Letter of Medical Necessity: Test Code 1200 / 1773

<<Today’s Date>>

<<Insurance Company Name>>

<<Address 1>>

<<Address 2>>

<<City, State ZIP>>

**Regarding:** <<Patient full name>>
**DOB:** <<MM/DD/YYYY>>

**Subscriber ID:** <<Member ID#>>

**Group ID:** <<Group ID#>>

**Re**: Request for prior authorization and coverage for PreventionGenetics’ Dystrophinopathy testing via deletion/duplication and sequencing assays. Billing is through <<billing institution>> with testing performed at PreventionGenetics, LLC.  The CPT code for PreventionGenetics’ deletion/duplication test code #1200 is 81161.  The CPT code for PreventionGenetics’ NGS sequencing is test code #1773 is 81479. The ICD 10 code(s) associated with the patient’s diagnosis include <<ICD code(s)>>.

**Duchenne and Becker Muscular Dystrophy**

Duchenne muscular dystrophy is the most common form of congenital muscular dystrophy in all ethnic groups. Becker muscular dystrophy is a less common, relatively less severe form of dystrophinopathy with later onset of proximal weakness and preservation of ambulation into the third decade of life.1 These conditions are caused by variants in the dystrophin-encoding *DMD* gene. Approximately 65% of the variants in DMD patients are deletions of one or more exons in this gene that often disrupt the reading frame. The occurrence of deletions is slightly higher in BMD patients, however most of these are in-frame and do not disrupt the open reading frame (hence the milder phenotype).2,6  Variants detectable by sequence analysis are found in approximately 30% of DMD cases and in approximately 20% of BMD cases. Therefore, it is more cost-efficient and clinically relevant to test for deletions/duplications first followed by reflex to sequencing. Once a variant is identified, carrier analysis can be performed for the mother and other female relatives. Carriers are mainly asymptomatic though there is a risk of cardiac involvement, which requires monitoring and intervention if abnormalities are detected.3

A timely genetic diagnosis is one of the standards of care for DMD. According to these standards, published in 2010, this is important for family planning and initiating proper care for the affected individual. Confirming carrier status in the mother affects family planning and means that her genetic female relatives are potentially at risk of being a DMD carriers. It is important to realize that even when the mother is not a carrier, it is still possible she has germline mosaicism for the mutation, and in turn, is still at risk of having another son with DMD.3  Mutation specific therapies for eligible patients have also emerged, allowing for better treatment and management of the disorders. Treatments should begin as soon as possible for the affected as DMD is a progressive disease whose effects on muscle loss are likely irreversible. Antisense-mediated exon skipping therapies are the most promising treatments at this time. These splice interventions can remove exons with variants and allow dystrophin expression by editing dystrophin pre-mRNA and restoring the open reading frame.4,5,6

Research suggests that up to 80% of individuals with DMD could be eligible for these exon skipping therapies.4 A drug candidate designed to skip exon 51 of the *DMD* gene was just granted accelerated FDA approval on September 19, 2016. Exon 53 and 45 skipping therapies are currently in clinical development, and many others have been discovered and are undergoing clinical trials.7,8 Based on this information, genetic testing is critical for the treatment of patients clinically diagnosed or suspected to have Duchenne or Becker muscular dystrophy. The specific variant that an individual carries needs to be known in order for proper treatment and family planning to begin. Without this testing / test results, clinicians do not have the information they need to determine appropriate treatments or clinical trials for their patients

**Personal History**

<<Personal Medical History: Include details of patient’s relevant medical history>>

**Family History**

<<Family History: Include list of relevant family history information if applicable. Appropriate risk assessment models or limited history should be noted >>

Testing of the *DMD* gene through the *DMD* Deletion/Duplication panel (#1200), with reflex to the *DMD* NextGen Sequencing panel (#1773) in event a pathogenic variant is not identified via deletion/duplication, will allow for delineation of appropriate management guidelines for this patient and his/her family members.

The laboratory providing the genetic testing is PreventionGenetics, LLC, (Tax ID: 83 0343803) who is a sponsor of Pediatric Lab Utilization Guidance Services ([PLUGS®](http://www.seattlechildrenslab.org/plugs.aspx)).  PreventionGenetics is committed to providing comprehensive, high quality, and affordable genetic testing that adds value to patient care.  Through utilization management strategies at PreventionGenetics, over 1.3 million healthcare dollars are saved annually. PreventionGenetics is also certified by the College of American Pathologists (CAP# 7185561), the Clinical Laboratory Improvement Amendments (CLIA ID# 52D2065132), and is an Internationally-Recognized Accredited Laboratory (ISO 15189#: 3950.01).

I am hopeful that we can work together for <<Mr/Mrs/Ms/Miss patient’s last name’s>> benefit.  Please contact me at <<Phone #>> with the result of this prior authorization and/or if you need additional information.

Sincerely,

<<Name, credentials>>

<<Title>>

<<Institution>>

References:

1. Hoffman EP, Fischbeck KH, Brown RH, Johnson M, Medori R, Loike JD, Harris JB, Waterston R, Brooke M, Specht L. Characterization of dystrophin in muscle-biopsy specimens from patients with Duchenne’s or Becker’s muscular dystrophy. *N. Engl. J. Med*. 1988 May; 318(21):1363–1368. PubMed ID: 3285207.
2. Monaco AP, Bertelson CJ, Liechti-Gallati S, Moser H, Kunkel LM. An explanation for the phenotypic differences between patients bearing partial deletions of the DMD locus. *Genomics*. 1988 Jan; 2(1): 90–95. PubMed ID: 3384440.
3. Bakker E, Van BC, Bonten EJ, van de Vooren MJ, Veenema H, Van HW, van Ommen GJ, Vandenberghe A, Pearson PL. Germline mosaicism and Duchenne muscular dystrophy mutations. *Nature* . 1987 Oct; 329(6139):554–556. PubMed ID: 2889144.
4. Aartsma-Rus A, Fokkema I, Verschuuren J, Ginjaar I, van Deutekom J, van Ommen GJ, den Dunnen JT. Theoretic applicability of antisense-mediated exon skipping for Duchenne muscular dystrophy mutations. *Hum Mutat*. 2009 Mar; 30(3):293-299. PubMed ID: 19156838.
5. Fletcher, Sue, Abbie M. Adams, Russell D. Johnsen, Kane Greer, Hong M. Moulton, and Steve D. Wilton. Dystrophin Isoform Induction *In Vivo* by Antisense-mediated Alternative Splicing.  *Molecular Therapy.* 2010 Jun; 18(6):1218-1223. PubMed ID: 20332768.
6. Anthony, Karen; Virginia Arechavala-Gomeza; Valeria Ricotti; et al. DMD Deletions Pertinent to Exon 44 or 45 Skipping.  *JAMA Neurol.* 2014 Jan; 71(1):32-40. PubMed ID: 24217213.
7. Sarepta Therapeutics. Exon-Skipping for Duchenne. <https://www.sarepta.com/pipeline/exon-skipping-duchenne> 11 Oct. 2016.
8. Muscular Dystrophy Association. Eteplirsen Granted Accelerated Approval! 19 Sept. 2016. <https://www.mda.org/eteplirsen> 11 Oct. 2016.