Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 04/11/2024

Duchenne Muscular Dystrophy Class Policy

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

HCPCS: Amondys 45: J1426; Exondys 51: J1428; Viltepso: J1427; Vyondys 53: J1429

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
    a. Coverage of the requested drug is considered investigational/experimental for all indications due to insufficient evidence of a clinical benefit
        i. BCBSM and BCN are awaiting the results of ongoing clinical trials to provide evidence of a clinical benefit.

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Duchenne muscular dystrophy (DMD) is a rare, life-limiting, progressive childhood disease that affects 1 in 3,500 – 5,000 live male births. It is characterized by progressive muscle weakness and wasting due to the absence of dystrophin protein that causes degeneration of skeletal and cardiac muscle. Affected individuals are unable to run and jump properly due to proximal muscle weakness of the leg and pelvic muscles. DMD occurs as a result of mutations in the dystrophin gene, located on the X-chromosome, which normally functions to generate dystrophin, a structural protein of muscle cells. Mutations in the dystrophin gene lead to an absence of or a defect in dystrophin protein resulting in the progressive symptoms seen in DMD patients.

- At present, there is no disease-modifying therapy for DMD available for the majority of boys. In addition to surgical and physical therapeutic measures, glucocorticosteroids are used in DMD. The 2018 treatment guidelines for DMD support the use of glucocorticosteroids as they are the only medication currently available to slow the decline in

muscle strength and function which in turn reduces the risk of scoliosis and stabilizes pulmonary function. Trials show muscle strength is improved when treated with prednisone at a dose of 0.75 mg/kg daily for up to 6 months. The goal of glucocorticoids in an ambulatory patient is the preservation of ambulation and the minimization of later cardiac, respiratory, and orthopedic complications. Continued treatment after the patient becomes non-ambulatory has shown reduction in the risk of progressive scoliosis and stabilization of pulmonary function tests. However, it is important to note that glucocorticosteroids are not able to induce the production of dystrophin-like proteins and therefore do not alter or impact the underlying cause of DMD.

- Exondys 51 received FDA approval on September 19, 2016 for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 51 skipping. Vyondys 53 was FDA approved on December 12, 2019 and Viltepso was FDA approved on August 12, 2020 for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping. Amondys 45 received FDA approval February 25, 2021 for the treatment of Duchenne muscular dystrophy in patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 45 skipping. The FDA labeled indications includes a statement that continued approval is contingent upon verification of a clinical benefit in ongoing confirmatory clinical trials. Prior to FDA approval, the Peripheral and Central Nervous System Drugs Advisory Committee of the FDA held a meeting and voted against approval of eteplirsen as treatment for DMD due to lack of substantial evidence of effectiveness.

- Exondys 51, Vyondys 53, Viltepso, and Amondys 45 were approved under the accelerated approval pathway using a surrogate endpoint of increase in dystrophin in skeletal muscle observed in some patients. There is no evidence the small observed increase in dystrophin results in a clinically meaning benefit. Therefore, establishment of a clinical benefit is needed in on-going clinical trials.

- There is an ongoing phase III confirmatory trial (PROMOVI) evaluating the efficacy and safety of Exondys 51 across two groups of patients (treated and untreated) with genotypically confirmed DMD. Patients in the treated group are amenable to exon 51 skipping and those in the untreated group are not amenable to exon 51 skipping. The PROMOVI trial has a target enrollment of 160 patients. Subjects will be administered 30 mg/kg/week for 96 weeks. Objectives include changes in the 6 minute walk test (6MWT), dystrophin and pulmonary function. The estimated completion date is January 2019.

- There is an ongoing phase III confirmatory trial (ESSENCE) evaluating the efficacy and safety of Vyondys 53 and Amondys 45 versus placebo with genotypically confirmed DMD amenable to either exon 53 skipping or exon 45 skipping. The ESSENCE trial has a target enrollment of 211 patients. Subjects will be administered 30 mg/kg/week or Vyondys 53 or Amondys 45 depending on their genetic mutation for 96 weeks. Objectives include changes in 6MWT, dystrophin and pulmonary function. The estimated completion date is sometime in 2024.

- There is an ongoing phase III confirmatory trial (RACER53) evaluating the safety and efficacy of Viltepso versus placebo with genotypically confirmed DMD amenable to exon 53 skipping. The RACER53 trial has a target enrollment of 74 patients. Subjects will be administered Viltepso 80 mg/kg/week or placebo for up to 48 weeks. Objectives include changes in time to stand, 6MWT, time to run/walk 10 meters, and time to climb 4 steps.

- Based on the current information available, there is insufficient evidence that Exondys 51, Vyondys 53, Viltepso, and Amondys 45 provide a clinical benefit in patients with DMD. Therefore, demonstration of a clinical benefit is warranted in on-going clinical trials.

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Policy History		
#	Date	Change Description
2.6	Effective Date: 04/11/2024	Annual review of criteria was performed, no changes were made
2.5	Effective Date: 04/06/2023	Annual review of criteria was performed, no changes were made
2.4	Effective Date: 04/14/2022	Annual review of criteria was performed, no changes were made.
2.3	Effective Date: 04/26/2021	UM medical management system update for BCBSM for Amondys 45
2.2	Effective Date: 04/08/2021	Added Amondys 45
2.1	Effective Date: 03/22/2021	UM medical management system update for BCN for Amondys 45
2.0	Effective Date: 10/08/2020	Added Viltepso
1.9	Effective Date: 10/01/2020	UM medical management system update for BCBSM for Viltepso
1.8	Effective Date: 09/01/2020	UM medical management system update for BCN for Viltepso
1.7	Effective Date: 06/01/2020	UM medical management system update for MAPPO and BCNA for Vyondys 53 and Exondys 51
1.6	Effective Date: 02/06/2020	Added Vyondys 53 and copied over all updated information from the Exondys 51 policy to the DMD policy
1.5	Effective Date: 02/01/2020	UM medical management system update for BCBS for Vyondys 53
1.4	Effective Date: 01/02/2020	UM medical management system update for BCN for Vyondys 53
1.3	Effective Date: 05/09/2019	Annual review of criteria was performed, no changes were made.
1.2	Effective Date: 05/03/2018	Annual Drug Review; new publications and long-term continuation data reviewed/added
1.1	Effective Date: 04/01/2017	PA added to BCBS for Exondys 51
1.0	Effective Date: 02/09/2017	New Coverage Guidelines. PA added to BCN for Exondys 51

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*