MEDICAL COVERAGE POLICY	
SERVICE:	**Eteplirsen (Exondys 51) for Muscular Dystrophy**
Policy Number:	**237**
Effective Date:	**08/01/2020**
Last Review:	**06/29/2020**
Next Review Date:	**06/29/2021**

Important note:
Unless otherwise indicated, this policy will apply to all lines of business.
Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

SERVICE: Eteplirsen (Exondys 51) for treatment of Duchenne muscular dystrophy (DMD)

PRIOR AUTHORIZATION: Not applicable.

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for coverage details.

For Medicare plans, please refer to appropriate Medicare LCD (Local Coverage Determination). If there is no applicable LCD, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid TMPPM.

Eteplirsen (Exondys 51™) for the treatment of Duchenne muscular dystrophy is considered not medically necessary as a clinical benefit has not been established.

Eteplirsen (Exondys 51™) for the treatment of all other indications is considered experimental, investigational and/or unproven.

OVERVIEW:

Duchenne muscular dystrophy (DMD) is an X-linked, recessive disorder that occurs in about 1 in every 3500 to 5000 males. The first signs or symptoms of DMD are noted at about 2.5 years. DMD occurs as a result of mutation(s) in the gene responsible for producing dystrophin, resulting in progressive muscle degeneration leading to a loss of ambulation and more. It's not unusual for this members to die in their late teens.

Eteplirsen is an "anti-sense" oligonucleotide of the phosphorodiamidate morpholino oligomer (PMO) class. PMOs are analogues that selectively bind to RNA to alter gene expression. In the case of eteplirsen, the PMO binds to exon 51 of the dystrophin pre-messenger RNA causing the exon to be skipped and prevents that part of the code from being read during mRNA processing, thereby partially repairing the mutated reading frame in the mRNA coding sequence. Thus, eteplirsen enables the production of an internally truncated, yet functional, dystrophin protein.

For individuals with confirmed mutation of the Duchenne muscular dystrophy gene, eteplirsen promotes exon 51 skipping as evidenced in 1 randomized controlled trial (RCT) and its open-labelled follow-up study, and interim data from an ongoing RCT.

Interim results from an ongoing study provided evidence that eteplirsen increased dystrophin levels in skeletal muscle in some patients. However, yet to be established is clinical benefit. Ongoing clinical trials are underway to determine the clinical benefit.

In a pooled analysis, Randeree and Eslick analyzed the results of previous studies to evaluate the safety and efficacy of eteplirsen. The average increase in percentage dystrophinpositive fibers after treatment with eteplirsen was 24.23% The average rate of decline in distance walked for the six-minute walk test was 65 meters. The authors concluded that whether or not this increase in percentage dystrophin-positive fibers and distance walked was clinically significant was unclear, and there is therefore a need for more clinical trials.

In a review article by Hwang and Yokota, they noted that results with eteplirsen appear promising. However, challenges remain as exon-skipping agents can have deleterious non-specific effects.

At this time the clinical benefit of this medication for the treatment of DMD has not been established.

CODES:

Important note:
CODES: Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.

CPT Codes:	
CPT Not Covered:	
ICD10 codes:	G71.0 - Muscular dystrophy [Duchenne muscular dystrophy (DMD)]
ICD10 Not covered:	
HCPCS	J1428 – Injection, eteplirsen (Exondys51)

CMS:

POLICY HISTORY:

Status	Date	Action
New	05/16/2017	New policy
Update	12/13/1017	Added new code for Exondys51 effective 1/1/18
Reviewed	01/16/2018	Confirmed coverage decision.
Reviewed	01/08/2019	No changes
Reviewed	01/23/2020	No changes
	06/29/2020	Language changed to include FC

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. SWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available and they are not included in the list, please forward the reference(s) to SWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol. Jan 2010; 9(1):77-93. PMID 19945913
2. Falzarano MS, Scotton C, Passarelli C, et al. Duchenne muscular dystrophy: from diagnosis to therapy. Molecules. Oct 07 2015; 20(10):18168-18184. PMID 26457695
3. Prescribing Label: EXONDYS 51 (eteplirsen) injection, for intravenous use. Sarepta Therapeutics, Inc. Available at: <http://www.accessdata.fda.gov>. Accessed November 2016.
4. Mendell JR, Rodino-Klapac LR, Sahenk Z, et al. Eteplirsen for the treatment of Duchenne muscular dystrophy. Ann Neurol. Nov 2013;74(5):637-647. PMID 23907995
5. Mendell JR, Goemans N, Lowes LP, et al. Longitudinal effect of eteplirsen versus historical control on ambulation in Duchenne muscular dystrophy. Ann Neurol. Feb 2016; 79(2):257-271. PMID 26573217
6. Kesselheim AS, Avorn J. Approving a Problematic Muscular Dystrophy Drug: Implications for FDA Policy. JAMA. Oct 24 2016. PMID 27775756
7. Confirmatory Study of Eteplirsen in DMD Patients (PROMOVI). Available at: <https://www.clinicaltrials.gov>.
8. Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. Lancet Neurol. Feb 2010; 9(2):177-189. PMID 19945914
9. Randeree L, Eslick G. Eteplirsen for paediatric patients with Duchenne muscular dystrophy: A pooled-analysis. J Clin Neuroscience. 2018; 49: 1-6
10. Hwang, J., & Yokota, T. (2019). Recent advancements in exon-skipping therapies using antisense oligonucleotides and genome editing for the treatment of various muscular dystrophies. Expert Reviews in Molecular Medicine, 21, E5. doi:10.1017/erm.2019.5