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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.

P&T Date: 04/10/2025

Duchenne Muscular Dystrophy Class Policy

Amondys 45™ (casimersen)

Exondys 51® (eteplirsén)

Viltepso™ (viltolarsen)

Vyondys 53™ (golodirsén)

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:
- Coverage of the requested drug is considered investigational/experimental for all indications due to insufficient evidence of a clinical benefit
 - 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

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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.

References:

1. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne's muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *Lancet Neurol*. 2018 March; 17 (3): 251 - 67.
2. Bushby K, Finkel R, Birnkrant D, et al. Diagnosis and management of duchenne's muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. *Lancet Neurol*. 2018 April; 17 (4): 347-61.
3. Falzarano M, Scotton C, Passarelli C, et al. Duchenne muscular dystrophy: from diagnosis to therapy. *Molecules*. 2015 Oct 7; 20 (10): 18168 - 84.
4. Blat Y & Blat S. Drug discovery of therapies for duchenne muscular dystrophy. *J Biomol Screen*. 2015 April: 1 - 10.
5. Voit T, Topaloglu H, Straub V, et al. Safety and efficacy of drisapersen for the treatment of duchenne muscular dystrophy (DEMAND II): an exploratory, randomized placebo-controlled phase 2 study. *Lancet Neurol*. 2014; 13: 987 - 96.
6. Mendell JR, Rodino-Klapac L, Sahenk Z, et al. Eteplirsen for the treatment of duchenne muscular dystrophy. *Ann Neurol*. 2013; 74: 637 - 47.
7. Mendell JR, Goemans N, Lowes L, et al. Longitudinal effect of eteplirsen versus historical control on ambulation in duchenne muscular dystrophy. *Ann Neurol*. 2016; 79 (2): 257 - 71.
8. BioMarin Completes Rolling NDA Submission to FDA for Drisapersen for Duchenne Muscular Dystrophy. http://www.drugs.com/nda/drisapersen_150427.html.
9. BioMarin Pipeline: Clinical Trials – Duchenne's Muscular dystrophy. Cited on October 2nd, 2015. <https://www.bmrn.com/pipeline/clinical-trials/DuchenneMuscularDystrophy.php>.
10. Mirski KT & Crawford TO. Motor and cognitive delay in duchenne's muscular dystrophy implication for early diagnosis. *J Pediatr*. 2014; 165: 1008.
11. Emery AE. The muscular dystrophies. *Lancet*. 2002; 359: 687 - 96.
12. McDonald CM, Henricson EK, Abresch RT, et al. The 6-minute walk test and other endpoints in Duchenne muscular dystrophy: a longitudinal natural history observations over 48 weeks from a multicenter study. *Muscle Nerve*. 2013; 48: 343 - 56.
13. McDonald CM, Henricson EK, Abresch RT, et al. The 6-minute walk test and other clinical endpoints in duchenne muscular dystrophy: reliability, concurrent validity and minimal clinically important differences from a multicenter study. *Muscle Nerve*. 2013; 48: 357 - 68.
14. National Human Genome Research Institute: Learning About Duchenne Muscular Dystrophy. April 2013. Cited on October 10th, 2015. <https://www.genome.gov/19518854>.
15. New data on first-class Duchenne Muscular Dystrophy tx. October 16th, 2015. Cited on October 31st, 2015. <http://www.empr.com/drugs-in-the-pipeline/translarna-ataluren-nonsense-mutation-duchenne-muscular-dystrophy-phase-3/article/447532/>
16. Exondys 51 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc; December 2024.
17. Highmark Preliminary Medication Review: New Molecular Entity – Musculoskeletal Agent – eteplirsen (Exondys 51TM) [Sarepta Therapeutics, Inc.] October 2016
18. Deconinck N & Dan Bernard. Pathophysiology of duchenne muscular dystrophy: current hypothesis. *Pediatr Neurol*. 2007 Jan; 36 (1): 1 - 7.
19. Express Scripts® Drug Evaluation: Exondys 51 (eteplirsen injection for intravenous use – Sarepta Therapeutics, Inc.) September 2016.
20. FDA rejects BioMarin Pharmaceutical's Duchenne Muscular Dystrophy Drug. *Tech Times*. January 15th, 2016 [cited October 1, 2016].
21. US National Institutes of Health. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2016 Oct 5]. Available from: <https://clinicaltrials.gov/ct2/results?term=eteplirsen&search=Search>
22. Eteplirsen. Food and Drug Administration (FDA) Briefing Document: Peripheral and Central Nervous System Drugs Advisory Committee Meeting. January 22, 2016a. Available at: <http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/drugs/peripheralandcentralnervoussystemdrugsadvisorycommittee/ucm481911.pdf>. Accessed on October 20th, 2016.

23. Exondys 51™ (eteplirsen) Injection, For Intravenous Use. Exon Skipping Phosphorodiamidate Morpholino Oligomer (PMO). Formulary Submission Dossier. Sarepta Therapeutics, Inc.
24. Kinane TB, Mayer OH, Duda PW, et al. Long-term pulmonary function in duchenne muscular dystrophy: comparison of eteplirsen-treated patients to natural history. *J Neuromuscul Dis.* 2017 Dec 20. Accessed January 2018.
25. Randeree L & Eslick GD. Eteplirsen for paediatric patients with Duchenne muscular dystrophy: a pooled-analysis. *J Clin Neurosci.* 2017 Dec 15. pii: S0967-5868(17)31142-6. Accessed January 2018.
26. Eteplirsen clinical resenatation. Sarepta Therapeutics, Inc. January 2018.
27. Vyondys 53 [prescribing information]. Cambridge, MA: Sarepta Therapeutics, Inc.; June 2024.
28. Mendell JR, Shilling C, Leslie ND, et al. Evidence-based path to newborn screening for Duchenne muscular dystrophy. *Ann Neurol.* 2012; 71 (3): 304 – 13.
29. Hoffman EP, Fischbeck KH, Brown RH, et al. Characterization of dystrophin in muscle-biopsy specimens from patients with Duchenne's or Becker's muscular dystrophy. *N Engl J Med.* 1988; 318 (21): 1363 – 8.
30. Koeks Z, Bladen CL, Salgado D, et al. Clinical outcomes in Duchenne muscular dystrophy: a study of 5345 patients from the TREAT-NMD DMD global database. *J Neuromuscul Dis.* 2017; 4 (4): 293 – 306.
31. Humbertclaude V, Hamroun D, Bezzou K, et al. Motor and respiratory heterogeneity in Duchenne patients: implication for clinical trials. *Eur J Paediatr Neurol.* 2012; 16 (2): 149 – 60.
32. Gloss D, Moxley RT, Ashwal S, Oskoui M. Practice guideline update summary: corticosteroid treatment of Duchenne muscular dystrophy: report of the guideline development subcommittee of the American Academy of Neurology. *Neurology.* 2018; 17 (4): 347 – 61.
33. Van Putten M, Hulsker M, Young C, et al. Low dystrophin levels increase survival and improve muscle pathology and function in dystrophin/utrophin double-knockout mice. *FASBE J.* 2013; 27 (6): 2484 – 95.
34. Waldrop MA, Gumienny F, EL Husayni S, et al. Low-level dystrophin expression attenuating the dystrophinopathy phenotype. *Neuromuscular Disord.* 2018; 28 (2): 116 – 21.
35. Muntoni F, Frank DE, Morgan J, et al. Goldirsen induces exon skipping leading to sarcolemmal dystrophin expression in patient with genetic mutations amenable to exon 53 skipping. *Neuromuscular Disord.* 2018; 28 (Supp 1): S5.
36. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of duchenne muscular rehabilitation, endocrine, and gastrointestinal and nutritional management. *Lancet Neuro.* 2018 Mar; 17 (3): 251 – 67.
37. Clinicaltrials.gov. A 2-part, randomized, double-blind, placebo-controlled, dose-titration, safety, tolerability, and pharmacokinetics study (Part 1) followed by an open-label efficacy and safety evaluation (part 2) of SRP-4053 in patients with duchenne muscular dystrophy amenable to exon 53 skipping (NCT02310906). Available at: <https://clinicaltrials.gov/ct2/show/NCT02310906>. Accessed on December 16, 2019.
38. Clinicaltrials.gov. Study of SRP-4045 and SRP-4053 in DMD patients (ESSENCE) (NCT02500381). Available at: <https://clinicaltrials.gov/ct2/show/NCT02500381?term=golodirsen&draw=2&rank=4>. Accessed on January 2, 2020.
39. Viltepso [prescribing information]. Paramus, NJ: NS Pharma, Inc.; March 2021.
40. Clinicaltrials.gov. A phase 3 randomized, double-blind, placebo-controlled, multi-center study to assess the efficacy and safety of viltolarsen in ambulant boys with duchenne muscular dystrophy (DMD) (NCT04060199). Available at: <https://clinicaltrials.gov/ct2/show/NCT04060199?term=NCT04060199&draw=2&rank=1>. Accessed on August 13, 2020.
41. Clinicaltrials.gov. Safety and dose finding study of NS-065/NCNP-01 in boys with duchenne muscular dystrophy (DMD) (NCT02740972). Available at: <https://clinicaltrials.gov/ct2/show/NCT02740972?term=NS-065&cond=Duchenne+Muscular+Dystrophy&rank=3>. Accessed on August 13, 2020.
42. Clinicaltrials.gov. Extension study of NS-065/NCNP-01 in boys with duchenne muscular dystrophy (DMD) (NCT03167255). Available at: <https://clinicaltrials.gov/ct2/show/NCT03167255?term=NS-065&cond=Duchenne+Muscular+Dystrophy&draw=2&rank=1>. Accessed on August 13, 2020.
43. Amondys 45 [prescribing information]. Cambridge, MA: Sarepta Therapeutics, Inc.; March 2023.
44. Clinicaltrials.gov. Study of SRP-4045 and SRP-4053 in DMD patients (ESSENCE) (NCT02500381). Available at: <https://clinicaltrials.gov/ct2/show/NCT02500381?term=NCT02500381&draw=2&rank=1>. Accessed on February 26, 2021.

Policy History		
#	Date	Change Description
2.7	Effective Date: 04/10/2025	Annual review of criteria was performed, no changes were made
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>.

Blue Cross Blue Shield/Blue Care Network of Michigan

Medication Authorization Request Form



This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

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PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	Name
ID Number	Specialty
D.O.B. <input type="checkbox"/> Male <input type="checkbox"/> Female	Address
Diagnosis	City /State/Zip
Drug Name	Phone/Fax: P: () - F: () -
Dose and Quantity	NPI
Directions	Contact Person
Date of Service(s)	Contact Person Phone / Ext.

STEP 1: DISEASE STATE INFORMATION

- Is this request for: ☐ Initiation ☐ Continuation Date patient started therapy: _____
- Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
- Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
☐ Hospital outpatient facility (go to #4) Reason for Hospital Outpatient administration: _____
☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
- Please specify location of administration if hospital outpatient infusion: _____
- Please specify location of administration if hospital inpatient infusion: _____
- Please provide the NPI number for the place of administration: _____
- Initiation AND Continuation of therapy:**
 - What is the patient's diagnosis? _____
 - What other medication has the patient received for their condition? Please list _____
 - Please describe the response to previous therapies: _____
 - Will the patient be receiving any other treatment for the listed condition while on this medication? Please list: _____
 - Please list any labs values important for diagnosing or monitoring this patient's condition: _____
- Continuation of therapy:**
 - Has the patient progressed while on this medication? ☐ yes ☐ no
 - How has the patient's condition changed while on this medication?

☐ Improved: Please describe: _____
 ☐ Stable: please describe: _____
 ☐ Worsened; Please describe: _____
 ☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review (required)

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	<input type="checkbox"/> Form Completely Filled Out <input type="checkbox"/> Provide chart notes	<input type="checkbox"/> Attach test results
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

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7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021