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

JENNIFER KENT
DIRECTOR

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GOVERNOR

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Index: Benefits

TO: ALL COUNTY CALIFORNIA CHILDREN SERVICES (CCS) ADMINISTRATORS, MEDICAL CONSULTANTS, AND STATE SYSTEMS OF CARE DIVISION STAFF

SUBJECT: NUSINERSEN (SPINRAZA™)

I. PURPOSE

The purpose of this Numbered Letter (N.L.) is to establish CCS Program policy regarding the authorization of nusinersen (Spinraza), as a treatment for 5q spinal muscular atrophy (SMA) for CCS Program clients with confirmed 5q spinal muscular atrophy.

II. BACKGROUND

5q SMA is an autosomal recessive neurodegenerative disorder, characterized by progressive muscle atrophy and weakness. The weakness is caused by low levels of spinal motor neuron (SMN) protein with resulting degeneration of anterior horn cells in the brain and motor neuron nuclei in the lower brainstem. The condition is the most common genetic cause of childhood mortality, with an incidence of approximately one in 10,000 live births.

The disorder is classified into four types based on age of onset and severity. SMA1, also known as infantile SMA, is the most common and severe type, affecting approximately 60% of all individuals with 5q SMA. Symptoms appear before six months of age, affected individuals never sit, and the majority do not survive past two years of age.

SMA2 has age of onset primarily between six (6) and twelve (12) months. These infants sit and may stand or walk with help. Life expectancy is reduced but the majority survive into adulthood.

Children and adults with SMA3 (juvenile) have onset of disease from 18 months to adulthood. These individuals exhibit atrophy and weakness of proximal limb muscles, with twitching, which starts after ambulation has been acquired. Affected individuals often have difficulty walking, running and climbing stairs. Pulmonary issues are a common complication in this group.

SMA4 (adult onset) may have different etiology and will not be referenced further in this policy.

The genetic basis for the disease is as follows: The SMN1 and SMN 2 genes are located on chromosome 5q. Transcription of the normal SMN1 gene leads to full length mRNA transcripts that encode complete SMN protein. SMN protein is critical for correct splicing of genes and survival of motor neurons. SMN protein is also encoded by a second back-up gene, SMN2 which is identical to SMN1 except for a single substitution. Usually SMN2 transcription leads to an incomplete mRNA fragment and an incomplete SMN protein. However, approximately 10 – 15% of SMN2 transcripts are complete and encode the full-length SMN protein.

Individuals with 5q SMA have a mutation in the SMN1 gene leading to reliance on the SMN2 gene, which leads to low levels of the SMN protein. The severity of disease varies between individuals in large part because of differences in the number of copies of SMN2. Individuals with SMA who have more copies of SMN2 genes generally have less severe forms of SMA. Rarely, an individual with SMA has a mutation of SMN1 that produces a limited amount of SMN so that there is no reliance on SMN2. These individuals usually fall into the SMA1 classification.

Advances in nutrition, and pulmonary care for SMA patients have increased survivability. There was no Food and Drug Administration (FDA) approved disease modifying treatment for 5q SMA, however, until nusinersen (Spinraza) received fast track approval from the FDA. Nusinersen is an oligonucleotide that interferes with transcription of the SMN2 gene, leading to functional SMN protein. During the largest study leading to drug approval (ENDEAR), infants with infantile-onset SMA who received the medication experienced significant stabilization and improvement in motor function compared to sham controls. Because of the clear association between the drug and improvement, the study was stopped early. Other studies supporting efficacy of nusinersen were an open label study of patients with infantile onset SMA, a study in presymptomatic infants (NURTURE) and finally an open label study in which patients with SMA2 and SMA3 received the drug for up to four years. This group saw stabilization, and at times, improvement, including ambulation.

While nusinersen is a critical part of care for the SMA patient, it is vital that other supportive care continue at or through the SCC, including nutrition support, pulmonary and physical therapy services, continue concurrently with nusinersen.

III. POLICY

A. Effective the date of this letter, nusinersen is a benefit for CCS Program clients when all the following criteria are met:

1. The client has SMA1, SMA2 or SMA3, based on genetic testing.

2. The genetic testing results include the number of copies of SMN2 and, in the rare case of impaired but functional SMN1, the specific SMN1 mutation.

3. The client is under the care of one of the following CCS Program approved center types: neuromuscular special care center, neuromusculoskeletal special care center or pediatric rehabilitation special care center.

4. The client has the following neuromotor status:

   a. Pre-symptomatic - if the client has genetic testing that confirms that the client has between one and three copies of SMN2.

   b. Clinical signs of SMA with level of function necessary to preserve communication, for instance finger or eye movements, with any number of copies of SMN2.

   c. Clinical signs of SMA with impaired but functional SMN1.

5. Nusinersen can be safely administered intrathecally (IT). Specifically, for older clients with SMA and scoliosis, the drug may only be authorized if client has:

   a. Scoliosis without spine surgery, or

   b. Is post spine surgery with preserved window of accessibility, by intrathecal injection under fluoroscopic or ultrasound guidance if needed, or

c. Is post spine surgery (e.g., fusion) without window of accessibility with surgical placement of an indwelling catheter or establishment a new window for IT accessibility.

6. The client does not have a coexisting terminal condition or a condition with which the risk of nusinersen treatment outweighs the potential benefit.

B. The CCS Program approved rehabilitation, neuromuscular or neuromusculoskeletal special care center has submitted the Nusinersen Request Form which contains all of the following information:

1. Patient demographics, including age of onset.

2. Results of genetic testing, including name of laboratory, number of copies of SMN2, and whether SMN1 sequencing was done.

3. Neurologic status, specifically if client is non-sitter, sitter or walker.

4. Results of neuromotor assessment, based on neurologic status of client. Specifically the tests to complete prior to each reauthorization are:

a. For non-sitters:

(1) CHOP Intend, OR

(2) Hammersmith Infant Neurological Exam-Part 2 (HINE-2).

b. For sitters: Hammersmith Functional Motor Scale (HFMS).

c. For walkers: the 6 minute walk test OR the 10 meter run/walk test.

5. Other medical condition.

6. For reauthorization, test results as well as response to medication.

C. The request is for the FDA approved dosage only, with the approved loading and maintenance schedules.

1. Nusinersen is a 12 mg suspension, to be administered intrathecally.

2. The nusinersen treatment schedule consists of four loading doses of 12 mg, at days 1, 15, 29, 59, and maintenance doses every 4 months thereafter.

IV. POLICY IMPLEMENTATION

A. Nusinersen requires a separate authorization.

1. Requesting CCS Program providers must submit the following items to their CCS program county office or Dependent County Regional Office: a CCS Program Service Authorization Request (SAR), a Nusinersen Request Form, completed by the CCS Program approved special care center, along with the required documentation from the CCS Program approved SCC and a copy of the signed prescription.

2. The local county CCS program office will pend a SAR and forward the SAR request and the completed Nusinersen Request Form to the Nusinersen e-mail inbox:

CCS_Operations@dhcs.ca.gov or via secure Rightfax number: (916) 440-5768.

B. All requests shall be reviewed by the SCD Medical Director or designee before authorization of nusinersen.

1. Initial Authorization:shall be for a period of six months. The initial authorization shall cover the four load loading doses and the first maintenance dose.

2. Extension of the authorization shall be granted with an updated Nusinersen Request Form every six months unless there are significant adverse effects. After two years of treatment, further authorizations will be done by the local CCS program county or Dependent County Regional Office.

C. Institutional providers purchasing and administering nusinersen must obtain SAR approval and bill with HCPCS code J3490, until a specific HCPCS code is assigned.

D. Currently, the manufacturer has authorized one specialty pharmacy to supply/dispense nusinersen. The pharmacy may obtain a SAR and bill by NDC if the administering facility is not directly purchasing the drug. The authorized pharmacy provider is contracted by the manufacturer to deliver directly to the facility administering nusinersen on the day of administration.

E. Exceptions will be reviewed on a case-by-case basis by the State CCS Program Medical Director or designee.

If you have any questions regarding this N.L., please contact Jill Abramson, M.D., Chief, Medical Policy & Consultation Section, at (916) 327-2108 or via e-mail at Jill.Abramson@dhcs.ca.gov.

Sincerely,

ORIGINAL SIGNED BY PATRICIA MCCLELLAND

Patricia McClelland, Chief
Systems of Care Division

Nusinersen Request Form

Full Name		CCS Case #		Date Completed	
County		Age		Nusinersen applicable 5q mutation (yes/no)	
SMA Type		Number of SMN2 copies (and laboratory name)			
SMN1 sequencing (and laboratory name) y/n					
Age of onset					
Other medical condition					
Neurologic status (check one): Non-sitter, Sitter, Walker					
I Clinical Baseline Prior to Loading Doses					
CHOP Intend total score, non-sitter				Date Completed	
Hammersmith Infant Neurological Exam-Part 2 (HINE-2) total score, non-sitter				Date Completed	
Hammersmith Functional Motor Scale (HFMS) total score, sitter				Date Completed	
6-minute walk test (6MWT), walker				Date Completed	
10 meter walk/run test (10MWR), walker				Date Completed	
Notes					
Anticipated dates for loading doses		1.		2.	
		3.		4.	
Form Completed By (Name/Title)		Special Care Facility Name		Date Completed	
II. Request For Authorization for Maintenance Doses					
CHOP Intend total score, non-sitter					
Hammersmith Infant Neurological Exam-Part 2 (HINE-2) total score, non-sitter				Date Completed	
Hammersmith Functional Motor Scale (HFMS) total score, sitter				Date Completed	
6-minute walk test (6MWT), walker				Date Completed	
10 meter walk/run test (10MWR), walker				Date Completed	
Actual dates of loading doses		1.		2.	
		3.		4.	
Anticipated dates for maintenance doses		1.		2.	
		3.		4.	
Any adverse reactions with Nusinersen					
Additional Details					
. Form Completed By (Name/Title)		Special Care Facility Name		Date Completed	
To be completed by CCS staff					
Approved ☐ Denied ☐ Reason for Denial:				Date:	
Reviewed By (SCD staff)					