CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
1Q17 January – February

BRAND NAME
Spinraza™

GENERIC NAME
Nusinersen

MANUFACTURER
Biogen Inc.

DATE OF APPROVAL
December 23, 2016

PRODUCT LAUNCH DATE
December 28, 2017

REVIEW TYPE

☒ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☐ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastic, antipsychotics, antiretrovirals, and immunosuppressants)

FDA APPROVED INDICATION(S)
Spinraza is indicated for the treatment of spinal muscular atrophy (SMA) in pediatric and adult patients.

OFF-LABEL USES
Not applicable

CLINICAL EFFICACY[1,2]
The efficacy of Spinraza was demonstrated in a randomized, double-blind, sham-procedure controlled study, ENDEAR, in 121 symptomatic infants ≤7 months of age diagnosed with spinal

muscular atrophy (SMA) and was supported by open-label studies conducted in presymptomatic and symptomatic SMA patients.

ENDEAR: This was a phase 3 study investigating Spinraza in 121 patients with infantile-onset SMA, including patients with the onset of signs and symptoms of SMA at up to seven months of age. Patients were randomized 2:1 to receive either Spinraza or sham injection. A planned interim efficacy analysis was conducted based on patients who died, withdrew, or completed at least 183 days of treatment. Eighty-two patients were included in the interim analysis. The primary endpoints pre-specified for the interim analysis of the study were the proportion of motor milestone responders from the motor component of the Hammersmith Infant Neurological Examination (HINE) and time to death or permanent ventilation. A statistically significant greater percentage of patients achieved a motor milestone response in the Spinraza group (40%) compared to the sham-control group (0%) ($p<0.0001$). Overall, there was a 29% reduction in the risk of death or permanent ventilation compared with the control (HR 0.71). Given the results of the positive interim analysis, the ENDEAR study was stopped and participants were transitioned into the SHINE open-label study, in which all patients received Spinraza.

CHERISH: This is a phase 3 randomized, double-blind, parallel-group, sham-procedure controlled study designed to assess clinical efficacy and safety of Spinraza in 117 patients with later-onset SMA aged 2-12 years. Patients were randomized 2:1 to receive either Spinraza or sham injection. The primary endpoint is change from baseline in Hammersmith Functional Motor Scale Expanded (HFMSE) score at 15 months. Secondary endpoints include proportion of patients achieving a 3-point increase from baseline in HFMSE score at 15 months, proportion of patients achieving any new motor milestone at 15 months, number of motor milestones achieved per patient at 15 months, change from baseline in Upper Limb Module Test at 15 months, proportion of patients achieving standing alone at 15 months, and proportion of patients achieving walking with assistance at 15 months. This study is ongoing and results are not available at this time.

Currently, ENDEAR study outcomes for time to death or permanent ventilation has not been published. However, in an open-label, phase 2, dose-escalation published study with 20 patients with infantile-onset SMA, results demonstrated positive clinical response in most. Median age at death or permanent ventilation was not reached as compared with published natural history ($p=0.0014$).[3]

CONTRAINDICATIONS
Not applicable

BLACK BOX WARNINGS
Not applicable

DRUG INTERACTIONS

Not applicable

ADVERSE REACTIONS[4]

Common

- Gastrointestinal: Constipation (30%)
- Musculoskeletal: Backache (41%)
- Neurologic: Headache (50%), Reaction to lumbar puncture (41%)
- Renal: Glomerulonephritis
- Respiratory: Lower respiratory tract infection (43%), Upper respiratory infection (39%)

Serious

- Endocrine metabolic: Hyponatremia (1.8%)
- Hematologic: Coagulation/bleeding tests abnormal, platelet count below reference range (11%)
- Respiratory: Atelectasis (14%)

DOSAGE AND ADMINISTRATION

- The recommended dosage is 12 mg (5 mL) per administration.
- Initiate Spinraza treatment with 4 loading doses. The first three loading doses should be administered at 14-day intervals. The 4th loading dose should be administered 30 days after the 3rd dose.
- A maintenance dose should be administered once every 4 months thereafter.

PRODUCT AVAILABILITY

Injection: 12 mg/5 mL (2.4 mg/mL) nusinersen as a clear and colorless solution in a single-dose vial free of preservatives

THERAPEUTIC ALTERNATIVES

Not applicable

Utilization Management Recommendation
• There is significant potential for inappropriate use and utilization management should be considered for the following reason(s): i) Exact CPAC rationale language (1) To ensure appropriate use of medications that have a significant potential for use that may lead to inferior or unpredictable outcomes. (a) Currently all the data is interim unpublished data so it is difficult to evaluate the outcomes and benefits. ii) Recommended utilization management tool(s): (check all that apply) (1) ☒ Prior authorization

(2) ☐ Quantity limits (3) ☐ Provider newsletter (4) ☐ Hard block (plan exclusion) (5) ☐ Messaging (6) ☐ Electronic step therapy (7) ☐ Clinical Program
Product Comparison
• Only available first line therapy for spinal muscular atrophy (Not scored) • There are no clinically appropriate therapeutic alternatives.

REFERENCES

[1] Spinraza [Prescribing Information]. Cambridge, MA: Biogen Inc.; December 2016. Available at: https://www.spinraza-hcp.com/. Accessed January 4, 2017.
[2] Formulary submission dossier: Spinraza (nusinersen) for spinal muscular atrophy. Cambridge, MA: Biogen Inc.; December 2016.
[3] Finkel RS, Chiriboga CA, Vajsar J, et al. Treatment of infantile-onset spinal muscular atrophy with nusinersen: a phase 2, open-label, dose-escalation study. *Lancet*. 2017;388(10063):3017-3026.
[4] Micromedex® Healthcare Series [Internet database]. Greenwood Village, CO: Thomson Healthcare. Updated periodically. Accessed January 6, 2017.