadofaragene firadenovec-vncg (Adstiladrin®)

Original Implementation Date : 5/24/2023
Version [B] Date : 7/1/2023
Last Reviewed Date: 7/1/2023

PRODUCT VARIATIONS

This policy applies to all Jefferson Health Plans product lines unless noted below.

POLICY STATEMENT

Jefferson Health Plans considers Etranacogene dezaparvovec-drlb (Hemgenix®), Viltolarsen (Viltepso®), Nadofaragene firadenovec-vncg (Adstiladrin®), and Delandistrogene moxeparvovec-rokl (Elevidys®) medically necessary for its FDA approved indications when the prior authorization listed in this policy are met.

FDA INDICATIONS

Gene Therapy is the introduction, removal, or change in the content of a person's genetic code with the goal of treating or curing a disease. It includes therapies such as gene transfer, gene modified cell therapy, and gene editing.

- Hemgenix® is an adeno-associated virus vector-based gene therapy indicated for the treatment of adults with Hemophilia B (congenital Factor IX deficiency) who:
    - Currently use Factor IX prophylaxis therapy, or
    - Have current or historical life-threatening hemorrhage, or
    - Have repeated, serious spontaneous bleeding episodes.

- **Viltepso®** is an antisense oligonucleotide indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in

patients treated with VILTEPSO. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

- **Adstiladrin®** is a non-replicating adenoviral vector-based gene therapy indicated for the treatment of adult patients with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

- **Elvedidys®** is an adeno-associated virus vector-based gene therapy indicated for the treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the DMD gene. This indication is approved under accelerated approval based on expression of ELEVIDYS microdystrophin in skeletal muscle observed in patients treated with ELEVIDYS. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

OFF-LABEL USE

N/A

PRIOR AUTHORIZATION CRITERIA

Prior authorization is required for Etranacogene dezaparvovec-drlb (Hemgenix®), Viltolarsen (Viltepso®), Nadofaragene firadenovec-vncg (Adstiladrin®), and Delandistrogene moxeparvovec-rokl (Elevidys®).

Etranacogene dezaparvovec-drlb (Hemgenix®)

Initial use of Etranacogene dezaparvovec-drlb (Hemgenix®) may be considered medically necessary when All of the following apply:

1. FDA approved indication.
2. FDA approved age (18 years and older).
3. 3) Must have severe disease defined as a factor IX levels less than 1% of normal or moderately severe hemophilia B defined as a Factor IX levels ≥ 1% ≤ 2% (greater than or equal to 0.01 IU/mL to less than or equal to 0.02 IU/mL) and one of the following:
4. current or historical life-threatening hemorrhage or
5. repeated, serious spontaneous bleeding episodes.
6. Must currently be on factor IX therapy with greater than 150 prior exposure days to treatment.

7. Must not have a history of inhibitors to factor IX or a positive inhibitor screen defined as greater than or equal to 0.6 Bethesda units prior to administration of etranacogene dezaparvovec.
8. Must not have received prior treatment with any gene therapy for hemophilia B or are being considered for treatment with any other gene therapy for hemophilia B.

Viltolarsen (Viltepso®)

1. Initial use of Viltolarsen (Viltepso®) may be considered medically necessary when All of the following apply: Individual is <10 years of age at the start of therapy.

2. Individual does not have symptomatic cardiomyopathy.

    a. Stable cardiac function with left ventricular ejection fraction (LVEF) ≥ 40%.

    b. Stable pulmonary function with predicted forced vital capacity (FVC) ≥ 50%.

3. Individual must have confirmed mutation of the DMD gene that is amendable to exon 53 skipping.

    a. Must have proper documentation of DMD.

    b. Medication is being prescribed by, or in consultation with, a Neurologist, Neuromuscular specialist, or by a Muscular Dystrophy Association (MDA) clinic.

    c. FDA approved dosing.

    d. Dose does not exceed 80 mg/kg per week.

4. Must be on stable dose of corticosteroids (unless contraindicated or intolerance) for at least 3 months.

5. Individual is not taking any other RNA antisense agent or any other gene therapy. E.g., exon skipping therapies (Amondys 45™, Exondys 51®, Vyondys 53™).

6. Individual is compliant with necessary monitoring parameters.

Nadofaragene firadenovec-vncg (Adstiladrin®)

Initial use of Nadofaragene firadenovec-vncg (Adstiladrin®) may be considered medically necessary when **all** of the following apply:

1. Individual must have a diagnosis of high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

2. Individual does not have a hypersensitivity to interferon alfa or any component of the product.

3. Has premedication with an anticholinergic before each instillation of the product.

4. FDA approved dosing.

    a. The dose is 75 mL of ADSTILADRIN at a concentration of 3 x 1011 viral particles (vp)/mL, instilled once every three (3) months.

5. Administered for intravesical instillation only.

6. If female, verify pregnancy status in females of reproductive potential prior to initiating product.

7. Individual is complaint with necessary monitoring parameters.

Delandistrogene moxeparvovec-rokl (Elevidys®)

Initial use of Delandistrogene moxeparvovec-rokl (Elevidys®) may be considered medically necessary when **all** of the following apply.

1. Individual aged 4 through 5 years with a diagnosis of Duchenne Muscular Dystrophy (DMD) and confirmed mutation within the DMD gene.

    a. Must have proper documentation of DMD.

    b. Medication is being prescribed by, or in consultation with, a Neurologist, Neuromuscular specialist, or by a Muscular Dystrophy Association (MDA) clinic.

    c. FDA approved dosing.

    d. Single-dose intravenous use only

e. 1.33×10^{14} vector genomes (vg) per kg

2. Eligible to receive premedication with corticosteroids 1 day prior to infusion and minimum of 60 days after (unless tapering is clinically indicated).

3. Does not have any deletion in exon 8 and/or exon 9 in the DMD gene.

4. Does not have any clinical signs or symptoms of active infection at the time of administration.

5. Individual does not have a pre-existing medical reason preventing treatment.

6. Individual is compliant with necessary monitoring parameters.

7. Individual has an anti-AAVrh74 total binding antibody titer <1:400.

8. Individual is not taking any other RNA antisense agent or any other gene therapy. E.g., exon skipping therapies (Amondys 45™, Exondys 51®, Vyondys 53™).

SAFETY AND MONITORING

Etranacogene dezaparvovec-drlb **(Hemgenix®)**

Risk factors:

1. **Infusion reactions**: Monitor during administration and for at least 3 hours after end of infusion. If symptoms occur, slow or interrupt administration. Re-start administration at a slower infusion once resolved.

2. **Hepatotoxicity:** Closely monitor transaminase levels once per week for 3 months after Hemgenix® administration to mitigate the risk of potential hepatotoxicity. Continue to monitor transaminases in all patients who developed liver enzyme elevations until liver enzymes return to baseline. Consider corticosteroid treatment should elevations occur.

3. **Hepatocellular carcinogenicity:** For patients with preexisting risk factors (e.g., cirrhosis, advanced hepatic fibrosis, hepatitis B or C, non-alcoholic fatty liver disease (NAFLD), chronic alcohol consumption, non-alcoholic steatohepatitis (NASH), and advanced age), perform regular (e.g., annual) liver ultrasound and alpha-fetoprotein testing following administration.

4. **Vector distribution in blood (within the body), and vector shedding in semen and other excreta and secreta can occur post-infusion**. It is not known how long this will continue. Patients should not donate blood, organs, tissues, or cells for transplantation.

Monitoring:

- After Hemgenix® administration, regularly monitor patient's Factor IX activity and Factor IX inhibitors.

- Hemgenix® can elevate certain liver enzymes. Weekly blood tests will be required to monitor for this for 3 months after treatment. Corticosteroid treatment may be necessary if this occurs.

Viltolarsen (Viltepso®)

Risk factors:

1) **Kidney Toxicity**: Based on animal data, may cause kidney toxicity. Kidney function should be monitored; creatinine may not be a reliable measure of renal function in DMD patients

2) **Adverse Reactions**: Upper resipiratory tract infection, injection site reaction, cough, pyrexia, contusion, arthralgia. Diarrhea, vominting, abdominal pain, ejection fraction decreased, urticaria

Monitoring:

- Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting Viltepso®. Consider measurement of glomerular filtration rate prior to initiation of Viltepso®.

- Monitoring for kidney toxicity during treatment is recommended. Obtain the urine samples prior to infusion of Viltepso® or at least 48 hours after the most recent infusion

Nadofaragene firadenovec-vncg, (Adstiladrin®)

Risk factors:

1. Metastatic Bladder Cancer with Delayed Cystectomy: delaying cystectomy in patients with BCG-unresponsive CIS could lead to development of muscle-invasive or metastatic bladder cancer.

2. Disseminated adenovirus infection: Patients who are immunocompromised or immunodeficient may be at risk for disseminated infection from Adstiladrin® due to low levels of replication-competent adenovirus. Avoid Adstiladrin® exposure to immunocompromised or immunodeficient individuals.

Monitoring:

- The most common (>10%) adverse reactions, including laboratory abnormalities (>15%), were glucose increased, instillation site discharge, triglycerides increased, fatigue, bladder spasm, micturition urgency, creatinine increased, hematuria, phosphate decreased, chills, dysuria, and pyrexia.

- Serious adverse reactions occurring in >1% of patients included coronary artery disease and hematuria.

Delandistrogene moxeparvovec-rokl (Elevidys®)

Risk Factors:

1. **Acute Serious Liver Injury:** Acute serious liver injury has been observed. If acute serious liver injury is suspected, a consultation with a specialist is recommended. Patients with preexisting liver impairment, chronic hepatic condition or acute liver disease may be at higher risk of acute serious liver injury.

2. **Immune-mediated Myositis:** Patients with deletions in the DMD gene in exons 1 to 17 and /or exons 59 to 71 may be at risk for severe immune-mediated myositis reaction. Consider additional immunomodulatory treatment if symptoms of myositis occur.

3. **Myocarditis**: Myocarditis and troponin-I elevations have been observed.

4. **Pre-existing Immunity against AAVrh74**: Perform baseline testing for presence of anti-AAVrh74 total binding antibodies prior to administration.

Monitoring:

- The most common adverse reactions (incidence ≥ 5%) reported in clinical studies were vomiting, nausea, liver function test increased, pyrexia, and thrombocytopenia.

- Liver function before infusion, and weekly for the first 3 months after infusion. Continue monitoring until results are unremarkable.

- Troponin-I before infusion, and weekly for the first month after infusion.

- Obtain platelet counts weekly for the first two weeks.

DOSAGE AND ADMINISTRATION

Hemgenix® is a suspension for intravenous infusion. Hemgenix® is provided in kits containing 10 to 48 single-use vials, each kit constituting a dosage unit based on the patient's body weight. Hemgenix® has a nominal concentration of 1 x 10^{13} gc/mL, and each vial contains an extractable volume of not less than 10 mL.

- **Administration:** Single-use intravenous infusion only.

- **Dose:** The recommended dose is 2 x 10^{13} genome copies (gc) per kilogram (kg) of body weight (or 2 mL/kg body weight) administered as an intravenous infusion after dilution with 0.9% sodium chloride solution (normal saline) at a constant infusion rate of 500mL/hour (8mL/min).

Viltepso® is a clear and colorless solution for intravenous infusion and is available as a 250 mg/5 mL (50 mg/mL) solution in a single-dose vial.

- **Administration**: Intravenous infusion over 60 minutes. If the volume of Viltepso® required is less than 100 mL, dilution in 0.9% Sodium Chloride Injection, USP, is required.

- **Dose:** Recommended dosage is 80 milligrams per kilogram of body weight once weekly.

Adstiladrin® is a suspension for intravesical instillation, supplied as single-use vials. Adstiladrin® is provided in a carton containing four (4) vials. All vials have a nominal concentration of 3 × 1011 viral particles (vp)/mL. Each vial of Adstiladrin® contains an extractable volume of not less than 20 mL.

- **Administration:** Premedication with an anticholinergic is recommended before each instillation of Adstiladrin®. Administer Adstiladrin® by intravesical instillation only.

- **Dose:** The dose is 75 mL of Adstiladrin® at a concentration of 3 x 10^{11} viral particles (vp)/mL, instilled once every three (3) months. Allow Adstiladrin® to be left in the bladder for 1 hour following instillation.

Elevidys® is a suspension for intravenous infusion with a nominal concentration of 1.33 × 10^{13} vg/mL, provided in a customized kit containing ten to seventy 10 mL single-dose vials, with each kit constituting a dosage unit based on the patient's body weight.

- **Administration:** One day prior to infusion, initiate a corticosteroid regimen for a minimum of 60 days. Recommend modifying corticosteroid dose for patients with liver function abnormalities. Administer as an intravenous infusion over 1-2 hours. Infuse at a rate of less than 10 mL/kg/hour**.**

- **Dose:** 1.33 $\times 10^{14}$ vector genomes (vg) per kg of body weight.

BENEFIT APPLICATION

Medical policies do not constitute a description of benefits. This medical necessity policy assists in the administration of the member's benefits which may vary by line of business. Applicable benefit documents govern which services/items are eligible for coverage, subject to benefit limits, or excluded completely from coverage.

This policy is invoked only when the requested service is an eligible benefit as defined in the Member's applicable benefit contract on the date the service was rendered. Services determined by the Plan to be investigational or experimental are excluded from coverage for all lines of business. For Medicaid members under 21 years old, benefits and coverage are always based on medical necessity review.

BACKGROUND

Etranacogene dezaparvovec-drlb (Hemgenix®). Hemophilia B is a rare genetic bleeding disorder in which affected individuals have insufficient levels of FIX due to a mutation on the F9 gene. Hemophilia B is classified as mild, moderate, or severe based upon the activity level of factor IX. Individuals with mild hemophilia have factor IX levels between 5 and 40% of normal. Those with moderate hemophilia have factor levels from 1 to 5% of normal. Patients with severe hemophilia have factor levels less than 1% of normal. Symptoms may vary greatly from one person to another depending on severity. Hemophilia B occurs in approximately 1 in 25,000 male births. Although many hemophilia B carrier females do not have symptoms, an estimated 10-25% will develop mild symptoms and females have also been reported with moderate and severe symptoms. Individuals with severe hemophilia B are usually diagnosed around birth or within the first 1-2 years of life; those with moderate hemophilia B, five to six years of age; and individuals with mild hemophilia B may not be diagnosed until later in life and even into adulthood. Clotting factors are the treatment of choice for people with hemophilia as they are very safe and effective for treating and preventing bleeds.

The World Federation of Hemophilia (WFH) 2020 treatment guidelines do not express a preference for recombinant over plasma-derived clotting factor concentrates and state the choice between these classes of product must be made according to availability, cost, and patient preferences. For patients with a severe phenotype, WFH strongly recommends patients be on prophylaxis sufficient to prevent bleeds at all times, but that prophylaxis should be individualized, taking into consideration patient bleeding phenotype, joint status, individual pharmacokinetics, and patient self-assessment and preference. Recombinant activated factor VIIa, a bypassing agent, is recommended for the treatment and prevention of bleeding complications in patients with hemophilia B who develop FIX inhibitors.

Hemgenix® (etranacogene dezaparvovec-drlb) is an adeno-associated viral vector-based gene therapy for intravenous infusion after dilution. Hemgenix® is a non-replicating recombinant AAV5 containing a codon-optimized DNA sequence of the gain-of-function Padua variant of human Factor IX (variant R338L), under control of a liver-specific promotor 1 (LP1).

Single intravenous infusion of H results in cell transduction and increase in circulating Factor IX activity in patients with Hemophilia B. The mean Factor IX activity levels over time, as measured by one-stage [activated Partial Thromboplastin Time (aPTT)-based] assay. Subjects achieved a mean (± SD) uncontaminated (i.e., excluding measurements within five half-lives of Factor IX replacement therapy) Factor IX activity levels of 39% (± 18.7), 41.5% (± 21.7), 36.9% (± 607 21.4) and 36.7 (± 19.0) of normal, respectively, at 6, 12, 18 and 24 months. The time to onset of Factor IX protein expression post-dose was detectable by first uncontaminated measurement at Week 3 in the clinical efficacy study (N = 54). ***Hemgenix®*** is not intended for administration in women. No adverse effects on mating rate and fertility indices or fetal weights were observed in healthy naïve female mice mated with healthy male mice that were intravenously administered a predecessor of Hemgenix® product 6 days prior to mating. Vector DNA was not detected in the uterus, placenta, or fetus.

Viltolarsen (Viltepso®). Viltolarsen is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) subclass. PMOs are synthetic molecules in which the five-membered ribofuranosyl rings found in natural DNA and RNA are replaced by a six-membered morpholino ring. Each morpholino ring is linked through an uncharged phosphorodiamidate moiety rather than the negatively charged phosphate linkage that is present in natural DNA and RNA. Each phosphorodiamidate morpholino subunit contains one of the heterocyclic bases found in DNA (adenine, cytosine, guanine, or thymine). Viltolarsen contains 21 linked subunits. The molecular formula of viltolarsen is C H N O P and the molecular weight is 6924. ***Viltepso®*** is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping. After treatment with Viltepso® 80 mg/kg once weekly, all patients evaluated (N=8) were found to produce mRNA for a truncated dystrophin protein, as measured by reverse transcription polymerase chain reaction (RT-PCR), and demonstrated exon 53 skipping, as measured by DNA sequence analysis. ***Viltepso®*** is approved for the treatment of Duchenne muscular dystrophy, a condition that primarily affects males. Animal reproduction studies have not been conducted and females were not included in the original studies.

Nadofaragene firadenovec-vncg, (Adstiladrin®). ***Adstiladrin®*** (nadofaragene firadenovec-vncg) is a non-replicating adenoviral vector-based gene therapy for intravesical instillation. It is a recombinant adenovirus serotype 5 vector containing a transgene encoding the human interferon alfa-2b (IFNα2b). ***Adstiladrin®*** is designed to deliver a copy of a gene encoding a human interferon-alfa 2b (IFNα2b) to the bladder urothelium. Intravesical instillation of Adstiladrin® results in cell transduction and transient local expression of the IFNα2b protein that is anticipated to have anti-tumor effects. After treatment with a single intravesical 75 mL dose of Adstiladrin® (3 × 1011 viral particles per mL), 53·4% (n=151) of patients with carcinoma in situ (with or without a high-grade Ta or T1 tumor) had a complete response within 3 months of the first dose and this response was maintained in 45·5% of patients at 12 months.

Adstiladrin® is approved for the treatment of adult patients with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors. Animal reproductive and developmental toxicities studies have not been

conducted.

Delandistrogene moxeparvovec-rokl (Elevidys®). ***Elevidys®*** is a recombinant gene therapy product that is comprised of a non-replicating, recombinant, adeno-associated virus (AAV) serotype rh74 (AAVrh74) capsid and a ssDNA expression cassette flanked by inverted terminal repeats (ITRs) derived from AAV2. The cassette contains: 1) an MHCK7 gene regulatory component comprising a creatine kinase 7 promoter and an α-myosin heavy chain enhancer, and 2) the DNA transgene encoding the engineered ELEVIDYS micro-dystrophin protein. ***Elevidys®*** is designed to carry a transgene encoding a micro-dystrophin protein consisting of selected domains of dystrophin expressed in normal muscle cells. Micro-dystrophin has been demonstrated to localize to the sarcolemma. Following IV administration, the drug's vector genome undergoes distribution via systemic circulation and distributes into target muscle tissues followed by elimination in the urine and feces. Its biodistribution and tissue transduction are detected in the target muscle tissue groups and quantified in the gastrocnemius or biceps femoris biopsies obtained from patients with mutations in the DMD gene. Evaluation of the drug's vector genome exposure in clinical muscle biopsies at Week 12 post-dose expressed as copies per nucleus revealed ELEVIDYS drug distribution and transduction with a mean change from baseline of 2.91 and 3.44 copies per nucleus at the recommended dose of 1.33×10^{14} vg/kg. ***Elevidys®*** is the first adeno-associated virus vector-based gene therapy indicated for the treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the DMD gene**.** It is not curative and can be administered in an outpatient setting.

CLINICAL EVIDENCE

Etranacogene dezaparvovec-drlb (Hemgenix®)

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. The efficacy of Hemgenix® was evaluated in a prospective, open-label, single-dose, single arm, multi-national study (N = 54). The study enrolled adult male subjects aged 19 to 75 years, with severe or moderately severe Hemophilia B, who received a single intravenous dose of 2×10^{13} gc/kg body weight of Hemgenix® and entered a follow-up period of 5 years. The study is on-going.

The main efficacy outcome was a non-inferiority test of annualized bleeding rate (ABR) during Months 7 to 18 after Hemgenix® treatment compared with ABR during the lead-in period. All bleeding episodes, regardless of investigator assessment, were counted. Subjects were allowed to continue prophylaxis during Months 0 to 6. The estimated mean ABR during Months 7 to 18 after Hemgenix® treatment was 1.9 bleeds/year with a 95% confidence interval (CI) of (1.0, 3.4), compared with an estimated mean ABR of 4.1 [95% CI: 3.2, 5.4] during the lead-in period. The ABR ratio (Months 7 to 18 post-treatment / lead-in) was 0.46 [95% CI: 0.26, 0.81], demonstrating non-inferiority of ABR during Months 7 to 18 compared to the lead-in period.

Viltolarsen (Viltepso®)

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The effect of Viltepso® on dystrophin production was evaluated in one study in Duchenne muscular dystrophy (DMD) patients with a confirmed mutation of the DMD gene that is amenable to exon 53 skipping.

The study was a multicenter, 2-period, dose-finding study conducted in the United States and Canada in males 4 years to less than 10 years of age on a stable corticosteroid regimen for at least 3 months. Patients were randomized to treatment (Viltepso®) or placebo groups. All patients then received 20-week of open-label Viltepso® 40 mg/kg once weekly (0.5 times the recommended dosage) (N=8) or 80 mg/kg once weekly (N=8). Efficacy was assessed based on change from baseline in dystrophin protein level (measured as % of the dystrophin level in healthy subjects, i.e., % of normal) at Week 25. In patients who received Viltepso 80 mg/kg once weekly, mean dystrophin levels increased from 0.6% (SD 0.8) of normal at baseline to 5.9% (SD 4.5) of normal by Week 25, with a mean change in dystrophin of 5.3% (SD 4.5) of normal levels (p=0.01) as assessed by validated Western blot (normalized to myosin heavy chain); the median change from baseline was 3.8%. All patients demonstrated an increase in dystrophin levels over their baseline values. As assessed by mass spectrometry (normalized to filamin C), mean dystrophin levels increased from 0.6% (SD 0.2) of normal at baseline to 4.2% (SD 3.7) of normal by Week 25, with a mean change in dystrophin of 3.7% (SD 3.8) of normal levels (nominal p=0.03, not adjusted for multiple comparisons); the median change from baseline was 1.9%

Nadofaragene firadenovec-vncg, (Adstiladrin®)

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. The efficacy of Adstiladrin® was evaluated in a phase 3, multicenter, open-label, repeat-dose study done in 33 centers (hospitals and clinics) in the USA in patients aged 18 years or older, with BCG-unresponsive non-muscle-invasive bladder cancer and an Eastern Cooperative Oncology Group status of 2 or less. Patients received a single intravesical 75 mL dose of Adstiladrin® (3×10^{11} viral particles per mL). Repeat dosing at months 3, 6, and 9 was done in the absence of high-grade recurrence. The study is ongoing with a 4-year treatment and monitoring phase. The primary endpoint was the proportion of patients with a complete response in the carcinoma in situ cohort at any time within 12 months after the first dose of Adstiladrin®. 55 (53·4%) of 103 patients (95% CI 43·3 to 63·3) in the carcinoma in situ cohort had a complete response, with all complete responses noted at month 3.

Delandistrogene moxeparvovec-rokl (Elevidys®)

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The expression of Elevidys micro-dystrophin in skeletal muscle and the effect on the North Start Ambulatory Assessment (NSAA) total score was evaluated in a two-part ongoing 1:1 randomized, double-blind, placebo-controlled study including 41 male DMD patients aged 4 through 7 with confirmed frameshift mutation, or a premature stop codon mutation between exons 18 to 58 in the DMD gene. Eight patients in the treatment group received 1.33×10^{14} vg/kg of ELEVIDYS, and 12 patients received lower doses. All subjects were on at least 12 weeks of corticosteroids prior to infusions, increased at least 1 mg/kg prior to infusion, and baseline anti-AAVrh74 titers <1:400. The difference between the ELEVIDYS and placebo groups was not statistically significant (p=0.37). The least squares (LS) mean changes in NSAA total score from baseline to Week 48 was 1.7 (standard error [SE]: 0.6) points for the ELEVIDYS group and 0.9 (SE: 0.6) points for the placebo group.

The effect of Elevidys micro-dystrophin expression was also evaluated in Study 2, an ongoing, open-label, multi-center study cohort consisting of 20 males DMD patients aged 4 through 7 years. All subjects received a single intravenous infusion of 1.33×10^{14} vg/kg. For subjects aged 4 through 5 years who received 1.33×10^{14} vg/kg, the mean (SD) micro-dystrophin expression levels at Week 12 following infusion were 95.7% (N=3, SD: 17.9%) in Study 1 Parts 1 and 2 and 51.7% (N=11, SD: 41.0%) in Study 2 Cohort 1. Evaluation of ELEVIDYS vector genome exposure in clinical muscle biopsies at Week 12 post-dose expressed as copies per nucleus revealed drug distribution and transduction with a mean change from baseline of 2.91 and 3.44 copies per nucleus at the recommended dose of 1.33×10^{14} vg/kg for Study 1 and Study 2 Cohort 1, respectively.

CODING

Note*:* The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that *may* be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT® is a registered trademark of the American Medical Association.

HCPCS Code	Description
J1411	Etranacogene dezaparvovec-drlb (Hemgenix®).
J9029	Nadofaragene firadenovec-vncg (Adstiladrin®).
J1427	Injection, viltolarsen, 10 mg (Viltepso®)

ICD-10 Codes	Description
N/A	N/A

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making.

Policy Bulletins are developed by Jefferson Health Plans to assist in administering plan benefits and constitute neither offers of coverage nor medical advice.

This Policy Bulletin may be updated and therefore is subject to change.

For Health Choices (Medicaid) and Children's Health Insurance Program (CHIP) products: Any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
July 2023 Code update. J9029 added to the coding table.	B	7/1/2023
New policy.	A	5/24/2023

REFERENCES

1. Package insert- *HEMGENIX.* CSL Behring: 2022. Available at: Hemgenix-Prescribing-Information.pdf (cslbehring.com).

2. Package insert- *HEMGENIX.* U.S. Food and Drug Administration: 2022. Available at: https://www.fda.gov/media/163467/download.

3. Etranacogene Dezaparvovec. Lexi-drugs. Lexicomp. Wolters Kluwer Health, Inc. Updated 1/19/23. https://online-lexi-com.libproxy.temple.edu/lco/action/doc/retrieve/docid/patch_f/7290387?cesid=9Z7486Gwmu3&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Dhemgenix%26t%3Dname%26acs%3Dfalse%26acq%3Dhemgenix#

4. CSL Behring. FDA accepts CSL Behring's biologics license application for etranacogene dezaparvovec for priority review. 2022 May 24. Available at: https://www.cslbehring.com/newsroom/2022/fda-bla-etranacogenedezaparvovec. Accessed on January 9, 2023.

5. Clinicaltrials.gov. HOPE-B: Trial of AMT-061 in severe or moderately severe hemophilia b patients (NCT03569891). Available at: https://clinicaltrials.gov/ct2/show/NCT03569891. Accessed on January 9, 2023.

6. Viltepso (Viltolarsen) prescribing information. New Jersey (NJ). NS Pharma. Revised 2021 March.

7. Boorjian SA, Alemozaffar M, Konety BR, et al. *Intravesical nadofaragene firadenovec gene therapy for BCG-unresponsive non-muscle-invasive bladder cancer: a single-arm, open-label, repeat-dose clinical trial.* Lancet Oncol. 2021;22(1):107-117. doi:10.1016/S1470-2045(20)30540-4.

8. *Package Insert - ADSTILADRIN*. U.S. Food and Drug Administration: 2022. Available at https://www.fda.gov/media/164029/download

9. Stewart J. *Adstiladrin*. Drugs.com: 2022. Available at: https://www.drugs.com/adstiladrin.html#warnings

10. Elevidys (delandistrogene moxeparvovec) [prescribing information]. Cambridge, MA: Sarepta Therapeutics Inc; June 2023.Accessed June 28, 2023. Available at https://www.fda.gov/media/169679/download

11. https://classic.clinicaltrials.gov/ct2/show/NCT05096221

12. https://classic.clinicaltrials.gov/ct2/show/NCT03375164?term=Delandistrogene+moxeparvovec&draw=2&rank=4