1. Is the treatment diagnosis Spinal Muscular Atrophy?
   a. Yes- Move to question 2
   b. No- Deny Cat 3 – Nusinersen is only indicated for use in the treatment of SMA

2. Is the diagnosis documented by genetic testing (Genetic documentation of 5q SMA homozygous gene deletion, homozygous mutation, or compound heterozygote) AND does the member have at least 2 copies of the SMN2 gene?
   a. Yes- Move to question 3
   b. No- Forward to Medical Director- *Medication is being prescribed outside of criteria required for participation in clinical trials.*

3. Does the member have a baseline motor function assessment using one of the assessment tools used in clinical trials?
   - HFSME Motor Function Score (Hammersmith Functional Motor Scale - Expanded) greater than or equal to 10 and less than or equal to 54?
   - Hammersmith Infant Neurological Exam (HINE-2)
   - Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)

   a. Yes- Move to question 4
   b. No- Forward to Medical Director- *Medication is being prescribed outside of criteria used for participation in clinical trials- Member must have baseline function assessed in order to determine efficacy of treatment.*

4. Does the member have ANY of the following:
   - Respiratory insufficiency, defined by the medical necessity for invasive or non-invasive ventilation for greater than 6 hours during a 24 hour period
   - Medical necessity for a gastric feeding tube, where the majority of feeds are given by this route,
   - Severe contractures or severe scoliosis evident on X-ray examination OR History of brain or spinal cord disease that would interfere with the LP procedure or CSF circulation
   - Hospitalization for surgery (i.e., scoliosis surgery, other surgery), pulmonary event, or nutritional support within 2 months
   - Presence of an untreated or inadequately treated active infection requiring systemic antiviral or antimicrobial therapy.
   - History of brain or spinal cord disease, including tumors, or abnormalities by MRI or CT that would interfere with the LP procedures or CSF circulation
   - Presence of an implanted shunt for the drainage of CSF or an implanted CNS catheter
   - History of bacterial meningitis.
   - Prior injury (e.g., upper or lower limb fracture) or surgical procedure which impacts the subject's ability to perform any of the outcome measure testing required in the protocol and from which the subject has not fully recovered or achieved a stable baseline
   - Clinically significant abnormalities in hematology (low platelet count) or clinical chemistry parameters or ECG.

- Treatment with another investigational drug (e.g., oral albuterol or salbutamol, riluzole, carnitine, creatine, sodium phenylbutyrate, et.c), biological agent, or device within 1-month OR Any history of gene therapy, antisense oligonucleotide therapy, or cell transplantation.
- Ongoing medical condition that would interfere with the assessment of safety or would compromise the ability of the subject to undergo administration procedures. Examples are medical disability (e.g., wasting or cachexia, severe anemia, etc.) OR life expectancy of less than 2 years at the time of request?

a. Yes – Forward to medical director – Member does not meet parameters of clinical trials used to establish safety and efficacy of this medication.
b. No- Move to question 5

5. Is the medication being prescribed by a pediatric neurologist with experience in SMA?
    a. Yes – Forward to Medical Director for final review of high impact medication- May approve for up to 5 doses over 8 months as initial approval
    b. No- Forward to Medical Director – *Medication should only be used by providers experienced with SMA to reduce risk of adverse outcome.*

Renewal Criteria

1. Has the member motor function improved as demonstrated by
    - Improvement in baseline motor function score documented a measured within one month of renewal request AND
    - More areas of motor function improved than worsened.

    a. Yes- Move to question 2
    b. No – Forward to Medical Director for evaluation of medication efficacy

2. No serious adverse drug effects (renal toxicity, thrombocytopenia, serious URI)
    a. Yes –Forward to Medical Director for final review of high impact medication
    b. No – Forward to Medical Director for evaluation of continued therapy

Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND)- developed by physical therapists to provide a method of evaluation of neck, limb and trunk strength in SMA patients. The assessment incorporates the limited abilities of SMA patients to sit and roll over and focuses on motor assessment in the prone position. It is a 16 item assessment of functional muscle strength and is scored on a 0–4 scale: no response (0), minimal (1), partial (2), nearly full (3) and complete (4) level of response; with a maximum score of 64 points- **Used in phase 2 trial, ENDEAR**

The Hammersmith Infant Neurological Exam (HINE) was developed by pediatric neurologists to assist in assessment of neurologic function of infants between 2 and 24 months of age. It includes 26 items assessing cranial nerve function, posture, quality and quantity of movements, muscle tone, and reflexes and reactions. Each item is scored individually (0, 1, 2, or 3), with a sum score of all individual items (range 0 to 78). At 9 or 12 months, a score greater than or equal to 73 is considered optimal. - **Used in ENDEAR trial**

The HINE-2 screening can be used as a tool to capture motor milestones in patients with SMA, including head control, sitting, voluntary grasp, ability to kick in supine, rolling, crawling or bottom shuffling, standing, and walking. An increased score indicates improved function with a maximum score between 2 to 4 points for each category and a total maximum score of 78. **- Used in phase 2 trial**

The Hammersmith Functional Motor Scale (HFMS) was developed by physical therapists to assess SMA type 2 and 3 patients. The assessment provides information on motor ability and clinical progression in children with limited amubulation.The HFMS motor assessment includes upper and lower limb activities as well as head and trunk control. Specific motor functions include rolling, sitting, lifting the head from prone to supine, propping on arms, 4 point kneeling, crawling and standing. Each item is scored on a 3 point scoring system: inability (0), assistance (1), and unaided (2). The total score ranges from 0 (all activities are failed) to 40 (all activities are achieved).

For ambulatory patients with SMA type 3, the HFMS was extended with 13 items to assess walking, running, and jumping which resulted in the HFMSE (HFMS Extended). It is scored on a 3 point scale similar to the HFSME, but scores range from 0 to 66.- **Used in phase 1 trial, CHERISH trial**

The Upper Limb Module (ULM) is used in non-ambulatory patients greater than 2 years of age. This assessment was designed to assist in evaluating the ability of young children to perform specific tasks such as lifting small objects, pushing buttons, or using a pencil. **NOT used in trials reviewed by FDA for approval**

The Six-Minute Walk Test is used only in ambulatory SMA patients more than 4 years of age- **NOT used in trials reviewed by FDA for approval**