Addendum to Protocol for Duchenne Muscular Dystrophy Products Approved October 2023

Approved July 2020
Updated July 2021 - Added viltolarsen (Viltepso®) – FDA-approved in August 2020
Updated October 2021:

a. Added casimersen (Amondys 45) – FDA-approved in February 2021
b. Changed name of protocol to "Protocol for Duchenne Muscular Dystrophy Products"

Exondys 51® (eteplirsen)
Vyondys 53® (golodirsen)
Viltepso® (viltolarsen)
Amondys 45® (casimersen)

Addendum:
Addition of Elevidys® (delandistrogene moexeparvovec-rokl) – FDA-approved July 22, 2023

Background:
Eteplirsen (Exondys 51®) 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 51 skipping.

Golodirsen (Vyondys 53®) 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.

Viltolarsen (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.

Casimersen (Amondys 45®) 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 45 skipping

Delandistrogene moxeparvovec-rokl (Elevidys®) 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.

Limitations:
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.)

Criteria for Initial Approval:

1. Patient must have the diagnosis of Duchenne Muscular Dystrophy (DMD).

2. Submission of medical records including the following:
   a. For Exondys 51: Genetic testing confirming the patient has a mutation of the DMD gene that is amenable to exon 51 skipping.
   b. For Vyondys 53 and Viltepso: Genetic testing confirming the patient has a mutation of the DMD gene that is amenable to exon 53 skipping.
   c. For Amondys 45: Genetic testing confirming the patient has a mutation of the DMD gene that is amenable to exon 45 skipping.
   d. For Elevidys:
      i. Genetic testing confirming the patient has any mutation in the DMD gene, except a deletion mutation in exon 8 and/or exon 9.
      ii. Elevidys is contraindicated for patients with deletion mutations in either exon 8 and/or exon 9 in the DMD gene.
   e. Baseline renal function tests (i.e., glomerular filtration rate GFR) as required by medication's label

3. Patient has been stable on a systemic corticosteroid regimen for at least 12 weeks, unless contraindicated or experienced significant adverse effects (must receive documentation)

4. Prescribed by or in consultation with a pediatric/adult neurologist or a physician who is an expert in the treatment of DMD and other neuromuscular disorders

5. Prescriber understands that continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials (PI)

6. Patient's kidney function will be evaluated before and during treatment as required by the medication label, except for Elevidys, for which the assessment of liver function is what is important

7. Weight must be received for drugs that have weight-based dosing

8. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Lexi-Drugs, national guidelines, or other peer-reviewed evidence

9. Patient will not use golodirsen (Vyondys 53®) together with viltolarsen (Viltepso®)

10. For Elevidys:
    a. Patient is 4-5 years old
    b. Patient is ambulatory (e.g., able to walk with or without assistance, not wheelchair dependent)
    c. Baseline anti-AAVrh74 antibody titers <1:400 as determined by a total binding antibody ELISA
    d. Baseline platelet count and troponin-I levels is obtained prior to initiating treatment
    e. Elevidys will not be used in combination at the same time as the exon-skipping therapies (casimersen, eteplirsen, golodirsen, viltolarsen), but can be used after discontinuation of the other treatment options.
    f. Treatment is one time only

Continuation of therapy:

1. Updated chart notes demonstrating positive clinical response to therapy (such as improvement and/or stabilization compared to baseline)

2. Prescribed by or in consultation with a pediatric/adult neurologist or a physician who is an expert in the treatment of DMD and other neuromuscular disorders

3. For dose increases, the member's weight must be received

4. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Lexi-Drugs, national guidelines, or other peer-reviewed evidence

5. Patient will not use golodirsen (Vyondys 53®) together with viltolarsen (Viltepso®)

Approval Duration:

- Elevidys - One month for a total of one dose
- All others - 6 months

Dosing and Quantity Level Limit:

Exondys 51

- Available as 100 mg/2 mL (50 mg/mL) single-dose vial - 120 vials (240 mL) per 28 days

- Available as 500 mg/10 mL (50 mg/mL) single-dose vial - 24 vials (240 mL) per 28 days

Vyondys 53

- Refer to product labeling at https://www.vyondys53.com/pi
- Available as 100 mg/2 mL single-dose vial

Viltepso

- Refer to product labeling at https://www.viltepso.com/prescribing-information
- Available as 250 mg/5 mL (50 mg/mL) single-dose vial

Amondys 45

- Refer to product labeling at https://www.amondys45.com/pi
- Available as 100 mg/2 mL single-dose vial

Elevidys

- Refer to product labeling at https://www.elevidys.com/downloads/elevidys-pi.pdf
- Member will not exceed a dose of 30 mg/kg once weekly

References:

1. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; September 2016.
2. Vyondys 53 [package insert]. Sarepta Therapeutics, Inc.; Cambridge, MA. March 2020.
3. Viltepso [package insert]. NS Pharma, Inc. Paramus, NJ 07652
4. Amondys 45 [package insert]. Sarepta Therapeutics, Inc; Cambridge MA. February 2021
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2019. URL: http://www.clinicalpharmacology.com. Updated periodically
6. Mendell JR, et al; Eteplirsen Study Group. Eteplirsen for the treatment of Duchenne muscular dystrophy. Ann Neurol. 2013;74(5):637-647.
7. Lee JJA, Saito T et al. Direct Reprogramming of Human DMD Fibroblasts into Myotubes for In Vitro Evaluation of Antisense-Mediated Exon Skipping and Exons 45-55 Skipping Accomplished by Rescue of Dystrophin Expression. Methods Mol Biol. 2018; 1828: 141-150
8. Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, et al. Diagnosis and management of Duchenne
9. muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol; 2010 Jan; 9(1):77 93.