HIGHMARK WHOLECARE

Updated: 04/2025
PARP Approved: 06/2025

Prior Authorization Criteria

Gene Therapy Agents

All requests for Gene Therapy Agents without their own policy require a prior authorization and will be screened for medical necessity and appropriateness using the criteria listed below.

Gene therapies include Kebilidi (eladocagene exuparvovec), Skysona (elivaldogene autotemcel), Hemgenix (etranacogene dezaparvovec), Roctavian (valoctocogene roxaparvovec), Elevidys (delandistrogene moxeparvovec-rokl), Lenmeldy (atidarsagene autotemcel) and Adstiladrin (nadogaragene firadenovec-vncg). New products with this classification will require the same documentation.

For all requests the following criteria must be met in addition to the diagnosis specific criteria below:

- Is prescribed for an indication that is included in the U.S. Food and Drug Administration (FDA)-approved package labeling OR a medically accepted indication
- The requested dose and frequency is in accordance with FDA-approved labeling, nationally recognized compendia, and/or evidence-based practice guidelines
- Must be age-appropriate according to FDA-approved labeling, nationally recognized compendia, or evidence-based practice guidelines
- The member is not currently enrolled in a clinical trial for the requested drug or has not previously received the requested gene therapy or any other gene therapy.
- Does not have any contraindications to the requested medication

For Hemgenix (etranacogene dezaparvovec) requests:

Coverage may be provided with a diagnosis of Hemophilia B (congenital Factor IX deficiency) and the following criteria is met:

- Member must have severe or moderately severe hemophilia B (congenital factor IX deficiency) defined as equal to or less than 2% of normal circulating factor IX confirmed by blood coagulation testing
- Must have baseline liver function tests assessed prior to and after therapy for at least three months and be within normal range
- Members with preexisting risk factors for hepatocellular carcinoma (e.g., members with cirrhosis, advanced hepatic fibrosis, hepatitis C or B, non-alcoholic fatty liver disease (NAFLD), chronic alcohol consumption, non-alcoholic steatohepatitis (NASH), and advanced age) must have abdominal ultrasound screenings and be monitored regularly (e.g., annually) for alpha-fetoprotein (AFP) elevations following administration
- Is prescribed by a hematologist or hemophilia treatment center practitioner
- Member has received IX prophylactic or on-demand replacement therapy for ≥ 150 accumulated days and is currently using factor IX prophylaxis therapy
- Member has ≥ 12 bleeding episodes if receiving on-demand therapy over the preceding 12 months. Does **not** apply to patients on prophylaxis.

- Member must have a baseline anti-AAV5 antibody titer of ≤ 1:678 measured by ELISA
- Member must not have any of the following:
    - Inhibitor antibodies to factor IX
    - A positive HIV test during time of screening that is not controlled with anti-viral therapy
    - Active infection with hepatitis B or C virus at screening
    - History of hepatitis B or C exposures, currently controlled by antiviral therapy
    - Prior hemophilia AAV-vector based gene therapy
- **Duration of Approval:** One lifetime dose

For Roctavian (valoctocogene roxaparvovec) requests:

Coverage may be provided with a diagnosis of Hemophilia A (congenital Factor VIII deficiency) and the following criteria is met:

- Member must have severe hemophilia A (congenital factor VIII deficiency) defined as equal to or less than 1% of normal circulating factor VIII confirmed by blood coagulation testing
- Member must not have any pre-existing antibodies to adeno-associated virus serotype 5 detected by an FDA approved test.
- Member must not have any contraindications to receiving therapy such as active infections (either acute or uncontrolled chronic), significant hepatic fibrosis (stage 3 or 4) or cirrhosis or a known hypersensitivity to mannitol.
- Member meets both of the following:
    - No previous documented history of a detectable FVIII inhibitor
    - Member has inhibitor level assay < 1 Bethesda units (BU) on 2 consecutive occasions at least one week apart within the last 12 months
- Must have baseline liver function tests assessed prior to and after therapy for at least three months and be within normal range
- Members with preexisting risk factors for hepatocellular carcinoma (e.g., members with cirrhosis, advanced hepatic fibrosis, hepatitis C or B, non-alcoholic fatty liver disease (NAFLD), chronic alcohol consumption, non-alcoholic steatohepatitis (NASH), and advanced age) must have abdominal ultrasound screenings and be monitored regularly (e.g., annually) for alpha-fetoprotein (AFP) elevations following administration
- Is prescribed by a hematologist or hemophilia treatment center practitioner
- Member has received VIII prophylactic or on-demand replacement therapy for ≥ 150 accumulated days
- Member has ≥ 12 bleeding episodes if receiving on-demand therapy over the preceding 12 months. Does not apply to patients on prophylaxis.
- Member must not have any of the following:
    - A positive HIV test during time of screening that is not controlled with anti-viral therapy
    - Active infection with hepatitis B or C virus at screening
    - History of chronic or active hepatitis B or active hepatitis C or currently controlled by antiviral therapy
    - Prior hemophilia AAV-vector based gene therapy

- **Duration of Approval:** One lifetime dose

For Elevidys (delandistrogene moxeparvovec-rokl) requests:

Coverage may be provided with a diagnosis of Duchenne muscular dystrophy (DMD) and the following criteria is met:

- A confirmed diagnosis of DMD by submission of lab testing demonstrating mutation of the dystrophin (DMD) gene by either:
  - A confirmed frameshift mutation OR
  - A premature stop codon mutation between exons 18 to 58 in the DMD gene
- Member meets either of the following criteria:
  - Member is ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent).
  - Member is non-ambulatory
- The member must not have any deletion in exon 8 and/or exon 9 in the DMD gene
- Member does not have signs of cardiomyopathy (e.g., ejection fraction < 40%)
- Member does not currently have an active infection
- The member must be on a stable dose of corticosteroids for DMD for at least 12 weeks prior to therapy unless contraindicated
- The member must have a baseline anti-AAVrh74 antibody titers <1:400 measured by ELISA
- Must be prescribed by or in consultation with a neurologist who has experience in the treatment and management of DMD
- Elevidys will not be used in combination with exon-skipping therapies (e.g., casimersen, eteplirsen, golodirsen, viltolarsen).
- There is documentation of a baseline evaluation, including a standardized assessment of motor function, by a neurologist with experience treating DMD and liver function, platelet count, and troponin-I levels have been assessed at baseline and will be monitored as clinically appropriate.
- **Duration of Approval:** One lifetime dose

For Skysona (elivaldogene autotemcel) requests:

Coverage may be provided with a diagnosis of **cerebral adrenoleukodystrophy (CALD)** and the following criteria is met:

- Must have early, active CALD defined by:
  - Elevated very long chain fatty acids (VLCFA) values
  - Active CNS disease established by central radiographic review of brain magnetic resonance imaging (MRI)
  - Loes score between 0.5 and 9
  - Gadolinium enhancement (GdE+) on MRI of demyelinating lesions
  - Neurologic function score (NFS) of ≤ 1 demonstrating asymptomatic or mild disease
- Member must have confirmed mutations in the ABCD1 gene

- Must be prescribed by a neurologist or ALD specialist. Adrenal symptoms must be managed by an endocrinologist.
- The requested dose and frequency is in accordance with FDA-approved labeling, nationally recognized compendia, and/or evidence-based practice guidelines
- Skysona should not be administered in members with active infections.
- Member must have a negative serology test for HIV.
- Member must not have been a recipient of an allogenic transplant or gene therapy
- **Duration of Approval:** One lifetime dose

For Lenmeldy (atidarsagene autotemcel) requests:

Coverage may be provided with a diagnosis of **metachromatic leukodystrophy (MLD)** and the following criteria is met:

- Member must have one of the following:
  - Pre-symptomatic late infantile (PSLI) MLD
  - Pre-symptomatic early juvenile (PSEJ) MLD
  - Early symptomatic early juvenile (ESEJ) MLD
- A confirmed diagnosis by **all** of the following:
  - Biochemical testing documenting human arylsulfatase A (ARSA) gene activity is below the normal range for the laboratory performing the test
  - The presence of two disease-causing ARSA alleles, either known or novel mutations, identified on genetic testing
  - If novel mutations are identified, a 24-hour urine collection showing elevated sulfatide levels
- Must be prescribed by or in consultation with a physician who specializes in the treatment of MLD
- The member does not have evidence of residual cells of donor origin if the member has received a prior allogeneic hematopoietic stem cell transplant (allo-HSCT).
- **Duration of Approval:** One lifetime dose

For Kebilidi (eladocagene exuparvovec-tneq) requests:

Coverage may be provided with a diagnosis of **aromatic L amino acid decarboxylase (AADC) deficiency** and the following criteria is met:

- Diagnosis must be confirmed based on **all** of the following:
  - Genetic testing showing biallelic mutations in the DOPA decarboxylase (DDC) gene
  - Reduced levels of 5-hydroxyindoleacetic acid (5-HIAA), homovanillic acid (HVA) and 3-methoxy-4hydroxyphenylglycol (MHPG) and high concentrations of 3-O-methyldopa (3-OMD), L-Dopa, and 5OH tryptophan (5-HTP) in the cerebral spinal fluid (CSF)
  - Reduced aromatic L-amino acid decarboxylase (AADC) activity in the plasma
- Must be prescribed by or in consultation with a pediatric neurologist

- Must present with classical clinical characteristics of AADC deficiency, such as oculogyric crises, hypotonia, and developmental delay
- Must not have any significant structural brain abnormality
- Must not have an anti-AAV2 neutralizing antibody titer over 1,200 folds
- Member must not have received prior treatment with any other AAV2-based gene therapy despite indication or are being considered for treatment with any other AAV2-based gene therapy
- **Duration of Approval**: One lifetime dose

For Adstiladrin (nadofaragene firadenovec-vncg) requests:
Coverage may be provided with a diagnosis of **non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS)** and the following criteria is met:

- The member has a confirmed diagnosis of NMIBC with CIS with or without papillary tumors
- The member's disease is high-risk and BCG unresponsive defined as:
    - Persistent disease following adequate BCG therapy,
    - Disease recurrence after an initial tumor-free state following adequate BCG therapy, or
    - T1 disease following a single induction course of BCG
- The member is not immunocompromised or immunodeficient
- Member must not have extra-vesical (i.e., urethra, ureter, or renal pelvis), muscle invasive (T2-T4), or metastatic urothelial carcinoma
- The member is ineligible for or has elected not to undergo cystectomy
- Member must have an ECOG performance status ≤ 2
- **Initial Duration of Approval:** 6 months
- **Reauthorization criteria:**
    - The member continues to meet the requirements for initial therapy and has been treated with Adstiladrin (nadofaragene firadenovec-vncg) with no adverse reactions.
    - The member has no signs of unacceptable toxicity (such as risk of disseminated adenovirus infection) while on treatment with Adstiladrin (nadofaragene firadenovec-vncg).
- **Reauthorization Duration of Approval**: 6 months

Coverage may be provided for any non-FDA labeled indication if it is determined that the use is a medically accepted indication supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis(es) for which it is prescribed. These requests will be reviewed on a case by case basis to determine medical necessity.

When criteria are not met, the request will be forwarded to a Medical Director for review. The physician reviewer must override criteria when, in their professional judgment, the requested medication is medically necessary.

HIGHMARK WHOLECARE

Updated: 04/2025
PARP Approved: 06/2025

GENE THERAPY AGENTS
PRIOR AUTHORIZATION FORM- Page 1 of 4

Please complete and fax all requested information below including any progress notes, laboratory test results, or chart documentation as applicable to Highmark Wholecare Pharmacy Services. **FAX:** (888) 245-2049
If needed, you may call to speak to a Pharmacy Services Representative. **PHONE**: (800) 392-1147 Mon – Fri 8:30am to 5:00pm

PROVIDER INFORMATION

Requesting Provider:	Provider NPI:
Provider Specialty:	Office Contact:
State license #:	Office NPI:
Office Address:	Office Phone:
	Office Fax:

MEMBER INFORMATION

Member Name:	DOB:	
Member ID:	Member weight:	Height:

REQUESTED DRUG INFORMATION

Medication:	Strength:	
Directions:	Quantity:	Refills:
Is the member currently receiving requested medication? ☐ Yes ☐ No	Date Medication Initiated:	

Billing Information

This medication will be billed: ☐ at a pharmacy **OR** ☐ medically, JCODE:_____
Place of Service: ☐ Hospital ☐ Provider's office ☐ Member's home ☐ Other

Place of Service Information

Name:	NPI:
Address:	Phone:

MEDICAL HISTORY (Complete for ALL requests)

Diagnosis:	ICD Code:

Hemophilia A:
Does the member have severe hemophilia A? ☐ Yes, normal factor activity level:_____ ☐ No
Does the member have any pre-existing antibodies to adeno-associated virus serotype 5 detected by an FDA approved test? ☐ Yes ☐ No
Does the member have any contraindications to receiving therapy? ☐ Yes ☐ No
Did the member have baseline liver function tests assessed prior to therapy and was it within normal range? ☐ Yes ☐ No
Will the member have liver function testing done for at least 3 months after therapy? ☐ Yes ☐ No
Did the member have abdominal ultrasound screenings if they have preexisting risk factors for hepatocellular carcinoma? ☐ Yes ☐ No
Has the member had any documented history of a detectable FVIII inhibitor or an inhibitor level assay <1 BU on 2 consecutive occasions at least one week apart with the last 12 months? ☐ Yes, please explain below. ☐ No
Has the member had ≥ 12 bleeding episodes if receiving on-demand therapy over the preceding 12 months? Does **not** apply to patients on prophylaxis. ☐ Yes ☐ No
Has the member received FVIII prophylactic or on-demand replacement therapy for ≥ 150 accumulated days and still on current therapy? ☐ Yes ☐ No
Does the member have a positive HIV test or active infection with Hepatitis B or C? ☐ Yes ☐ No
Has the member had prior hemophilia AAV-vector based gene therapy? ☐ Yes ☐ No

Hemophilia B:
Does the member have severe or moderately severe B? ☐ Yes, normal factor activity level:_____ ☐ No
Did the member have baseline liver function tests assessed prior to therapy and was it within normal range? ☐ Yes ☐ No
Will the member have liver function testing done for at least 3 months after therapy? ☐ Yes ☐ No
Did the member have abdominal ultrasound screenings if they have preexisting risk factors for hepatocellular carcinoma? ☐ Yes ☐ No

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GENE THERAPY AGENTS
PRIOR AUTHORIZATION FORM (CONTINUED)– PAGE 2 of 4

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MEMBER INFORMATION

Member Name:	DOB:	
Member ID:	Member weight:	Height:

MEDICAL HISTORY (Complete for ALL requests)

Hemophilia B (continued):

Has the member had ≥ 12 bleeding episodes if receiving on-demand therapy over the preceding 12 months? Does **not** apply to patients on prophylaxis. ☐ Yes ☐ No

Has the member received IX prophylactic or on-demand replacement therapy for ≥ 150 accumulated days and still on current therapy? ☐ Yes ☐ No

What is the members baseline anti-AAV5 antibody titer measured by ELISA? _____

Does the member have inhibitor antibodies to factor IX? ☐ Yes ☐ No

Does the member have a positive HIV test or active infection with Hepatitis B or C? ☐ Yes ☐ No

Has the member had prior hemophilia AAV-vector based gene therapy? ☐ Yes ☐ No

DMD:

Does the member have a diagnosis of DMD confirmed by submission of lab testing demonstrating mutation of the dystrophin (DMD) gene by either a confirmed frameshift mutation OR a premature stop codon mutation between exons 18 to 58 in the DMD gene? ☐ Yes ☐ No

Is the member ambulatory? ☐ Yes ☐ No

Is the member non-ambulatory? ☐ Yes ☐ No

Does the member have any deletion in exon 8 and/or exon 9 in the DMD gene? ☐ Yes ☐ No

Does the member have cardiomyopathy with an ejection fraction less than 40%? ☐ Yes ☐ No

Does the member currently have an active infection? ☐ Yes ☐ No

Is the member on a stable dose of corticosteroids for DMD for at least 12 weeks prior to therapy? ☐ Yes ☐ No

What is the member's baseline anti-AAVrh74 antibody titers level measured by ELISA? _____

Is the requested medication being used in combination with exon-skipping therapies? ☐ Yes ☐ No

Is there documentation of a baseline evaluation including a standardized assessment of motor function done by a neurologist with experience in treating DMD and liver function, platelet count and troponin-I levels assessed to be clinically appropriate? ☐ Yes ☐ No

CALD:

Does the member have early, active CALD? ☐ Yes ☐ No

Does the member have elevated VLCFA? ☐ Yes ☐ No Value: _____

Has the member had an MRI establishing active CNS disease with GdE+ of demyelinating lesions? ☐ Yes ☐ No

What is the Loes score? _____

What is the NFS score? _____

Does the member have confirmed mutations in the ABCD1 gene? ☐ Yes ☐ No

Does the member have an active infection? ☐ Yes ☐ No

Does the member have HIV? ☐ Yes ☐ No

Has the member received an allogenic transplant or gene therapy previously? ☐ Yes ☐ No

Metachromatic Leukodystrophy (MLD):

Does the member have one of the following (please select the appropriate one): ☐ Yes ☐ No ☐ Other:_____

☐ Pre-symptomatic late infantile (PSLI) MLD
☐ Pre-symptomatic early juvenile (PSEJ) MLD
☐ Early symptomatic early juvenile (ESEJ) MLD

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GENE THERAPY AGENTS
PRIOR AUTHORIZATION FORM (CONTINUED) – PAGE 3 OF 4

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MEMBER INFORMATION

Member Name:	DOB:	
Member ID:	Member weight:	Height:

MEDICAL HISTORY (Complete for ALL requests)

Diagnosis:	ICD Code:

MLD continued:

Has the diagnosis been confirmed by all of the following (submit confirmatory laboratory results): biochemical testing documenting human arylsulfatase A (ARSA) gene activity is below the normal range for the laboratory performing the test, the presence of two disease-causing ARSA alleles, either known or novel mutations, identified on genetic testing, and if novel mutations are identified, a 24-hour urine collection showing elevated sulfatide levels? ☐ Yes ☐ No

Is the requested medication being prescribed by or in consultation with a physician who specializes in the treatment of MLD? ☐ Yes ☐ No

Is there evidence of residual cells of donor origin if the member has received a prior allogeneic hematopoietic stem cell transplant (allo-HSCT)? ☐ Yes ☐ No

Aromatic L amino acid decarboxylase (AADC) deficiency:

Has the diagnosis been confirmed based on **all** of the following (submit confirmatory laboratory results): ☐ Yes ☐ No

- Genetic testing showing biallelic mutations in the DOPA decarboxylase (DDC) gene
- Reduced levels of 5-hydroxyindoleacetic acid (5-HIAA), homovanillic acid (HVA) and 3-methoxy-4hydroxyphenylglycol (MHPG) and high concentrations of 3-O-methyldopa (3-OMD), L-Dopa, and 5OH tryptophan (5-HTP) in the cerebral spinal fluid (CSF)
- Reduced aromatic L-amino acid decarboxylase (AADC) activity in the plasma

Is the requested medication being prescribed by or in consultation with a pediatric neurologist? ☐ Yes ☐ No

Does the member present with classical clinical characteristics of AADC deficiency, such as oculogyric crises, hypotonia, and developmental delay? ☐ Yes ☐ No

Does the member have any significant structural brain abnormality? ☐ Yes ☐ No

Does the member have anti-AAV2 neutralizing antibody titer over 1,200 folds? ☐ Yes ☐ No

Has the member received prior treatment with any other AAV2-based gene therapy despite indication or are being considered for treatment with any other AAV2-based gene therapy? ☐ Yes ☐ No

Non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS):

Does the member have a diagnosis of NMIBC with CIS with or without papillary tumors? ☐ Yes ☐ No

Is the member's disease high-risk and BCG unresponsive? ☐ Yes ☐ No

Is the member immunocompromised or immunodeficient? ☐ Yes ☐ No

Does the member have extra-vesical (i.e., urethra, ureter, or renal pelvis), muscle invasive (T2-T4), or metastatic urothelial carcinoma? ☐ Yes ☐ No

Is the member ineligible for or has elected not to undergo cystectomy? ☐ Yes ☐ No

Does the member have an ECOG performance status ≤2? ☐ Yes ☐ No

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HIGHMARK WHOLECARE

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GENE THERAPY AGENTS
PRIOR AUTHORIZATION FORM (CONTINUED) – PAGE 4 OF 4

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MEMBER INFORMATION

Member Name:	DOB:	
Member ID:	Member weight:	Height:

MEDICAL HISTORY (Complete for ALL requests)

Diagnosis:	ICD Code:

Non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS):
Does the member have a diagnosis of NMIBC with CIS with or without papillary tumors? ☐ Yes ☐ No
Is the member's disease high-risk and BCG unresponsive? ☐ Yes ☐ No
Is the member immunocompromised or immunodeficient? ☐ Yes ☐ No
Does the member have extra-vesical (i.e., urethra, ureter, or renal pelvis), muscle invasive (T2-T4), or metastatic urothelial carcinoma? ☐ Yes ☐ No
Is the member ineligible for or has elected not to undergo cystectomy? ☐ Yes ☐ No
Does the member have an ECOG performance status ≤2? ☐ Yes ☐ No

CURRENT or PREVIOUS THERAPY

Medication Name	Strength/ Frequency	Dates of Therapy	Status (Discontinued & Why/Current)

REAUTHORIZATION

Non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS):
Does the member continue to meet the requirements for initial therapy and has been treated with nadofaragene firadenovec-vncg (Adstiladrin) with no adverse reactions? ☐ Yes ☐ No
Does the member have no signs of unacceptable toxicity (such as risk of disseminated adenovirus infection) while on treatment with nadofaragene firadenovec-vncg (Adstiladrin)? ☐ Yes ☐ No

SUPPORTING INFORMATION or CLINICAL RATIONALE

Prescribing Provider Signature	Date