Medicaid Drug Cap Initiative:

Nusinersen (Spinraza®)

Presentation for
Drug Utilization Review Board
July 23, 2020
Purpose

- Spinraza® has been identified as contributing to pharmacy expenditures exceeding the Medicaid Drug Cap as defined in NYS Public Health Law, article 2-A, title 2 section 280.

- To evaluate the utilization of Spinraza® (nusinersen) across the entire New York State (NYS) Medicaid population including the fee-for-service (FFS) program and managed care organizations (MCOs).

- To assist in the formulation of a target manufacturer supplemental rebate amount for Spinraza®.
Spinraza®: Background

**Agent** | **Dosage formulation/ Strength** | **Manufacturer**
--- | --- | ---
Spinraza® (nusinersen) | • Injection for intrathecal use  
• 12 mg/5 mL (2.4 mg/1 mL) single-dose vial | Biogen

- **Food and Drug Administration (FDA) approval:**
  - Date: December 2016
  - Indication: Treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

- Nusinersen is a survival motor neuron-2 (SMN2)-directed antisense oligonucleotide.
Nusinersen: Background

**SMA**
- SMN protein deficiency leads to motor neuron degeneration, muscle atrophy.

**SMN Protein**
- Production depends on SMN1 gene on chromosome 5q13.
- In SMA, SMN1 gene mutations reduce functional protein expression.

**Mechanism of Action**
- Paralogous SMN2 gene also codes for SMN protein but produces very little functional SMN protein due to aberrant splicing.
- Nusinersen modifies the SMN2 pre-messenger RNA splicing, resulting in the creation of functional full-length SMN protein.
Nusinersen Dosing

• 1 dose of nusinersen: 12 mg/5 mL via intrathecal injection.

• Initiation: 4 loading doses (LD)
  – 3 doses at 14 day intervals; fourth dose 30 days after third.

• Maintenance dose (MD): 1 dose every 4 months.
Nusinersen: Background

• Information related to the following will not be discussed during the presentation but details are available in the report:
  – Contraindications;
  – Warnings and precautions;
  – Adverse events;
  – Drug interactions; and
  – Special populations.
Legislative Overview by Subsection

• Medicaid drug cap law:
  – Law lists factors the Board may consider when formulating drug rebate recommendation.
  – Presentation reviews findings related to each item.
In formulating a recommendation concerning a target rebate amount for a drug, the drug utilization review board may consider:

(i) Publicly available information relevant to the pricing of the drug;
Public Drug Pricing Information

WAC for Initial Year of Nusinersen Therapy

<table>
<thead>
<tr>
<th>Year 1</th>
<th>WAC ($) 12 mg/5 mL dose*</th>
<th>WAC Total ($)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loading Dose 1 (Day 0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loading Dose 2 (Day 14)</td>
<td>$127,500</td>
<td>$510,000</td>
</tr>
<tr>
<td>Loading Dose 3 (Day 28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loading Dose 4 (Day 58)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintenance Therapy (Day 180)</td>
<td>$127,500</td>
<td>$255,000</td>
</tr>
<tr>
<td>Maintenance Therapy (Day 300)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL WAC FOR YEAR 1 OF THERAPY</strong></td>
<td></td>
<td><strong>$765,000</strong></td>
</tr>
</tbody>
</table>

Note: The wholesale acquisition cost (WAC) is an estimate of the manufacturer's list price for a drug to wholesalers or direct purchasers, but does not include discounts or rebates.

## Public Drug Pricing Information

### WAC for Maintenance Year of Nusinersen Therapy

<table>
<thead>
<tr>
<th>Year of Maintenance Therapy</th>
<th>WAC ($) 12 mg/5 mL dose*</th>
<th>WAC Total ($)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintenance Therapy Dose 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintenance Therapy Dose 2</td>
<td>$127,500</td>
<td>$382,500</td>
</tr>
<tr>
<td>Maintenance Therapy Dose 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ANNUAL MAINTENANCE WAC</strong></td>
<td></td>
<td>$382,500</td>
</tr>
<tr>
<td><strong>WAC for First 2 Years of Therapy</strong></td>
<td></td>
<td>$1,147,500</td>
</tr>
</tbody>
</table>

In formulating a recommendation concerning a target rebate amount for a drug, the drug utilization review board may consider:

• (ii) Information supplied by the department relevant to the pricing of the drug;
  – The department will provide the DURB with information relevant to the pricing of Spinraza® (nusinersen) at today’s executive session.
In formulating a recommendation concerning a target rebate amount for a drug, the drug utilization review board may consider:

(iii) Information relating to value-based pricing
Value-Based Pricing

• The Institute for Clinical and Economic Review (ICER) will provide an economic review related to the value-based pricing of Spinraza® (nusinersen).
Nusinersen Coverage: Medicaid Programs

• NYS Medicaid (MCOs and FFS): covered as a medical benefit.

• Review of 7 other state Medicaid programs:
  – Coverage criteria were available for 5 states: California, Florida, Illinois, Massachusetts, and Texas.
  – Criteria for nusinersen initiation:
    • Confirmation of SMA diagnosis, genetic testing, baseline assessment of motor function, specialist consulted, patient not ventilator-dependent.
  – Criteria for nusinersen continuation:
    • Response to therapy/lack of deterioration, adherence.
Nusinersen Coverage: Commercial Health Insurance

• 5 largest US healthcare insurance companies by membership:
  – All have nusinersen coverage criteria.
  – Criteria for nusinersen initiation:
    • Confirmation of SMA diagnosis, genetic testing, baseline assessment of motor function, specialist consulted, patient not ventilator-dependent.
    • 4 companies: varying age edits, all precluding adult use.
  – Criteria for nusinersen continuation:
    • Response to therapy/lack of deterioration, adherence.
Nusinersen Coverage: Other Countries

• Nusinersen guidance and coverage policies from 6 non-US government agencies were reviewed:
  – Australia, Brazil, Canada, European Union, Scotland, United Kingdom (UK).

• Most restrict coverage:
  – Diagnosis requirement, prescribing limited to specialists.

• Some countries have implemented pricing agreements as a condition of coverage.
In formulating a recommendation concerning a target rebate amount for a drug, the drug utilization review board may consider:

(iv) The seriousness and prevalence of the disease or condition that is treated by the drug;
SMA: Seriousness and Prevalence

• The type of SMA is based on the patient’s age of onset and the highest physical milestones reached.
• Patients with more copies of the SMN2 gene generally have a less severe form of SMA.

<table>
<thead>
<tr>
<th>SMA Type</th>
<th>SMN2 Copies</th>
<th>Disease Presentation</th>
<th>Life Expectancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>Severe weakness and hypotonia, rapid progression, failure to thrive</td>
<td>&lt;6 months</td>
</tr>
<tr>
<td>1</td>
<td>1-3</td>
<td>Difficulty swallowing, breathing</td>
<td>&lt;2 years</td>
</tr>
<tr>
<td>2</td>
<td>2-3</td>
<td>Unable to walk</td>
<td>Typically &gt;20 years</td>
</tr>
<tr>
<td>3</td>
<td>3-4</td>
<td>Achieve ability to walk, but increasingly limited mobility over time</td>
<td>Adulthood</td>
</tr>
<tr>
<td>4</td>
<td>≥4</td>
<td>Able to attain motor milestones and maintain mobility throughout life</td>
<td>Adulthood</td>
</tr>
</tbody>
</table>
SMA: Seriousness and Prevalence

• SMA affects 10,000 – 25,000 people in the US.
  – Prevalence: 1 to 2 per 100,000 persons.
  – Incidence: 10 per 100,000 live births.

• Incidence in NYS:
  – 20 – 30 per 235,000 births per year.

• Childhood onset more common than adult:
  – Type 1: >50% of all new SMA cases
  – Type 2: 30% of overall cases
  – Type 3: 10% of overall cases
In formulating a recommendation concerning a target rebate amount for a drug, the drug utilization review board may consider:

(v) The extent of utilization of the drug;
Nusinersen Utilization Analysis: Purpose

- The purpose of this analysis is to provide an overview of nusinersen utilization in the NYS Medicaid Program.
  - The analysis includes both fee-for-service (FFS) and Medicaid managed care (MC) plans.
Methods

• A retrospective analysis of nusinersen utilization was conducted.

• The data source was the Medicaid Data Warehouse (MDW).

• The timeframe of the analysis was April 1, 2017 through September 30, 2019.
Results

• <100 unique NYS Medicaid members (FFS+MC) had a claim for nusinersen resulting in 336 claims during the timeframe of the analysis.

• Patients ranged in age from <1 year to 58 years of age.
Members Utilizing Nusinersen by Age

Timeframe: April 1, 2017 through September 30, 2019

- ≤6 years: 45%
- 7-20 years: 30%
- ≥21 years: 25%
- <100 members (FFS+MC)

Data source: MDW
Extract date: February 2020
## Nusinersen Utilization

<table>
<thead>
<tr>
<th>SFY</th>
<th>FFS + MC # Claims</th>
<th>FFS # Claims</th>
<th>MC # Claims</th>
</tr>
</thead>
<tbody>
<tr>
<td>SFY 2018</td>
<td>87</td>
<td>13</td>
<td>74</td>
</tr>
<tr>
<td>SFY 2019</td>
<td>164</td>
<td>51</td>
<td>113</td>
</tr>
<tr>
<td>SFY 2020</td>
<td>85</td>
<td>29</td>
<td>56</td>
</tr>
<tr>
<td>(6 months only)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>336</td>
<td>93</td>
<td>243</td>
</tr>
</tbody>
</table>

FFS = fee-for-service, MC = managed care, SFY = state fiscal year

Data source: MDW
Extract date: February 2020
In formulating a recommendation concerning a target rebate amount for a drug, the drug utilization review board may consider:

(vi) The effectiveness of the drug in treating the conditions for which it is prescribed, or in improving a patient's health, quality of life, or overall health outcomes;
Effectiveness: Place in Therapy

• SMA Care Group: 2018 guideline on diagnosis and management of SMA
  – Acknowledges nusinersen as an FDA-approved agent for SMA, but does not provide detail as to its place in therapy.

• CureSMA: 2018 algorithm for treatment of infants diagnosed with SMA via newborn screening
  – In NYS, testing for SMA is currently included in newborn screening.
  – 2 or 3 copies of SMN2 → Probable SMA types 1 or 2:
    • Start treatment with SMN-up-regulating therapies immediately.
  – 4 or more copies of SMN2 → Probable SMA types 3 or 4:
    • Wait to treat; monitor and then treat at onset of symptoms.
Clinical Trials: Finkel 2017
Phase 3 ENDEAR Trial in Infantile-Onset SMA

• Randomized, sham-controlled, double blind, multicenter trial
  – In infants age ≤7 months at screening with SMA symptom onset age ≤6 months.

• Treatment groups (randomized 2:1)
  – Nusinersen group:
    • 12 mg intrathecal dose equivalent (volume adjusted by age) on days 1, 15, 29, 64, 183 and 302 (n=80).
  – Control group:
    • Sham procedures on same schedule (n=41).

• Primary outcomes:
  – Motor-milestone response per Hammersmith Infant Neurologic Examination Part 2 (HINE-2), with interim analysis (response = improvement in ≥1 category[ies] and more categories with improvement than worsening); event-free survival (time to death or permanent assisted ventilation [PAV]).
Clinical Trials: Finkel 2017, Interim Analysis

- 13 month duration planned.

- Prespecified interim analysis
  - Conducted when ~80 infants had been enrolled for ≥6 months.

<table>
<thead>
<tr>
<th>HINE-2 Motor-Milestone Response Achieved</th>
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<tbody>
<tr>
<td>Nusinersen: 21/51 (41%)</td>
</tr>
<tr>
<td>Control: 0/27 (0%)</td>
</tr>
<tr>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

- Results prompted early trial termination; end-of-trial visits were conducted for final analysis.
Clinical Trials: Finkel 2017, Final Analysis

- Final analysis
  - Included 121 infants (nusinersen: n=80; control: n=41) who had undergone assigned procedure at least once.

<table>
<thead>
<tr>
<th>Event-Free Survival (no death or use of PAV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nusinersen: 49/80 (61%)</td>
</tr>
<tr>
<td>Control: 13/41 (32%)</td>
</tr>
<tr>
<td>HR (95% CI): 0.53 (0.32–0.89)</td>
</tr>
<tr>
<td>P=0.005</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Median Time to Death or PAV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nusinersen: not reached</td>
</tr>
<tr>
<td>Control: 22.6 weeks</td>
</tr>
</tbody>
</table>

- Likelihood of event-free survival was higher in infants treated with nusinersen who had disease duration ≤13.1 weeks at screening.
Clinical Trials: Mercuri 2018
Phase 3 CHERISH Trial in Later-Onset SMA

- Randomized, sham-controlled, double blind, multicenter trial
  - In children age 2-12 years with SMA symptom onset age >6 months.
- Treatment groups (randomized 2:1).
  - Nusinersen group:
    - 12 mg intrathecally on days 1, 29, 85, and 274, with 6 months of follow-up (n=84).
  - Control group:
    - Sham procedures on same schedule (n=42).
- Primary outcomes:
  - Hammersmith Functional Motor Scale Expanded (HFMSE) score (least-squares mean change from baseline at 15 months), with interim analysis.
Clinical Trials: Mercuri 2018, Interim Analysis

- 15 month duration planned.
- Prespecified interim analysis:
  - Conducted when all patients were enrolled ≥6 months and ≥39 completed 15-month assessment.

<table>
<thead>
<tr>
<th>HFMSE Score: Least-Squares Mean Difference vs. Baseline (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nusinersen: 4.0 (2.9 to 5.1)</td>
</tr>
<tr>
<td>Difference: 5.9 (3.7 to 8.1)</td>
</tr>
</tbody>
</table>

- Results prompted early trial termination; patients who had not yet had a 15-month assessment were evaluated at a final visit.
Clinical Trials: Mercuri 2018, Final Analysis

- Final analysis
  - 66/84 patients in the nusinersen group and 34/42 in the control group completed the 15-month assessment.

<table>
<thead>
<tr>
<th>HFMSE Score: Least-Squares Mean Difference vs. Baseline (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nusinersen: 3.9 (3.0 to 4.9)</td>
</tr>
<tr>
<td>Control: −1.0 (−2.5 to 0.5)</td>
</tr>
<tr>
<td>Difference: 4.9 (3.1 to 6.7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patients with HFMSE Score Change of ≥3 Points (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nusinersen: 57% (46 to 68)</td>
</tr>
<tr>
<td>Control: 26% (12 to 40)</td>
</tr>
<tr>
<td>Difference: 30.5% (12.7 to 48.3)</td>
</tr>
<tr>
<td>Odds ratio: 6 (2 to 15)</td>
</tr>
<tr>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>
In formulating a recommendation concerning a target rebate amount for a drug, the drug utilization review board may consider:

(vii) The likelihood that use of the drug will reduce the need for other medical care, including hospitalization;
Post-Marketing Outcomes: Hagenacker 2020, Nusinersen in Adults

- Post-marketing observational cohort study on safety and effectiveness of nusinersen treatment in adults with SMA.

- Primary outcome: change in HFMSE score at 6, 10, and 14 months.
  - Clinically meaningful improvement = HFMSE score increase ≥3 points.

- 124 patients included in the 6-month analysis.
  - SMA type 1: n=2 (2%); SMA type 2: n=45 (36%); SMA type 3: n=77 (62%).

- No serious adverse events reported.
  - Most frequent adverse events at 14 months included headache (35%), back pain (22%), and nausea (11%).

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Patients</th>
<th>Mean HFMSE Score Change</th>
<th>95% CI</th>
<th>Patients with Clinically Meaningful Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>n=124</td>
<td>1.73</td>
<td>1.05-2.41</td>
<td>35/124 (28%)</td>
</tr>
<tr>
<td>10 months</td>
<td>n=92</td>
<td>2.58</td>
<td>1.76-3.39</td>
<td>33/92 (36%)</td>
</tr>
<tr>
<td>14 months</td>
<td>n=57</td>
<td>3.12</td>
<td>2.06-4.19</td>
<td>23/57 (40%)</td>
</tr>
</tbody>
</table>
Post-Marketing Outcomes: Weaver 2020, Quality of Life (QoL) Study

• Prospective, randomized, longitudinal, crossover survey study.
• Assessed QoL and family experience for children with SMA, with and without nusinersen.
• Patients and parents were randomized to complete 4 survey instruments in a crossover fashion.
• Participants included 58 pediatric patients with SMA (age 0.25-20 years) and parents at US specialty clinics.
  – SMA type I (n=26) 12/26 (50%) received nusinersen
  – SMA type II (n=23) 8/23 (35%) received nusinersen
  – SMA type III (n=9) 1/9 (11%) received nusinersen
• Impact of nusinersen use:
  – No significant differences in scores on any of the 4 surveys.
  – However, many patients had just begun nusinersen treatment; further study needed.
Expanded Access Program (EAP) Outcomes: Ali 2019, Study of Hospital Utilization

• Retrospective cohort study in one UK hospital, assessing hospital utilization over 24-month study period.

• Patients:
  – 11 children with SMA type 1 receiving nusinersen via Expanded Access Program.
  – Median age at initiation of nusinersen: 8.1 (range 0-85.7) months

• Total number of hospital admissions since nusinersen initiation: 107.
  – Median admissions per child: 11 (range 1-25).
  – Most common reasons for admission: lower respiratory tract infection (n=42), nusinersen administration (n=38).

• Median hospital days since diagnosis per child: 118 (range 7-235).
  – Patients were hospitalized for a median of 20% (range 2-72%) of their lives.

• Overall, a total of 762 days was spent in a high-dependency unit and 248 days in pediatric intensive care unit during the 2-year study period. This equated to an estimated additional cost of £2.2M (approximately $2.7M USD at April 2020 exchange rate).
(viii) The average wholesale price, wholesale acquisition cost, retail price of the drug, and the cost of the drug to the Medicaid program minus rebates received by the state;
- WAC was $25,500/mL as of February 2020 per eMedNY.
- Product is only available in 12 mg/5 mL single-use vial. Based on WAC/mL, the WAC for the 5 mL single-use vial would be $127,500.

(ix) In the case of generic drugs, the number of pharmaceutical manufacturers that produce the drug;
- Spinraza® is a single-source product; currently there is no equivalent (AB-rated) generic drug.
In formulating a recommendation concerning a target rebate amount for a drug, the drug utilization review board may consider:

• (x) Whether there are pharmaceutical equivalents to the drug; and
  – Spinraza® is a single-source product and there are no pharmaceutical equivalents to the product.

• xi) Information supplied by the manufacturer, if any, explaining the relationship between the pricing of the drug and the cost of development of the drug and/or the therapeutic benefit of the drug, or that is otherwise pertinent to the manufacturer's pricing decision; any such information provided shall be considered confidential and shall not be disclosed by the drug utilization review board in a form that identifies a specific manufacturer or prices charged for drugs by such manufacturer.
  – Information supplied by the manufacturer will be provided to the DURB.
Summary

• Total WAC for initial year of nusinersen therapy: $765,000; total WAC for maintenance year of therapy: $382,500.

• Coverage policies for other states’ Medicaid programs, commercial health insurance, and other countries were reviewed; most specified criteria and/or restrictions for nusinersen coverage.

• SMA affects 10,000 – 25,000 people in the US; incidence in NYS: 20–30 per 235,000 births per year. NYS includes SMA testing in newborn screening.

• Patients with severe forms of SMA may struggle to swallow or breathe, and have life expectancy of <2 years. Patients with less severe disease can survive into adulthood, but may experience mobility limitations. Severe SMA is more common, with Type 1 accounting for >50% of all new SMA cases.
Summary

• From April 2017 through September 2019, <100 unique NYS Medicaid members (FFS+MC) had a claim for nusinersen, resulting in 336 claims during the timeframe of the analysis.

• Two phase 3 clinical trials for nusinersen were terminated early after interim analyses found that treatment produced favorable results.

• Post-marketing studies also showed benefits of nusinersen in adults with SMA.
References


