University of Michigan Health Plan

DRUG DETERMINATION POLICY

Title: DDP-39 Gene Therapy Agents

Effective Date: 12/18/24

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by UM Health Plan and may not be covered by all UM Health Plan. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact UM Health Plan Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Luxturna, Zolgensma, and Evrysdi are specialty drugs indicated for very specific diagnoses and are associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the intended diagnosis and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. Luxturna subretinal injection (voretingene neparvovec) [must meet all listed below]:

   A. Age: at least four years (no study on patients less than four years of age).

   B. Prescriber: ophthalmologist or retinal surgeon.

   C. Diagnosis and severity [must meet all listed below]:

      1. Diagnosis: biallelic PRE65 mutation-associated retinal dystrophy dystrophy [e.g. Leber's congenital amaurosis (LCA), retinitis pigmentosa (RP), early onset severe retinal dystrophy (ERSOD)].

      2. Genetic testing: documenting biallelic mutation of RPE65 gene.

      3. Sufficient viable retinal cell determined by optical coherence tomography [must meet one listed below]:

a. Confirming an area of the retina with the posterior pole of greater than 100 um thickness.

b. At least three disc areas of the retina without atrophy or pigmentary degeneration with the posterior pole.

c. Remaining visual field within 30 degrees fixation as measured by III4e isopter or equivalent.

D. Other therapies: none.

E. Dosage regimen: Luxterna subretinal injection (voretingene neparvovec) [must meet all listed below]:

1. Dose: 1.5 x 10^{11} vector genomes subretinal injection in a total volume of 0.3 mL.

2. Administration: each eye on separate days within a close interval, but no fewer than six days apart by an ophthalmologist or retinal surgeon.

3. Concomitant oral corticosteroid therapy: prednisone 1 mg per kg per day (or equivalent) times seven days beginning three days before gene therapy, then tapering over the next ten days.

4. Limited activities: no air travel and/or scuba diving post-treatment until all intraocular air bubbles have been absorbed.

F. Approval: one injection per eye per lifetime.

G. Exclusions:

1. Intraocular surgery: surgery within six months of the time of therapy.

2. Ocular or systemic conditions that would interfere with therapy.

a. Malignancy treatment that affects the central nervous system (CNS): radiation of the orbit, CNS leukemia with optic nerve involvement.

b. Diabetes or sickle cell disease with advanced retinopathy: macular edema, proliferative changes.

c. Immunodeficiency susceptible to opportunistic inecions: e.g., cytomegalovirus retinitis.

d. Pregnant or breastfeeding.

II. Spinal Muscular Atrophy Agents

A. Zolgensma intravenous (onasennogene beparvovec-xioi IV) [must meet all listed below]

1. Age [must meet both listed below]:

a. Six months to less than two years.

b. Prematurity: full-term gestational age reached before use.

2. Weight: 2.6 kg – 21 kg

3. Prescriber: neurologist.

4. Diagnosis and severity.
    a. Spinal muscular atrophy (SMA) diagnosis [must meet all listed below]:
        i. Symptomatic disease that is diagnosed by a neurologist with expertise in SMA.
        ii. Diagnosis of likely Type I or II SMA based on SMA newborn screening.
        iii. Medical records documenting that the patient has three or fewer copies of the SMA2 gene.
    b. Genetic testing [must meet one listed below]:
        i. Homozygous gene deletion of genes or mutation of SMN1 gene (e.g., deletion of SMN1 exon 7 at locus 5q13)
        ii. Compound heterozygous mutation of SMN1 gene (e.g., deletion of SMB1 exon7 [allele 1] and mutation of SMN1 [allele 2]).
    c. Severity [must meet all listed below]:
        i. Severity score: Children's Hospital of Philadelphia Infant Test of Neuromuscular Disease (CHOP INTEND) score of at least 40 indicating disease severity is not an advanced stage. http://columbiasma.org/docs/cme-2010/CHOP%20INTEND%20for%SMA%20Type%201%20-%20Score%20Sheet.pdf.
        ii. Degree of ventilation assistance: use of non-invasive ventilation only during naps and nighttime sleep.
        iii. Degree of paralysis: does not have paralysis of all limbs.
5. Other therapies: none.
6. Dosage regimen [must meet all listed below]:
    a. 1.1×10^{14} vector genomes per Kg of body weight (limit of one kit of Zolgensma).
    b. Must be administered with prophylactic prednisolone (or glucocorticoid equivalent) prior to and following receipt of Zolgensma as indicated by the package insert.
7. Approval.
    a. Initial: one month.
    b. Re-approval: limited to one injection per lifetime.

B. Evrysdi (risdiplam) [must meet all listed below]:
1. Age: two months to 25 years.
2. Prescriber: neurologist.
3. Diagnosis and severity
    a. Spinal muscular atrophy (SMA) diagnosis [must meet all listed below]:

i. Symptomatic disease that is diagnosed by a neurologist with expertise in SMA.

ii. Diagnosis: Type I, II, or III SMA.

iii. Medical records documenting that the patient has three or fewer copies of the SMA2 gene.

b. Genetic testing [must meet one listed below]:

i. Homozygous gene deletion of genes or mutation of SMN1 gene (e.g., deletion of SMN1 exon 7 at locus 5q13)

ii. Compound heterozygous mutation of SMN1 gene (e.g., deletion of SMB1 exon7 [allele 1] and mutation of SMN1 [allele 2]).

c. Severity [must meet both listed below]:

i. Degree of ventilation assistance: use of non-invasive ventilation only during naps and nighttime sleep.

ii. Degree of paralysis: does not have complete paralysis of all limbs.

4. Other therapies: none.

5. Dosage regimen: Evrysdi (risdiplam).

a. Two months to less than two years: 0.2 mg per Kg once daily.

b. Two years of age and older weighing less than 20 Kg: 0.25 mg per Kg once daily

c. Two years of age and older weighing 20 Kg or more: 5 mg once daily.

6. Approval

a. Initial: four months.

b. Re-approval:

i. Duration: six months.

ii. Documentation of a positive response to therapy as demonstrated by clinically significant improvement or maintenance of function from pretreatment baseline status.

iii. Adherence: consistent (at least 80% of days covered) fill history electronically or verbally from the pharmacy.

C. Exclusions:

1. Treatment of pre-symptomatic patients diagnosed by newborn screening who are unlikely to develop Type I or II SMA.

2. Late-onset SMA greater than two years old.

3. SMA without chromosome 5q deletions.

4. Anti-AAV9 antibody titer at or above 1:50 before administration.

5. Combination of SMA with concomitant SMN modifying therapy (e.g., Spinraza) or previous treatment with Spinraza with evidence of clinical decline while receiving it.

6. Prior use of gene replacement therapy for the treatment of SMA (e.g., Zolgensma – nasemnogene abeparvovee-xioi).

4.0 Coding:

COVERED PRODUCTS – PHARMACY BENEFIT	
Medication Name	**Prior Approval**
Evrysdi	Y

COVERED CODES – MEDICAL BENEFIT				
Code	**Brand Name**	**Generic Name**	**Billing Units (1 unit)**	**Prior Approval**
J3398	Luxturna	voretingene neparvovec	1 billion vector genomes	Y
J3399	Zolgensma	Onasemnogene abreparvovec-XIOI	Up to 5x10^15 vector genomes	Y

5.0 References, Citations & Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Luxturna accessed October 2021.
2. Efficacy and safety of voretingene neparvovec (AAV2-hRPE65v2) in patients with RPE65-mediated inherited retinal dystrophy: a randomized, controlled, open-label, phase 3 trial. Lancet 2017;390(10097):849-860.
3. Improvement and decline in vision with gene therapy om childhood blindness. N Eng J Med 2015;372:1920.
4. *RPE65*-associated inherited retinal diseases: Consensus recommendations for eligibility to gene therapy. Orphanet J Rare Dis 2021;16:257
5. Lexi comp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Zolgensma, Evrysdi accessed J October 2021.
6. Single-dose gene-replacement therapy for spinal muscular atrophy. N Engl J med. 2017;377:1713-22.
7. Treatment algorithm for infants diagnosed with spinal muscular atrophy through newborn screening. Journal of Neuromuscular Disease. 2018;5(2):145-58. 4. Cure SMA: Clinical Guidelines. https://www.curesma.org/clinical-guidelines/ accessed October 2022.

6.0 Appendices:

None.

7.0 Revision History:

Original Effective Date: 12/11/2019

Next Review Date: 11/10/2025

Revision Date	Reason for Revision
11/19	New policy, split into two policies
10/20	Annual review; clarified criteria instructions, replaced abbreviations, formatting, approved by P&T Committee 12/9/20
10/21	Annual review; reformatting
10/22	Annual review; added reference
9/23	Annual Review – DDP-40 regarding Zolgensma, and Evrysdi merged into this policy. New policy title. minor grammatical changes, coding updated, added weight range to Zolgensma pursuant to prescribing information, adherence requirement added to Evrysdi
9/24	Annual review; removed Patient Safety and Monitoring Appendix, Added Pharmacy Benefit coverage to coding section