



State of California—Health and Human Services Agency
Department of Health Care Services



GAVIN NEWSOM
GOVERNOR

DATE: December 8, 2020

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Index: Benefits

TO: All California Children Services Program County Administrators,
Medical Consultants, Genetically Handicapped Person Program staff
and Integrated Systems of Care Division Staff

SUBJECT: Antisense Oligonucleotide Treatment of Duchenne Muscular Dystrophy

I. PURPOSE

This Numbered Letter (N.L.) establishes California Children's Services (CCS) and Genetically Handicapped Person Program (GHPP) Program policy regarding the authorization of antisense oligonucleotide treatments for Duchenne muscular dystrophy (DMD).¹

The CCS Program publishes this N.L. under the program's authority to authorize services that are medically necessary to treat CCS-eligible conditions.^{2,3,4}

II. BACKGROUND

DMD is a genetic disorder causing progressive muscle deterioration and weakness. The absence or deficient levels of dystrophin protein, which maintains intact muscle cells, causes muscle deterioration and weakness. DMD primarily affects a patient's skeleton, diaphragm, and heart muscle. DMD occurs in about 1 in 3,600 male infants worldwide. DMD rarely occurs in females.

Symptoms typically appear in the first three years of life and progressively worsen over time. Affected individuals gradually lose their ability to perform daily activities and are usually wheelchair bound by adolescence and ventilator dependent by their 20s or 30s.

Clients with gene variants amenable to skipping of certain exons can produce functional, although truncated, dystrophin protein in the presence of eteplirsen, golodirsen, or viltolarsen, respectively.

Eteplirsen (Exondys 51™) is an antisense oligonucleotide that targets mutations amenable to exon 51 skipping, was the first treatment for DMD approved in the United States. It received accelerated approval on September 19, 2016 by the U.S.

Food and Drug Administration (FDA) for treatment of DMD in patients who have a confirmed DMD gene mutation amenable to exon 51 skipping. About 13 percent of DMD patients have a genetic mutation of the dystrophin gene amenable to exon 51 skipping.

Golodirsen (Vyondys 53™), which targets mutations amenable to exon 53 skipping, received accelerated FDA approval on December 12, 2019 for treatment of DMD in patients who have a dystrophin gene mutation amenable to exon 53 skipping. About eight percent of DMD patients have the genetic mutation of the dystrophin gene amenable to exon 53 skipping.

Viltolarsen (Viltepso) was approved on August 12, 2020, becoming the second drug treatment in patients with dystrophin gene mutation amenable to exon 53 skipping.

All three drugs are antisense oligonucleotides that are approved for use as a once-weekly intravenous infusion for the treatment of DMD in patients who have a confirmed mutation in the DMD gene that is amenable to exon 51 skipping (eteplirsen) or exon 53 skipping (golodirsen and viltolarsen).

III. POLICY

A. Initial Authorization

Effective the date of this N.L., the CCS Program shall authorize eteplirsen, golodirsen, or viltolarsen for up to twelve months when the following criteria are met:

1. Client has documented DMD with dystrophin gene mutation, amenable to exon 51 skipping for eteplirsen or amenable to exon 53 skipping for golodirsen or viltolarsen, as documented by genetic test(s).⁵
2. Client is at least two years of age for eteplirsen and golodirsen and four years of age for viltolarsen.
3. Client is currently under the supervision and monitoring of a CCS-paneled neurologist or physical medicine and rehabilitation specialist who is fellowship trained in neuromuscular medicine, at a CCS Neuromuscular Medicine Special Care Center (SCC), or at a neurology clinic.
4. The following are completed as part of the assessment for antisense oligonucleotide therapy:
 - a. Forced Vital Capacity (FVC),
 - b. Brooke score,
 - c. 6 minute walk test (6MWT), if ambulatory, and

- d. Renal toxicity screening with urinalysis, creatinine/protein ratio or serum cystatin C.
5. The FVC is >30% predicted OR the Brooke score is ≤ 5 .
6. Request for antisense oligonucleotide therapy is for the FDA-approved dosage only.
7. Only one antisense oligonucleotide treatment shall be authorized at a time.
8. Client is on a corticosteroid, or has documented medical reason not to be on this medication.

B. Reauthorization

The CCS Program may re-authorize eteplirsen, golodirsen, or viltolarsen for up to one year when a client has finished the initial course of treatment and all of the following apply:

1. Client has not had significant decline in FVC beyond the pre-treatment disease trajectory while on the antisense oligonucleotide treatment.
2. Motor function has improved or has not declined beyond pretreatment trajectory, evidenced by improved or maintained score in 6MWT, timed function tests, Performance of Upper Limb (PUL), Brooke score, other standardized assessment of motor function, or quantifiable description of improvement by the physician or physical therapist in the medical record.
3. Client has not experienced significant adverse effects attributable to the antisense oligonucleotide treatment.

C. CCS Program clients with a FVC score of ≤ 30 percent and Brooke score of six will not be granted Service Authorization Request (SAR) authorizations because, at the time of this N.L., there is insufficient evidence of efficacy in that population.

D. Additional consideration for medical necessity determination:

For clients who do not meet the criteria described in sections III.A. or III.B., SCCs may also submit other clinical documentation and/or evidence that would support the medical necessity for initial or reauthorization of the client's antisense oligonucleotide treatments. SCCs should submit this documentation to the Integrated Systems of Care Division (ISCD) Medical Director or designee.

E. Whole Child Model (WCM) Counties:

For CCS clients who are enrolled in a Medi-Cal managed care plan (MCP) and reside in a WCM county, the client's MCP shall be responsible for authorizing, coordinating, and covering antisense oligonucleotide treatments. MCPs operating in WCM counties should use the authorization guidelines described in this N.L., or utilize the MCP's existing antisense oligonucleotide treatment policies, whichever is less restrictive.

IV. POLICY IMPLEMENTATION

- A. Submissions of authorization requests for eteplirsen, golodirsen, or viltolarsen are not included in Service Code Groupings.⁶ Until 4/1/21, providers should submit a separate SAR with the following documentation: a copy of the prescription, genetic laboratory test result with specific mutation, and clinical progress notes from a visit within the past 6 months.
1. For clients residing in an independent county, SARs should be submitted to the CCS independent county office, which shall review and authorize according to the policy above.
 2. For clients residing in a dependent county, SARs should be submitted to the CCS dependent county office. The dependent county program office shall pend and submit the SAR and supporting documentation to the Department of Health Care Services (DHCS) ISCD Special Populations Authorization Unit e-mail at CCSExpeditedReview@dhcs.ca.gov or via secure RightFax (916) 440-5306
- B. All antisense oligonucleotide requests shall be reviewed by a CCS Program Medical Director or designee before authorization.
- C. J1428 is the approved Healthcare Common Procedure Coding System (HCPCS) code for eteplirsen.
- Authorization of this code is required for physician or clinic administered eteplirsen. One unit of J1428 = 10mg of eteplirsen. The approved dosage is 30mg/kg, once weekly.
- D. J1429 is the approved Healthcare Common Procedure Coding System (HCPCS) code for golodirsen, beginning with dates of service July 1, 2020. Authorization of this code is required for physician or clinic administered golodirsen. One unit of J1429 = 10mg of golodirsen. The approved dosage is 30mg/kg, once weekly.
- E. The temporary HCPCS code C9071 is assigned to viltolarsen starting with date of service January 1, 2021. Authorization of this code is required for physician or clinic administered viltolarsen. One unit of C9071 = 10 mg viltolarsen. The recommended dosage is 80mg/kg, once weekly.
- F. Review This Computes #329⁷ for coding a HCPCS on a SAR.

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If you have any questions regarding this N.L., please contact the ISCD Medical Director or designee, via e-mail at ISCD-MedicalPolicy@dhcs.ca.gov.

Beginning April 1, 2021, all requests for prior authorization of medications billed by National Drug Code and dispensed by a Medi-Cal enrolled pharmacy provider, shall be sent from the pharmacy provider to the Medi-Cal Rx vendor, Magellan Medicaid Administration, Inc. (Magellan). The Medi-Cal RX website provides guidance: <https://medi-calrx.dhcs.ca.gov/home/>.

Sincerely,

ORIGINAL SIGNED BY

Roy Schutzengel
Medical Director
Integrated Systems of Care Division

Attachment(s):

Attachment : Deletions Potentially Amenable to Exon skipping

¹ Muscular dystrophy is not a GHPP eligible condition

² 22 Cal. Code Regs. § 41515.1 et. seq. Determination of Medical Eligibility
<https://govt.westlaw.com/calregs/Document/I28E30090D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=CategoryPageItem&contextData=%28sc.Default%29>

³ 22 Cal. Code Regs. § 41700 Availability
[https://govt.westlaw.com/calregs/Document/I2F1A7E70D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=CategoryPageItem&contextData=\(sc.Default\)&bhcp=1&ignorebhwarn=IgnoreWarns](https://govt.westlaw.com/calregs/Document/I2F1A7E70D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=CategoryPageItem&contextData=(sc.Default)&bhcp=1&ignorebhwarn=IgnoreWarns)

⁴ 22 Cal. Code Regs. § 41740 Eligibility for Treatment Services
<https://govt.westlaw.com/calregs/Document/I2FDD8050D4B811DE8879F88E8B0DAAAE?viewType=FullText&originationContext=documenttoc&transitionType=StatuteNavigator&contextData=%28sc.Default%29>

⁵ See Attachment 2: Deletions Potentially Amenable to Exon Skipping

⁶ Service Authorization Request Tools
<https://www.dhcs.ca.gov/services/ccs/cmsnet/Pages/SARTools.aspx#service>

⁷ This Computes #329: Determining Units and Quantity on SARs.
<http://dhcs-sp2010-archive/services/ccs/cmsnet/Documents/thiscomputes329.pdf>

Deletions That May be Amenable to Exon Skipping

The chart displays common Duchenne Muscular Dystrophy (DMD) deletions that are potentially amenable to exon skipping.^{1,2}

Exon Deletions Potentially Amenable to Exon 51		Exon Deletions Potentially Amenable to Exon 53	
3-50	33-50	3-52	33-52
4-50	34-50	4-52	34-52
5-50	35-50	5-52	35-52
6-50	36-50	6-52	36-52
9-50	37-50	9-52	37-52
10-50	38-50	10-52	38-52
11-50	39-50	11-52	39-52
13-50	40-50	13-52	40-52
14-50	41-50	14-52	41-52
15-50	42-50	15-52	42-52
16-50	43-50	16-52	43-52
17-50	45-50	17-52	45-52
19-50	47-50	19-52	47-52
21-50	48-50	21-52	48-52
23-50	49-50	23-52	49-52
24-50	50	24-52	50-52
25-50	52	25-52	52
26-50	52-58	26-52	54-58
27-50	52-61	27-52	54-61
28-50	52-63	28-52	54-63
29-50	52-64	29-52	54-64
30-50	52-66	30-52	54-66
31-50	52-76	31-52	54-76
32-50	52-77	32-52	54-77

¹ Dystrophin Isoform Induction *In Vivo* by Antisense-mediated Alternative Splicing

Fletcher S, Adams AM, Johnsen RD, Greer K, Moulton HM, Wilton SD. *Mol Ther*. 2010; 18(6):1218-1223.

<https://www.sciencedirect.com/science/article/pii/S1525001616310619#fig2>

² Duchenne Population Potentially Amenable to Exon Skipping

<https://www.cureduchenne.org/wp-content/uploads/2016/11/Duchenne-Population-Potentially-Amenable-to-Exon-Skipping-11.10.16.pdf>