GENE AND CELLULAR THERAPY - Exon Skipping Agents

Viltolarsen (Viltepso; NS Pharma, Inc.)
FDA Approval Date: 8/12/2020

AHFS PHARMACOLOGIC THERAPEUTIC CLASS
92:18 - Antisense Oligonucleotides
LEXI-COMP PHARMACOLOGIC THERAPEUTIC CLASS
Antisense Oligonucleotide

CURRENT FORMULARY STATUS WITHIN ENTERPRISE
Non-formulary

AVAILABLE FORMULATIONS[1]

- Solution, Intravenous [preservative free]: 250 mg/mL (5 mL) in a single dose vial.

INDICATIONS[2]
FDA Approved

- Treatment of Duchenne muscular dystrophy (DMD) in patients who have confirmed mutation of the DMD gene that is amenable to exon 53 skipping.
- DMD primarily affects males. Therefore, clinical trial experience is limited to the male population.

Off-Label uses

- None

DESCRIPTION AND CLINICAL PHARMACOLOGY[1]
Viltepso binds to exon 53 of dystrophin pre-messenger RNA (mRNA), excluding this exon during processings. Exon 53 skipping allows for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping.

PHARMACODYNAMICS AND PHARMACOKINETICS[1]

Distribution	V_{dss}: 300 mL/kg
Protein binding	~40%
Metabolism	Metabolically stable; no metabolites present in plasma or urine
Bioavailability	100%
Half-life elimination	2.5 hours
Time to peak	~1 hour
Excretion	Urine (mostly unchanged)

DOSING AND ADMINISTRATION[1]

Indication	Dosing
DMD	IV: 80 mg/kg once weekly

Geriatric
- Refer to adult dosing.

Pediatric
- Refer to adult dosing.

Renal impairment
- Has not been studied - There are no dosage adjustments provided in the manufacturer's labeling.
- Monitor closely.
- Viltolarsen is mainly excreted unchanged in the urine and renal impairment may increase exposure.
- Creatinine is not a reliable measurement of kidney function due to reduced skeletal mass in patients with DMD so no specific dosage adjustment can be recommended based on eGFR.

Hepatic impairment
- There are no dosage adjustments provided in the manufacturer's labeling.
- Viltolarsen is not hepatically eliminated.

LITERATURE REVIEW AND CLINICAL EFFICACY[3,4]

In a phase 2 trial, Viltepso demonstrated increases in mean dystrophin levels from 0.6% (SD 0.8) of normal at baseline to 5.9% (SD 4.5) of normal by week 25, with a mean change in dystrophin of 5.3% (SD 4.5) of normal levels (p=0.01). Viltepso gained an accelerated approval based on this biomarker of dystrophin production in skeletal muscle as a surrogate marker of efficacy. Viltepso's phase 3 RACER53 trial began as the confirmatory trial and is expected to conclude in 2024.

CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS[2]

Black Box Warnings
- N/A

Contraindications
- There are no contraindications listed in the manufacturer's labeling.

Warnings and Precautions
- Kidney toxicity
    - Observed in animal studies.
    - Including potentially fatal glomerulonephritis have been observed with some antisense oligonucleotides.
    - Creatinine may not be a reliable measure of kidney function in patients with DMD. Refer to a nephrologist if persistent increases in serum cystatin C or proteinuria occur.

ADVERSE REACTIONS[5]

Common
- Dermatologic: Injection site reaction
- Respiratory: Cough (19%), Upper respiratory infection
- Other: Fever (19%)

Serious
- N/A

RISK EVALUATION AND MITIGATION STRATEGIES

There is no REMS program associated with Viltepso.

MAJOR INTERACTIONS[2]

Drug-Drug

- There are no known significant interactions.

Drug-Disease

- May interfere with detection of urine protein (false positive) when pyrogallol red reagent is used.
    - Use a laboratory test that does not contain pyrogallol red reagent or use urine free of viltolarsen (e.g. urine obtained prior to infusion or ≥ 48 hours after infusion).

MONITORING REQUIREMENTS[1]

- Urine dipstick baseline and monthly.
- Serum cystatin C baseline and every 3 months.
- Urine protein-to-creatinine ratio baseline and every 3 months.
- GFR using exogenous filtration markers at baseline.
- Signs and symptoms of kidney toxicity.

PREGNANCY/BREASTFEEDING[1]

- Viltepso has not been studied in females. Animal reproduction studies have not been conducted.
- It is not known if Viltepso is present in breast milk.

MEDICATION SAFETY ISSUES[1]

Sound/Look Alike issues

- N/A

High Alert Medication

- N/A

SPECIAL STORAGE PRECAUTIONS[2]

- Store at 2 to 8°C (36 to 46°F). Do not freeze.
- The diluted solution may be stored at 2 to 8°C (36 to 46°F) for up to 24 hours.

SPECIAL HANDLING/ADMINISTRATION[2]

- Allow vials to reach room temperature prior to dilution.
- Mix the contents of each vial by gently inverting 2 or 3 times (do not shake).
- Withdraw the calculated volume.
    - If volume is <100 mL, dilute in NS by withdrawing an equivalent volume from a 100 mL NS infusion bag and injecting viltolarsen to achieve a total volume in the infusion bag of 100 mL.
    - If volume is ≥ 100 mL, dilution is not required.
- Place viltolarsen into an empty infusion bag.
- Discard unused portions.
- Administer by IV infusion over 60 minutes via central or peripheral catheter.
- Administration should begin as soon as possible after preparation or within 5 hours of preparation; complete infusion within 6 hours of preparation.
- Do not mix with other medications or infuse other medications concomitantly via the same IV access line.
- Flush IV access line with NS after infusion.

COST AND REIMBURSEMENT INFORMATION[2,6]

Cost (Estimated WAC)	Annual cost for 30-kg person: $703,872
Sales Projections (Estimated)	Unknown; however, some analysts project that Viltepso sales can surpass Vyondys sales by 2022
Medical/Pharmacy Benefit	Medical
Inpatient/Outpatient	Outpatient hospital, physician office, home infusion
Reimbursement Code	NDC 73292-0011-01: Single-dose vials containing 250mg/5L (50mg/mL)
NOC Code Billing Guide	NOC J3490 or C9399; See IPD COSESOURxCE

HCPS	Billing Unit	GPO Cost /Billing Unit	340 B Cost/ Billing Unit	Medicare	Traditional WV Medicaid	Aetna Better Health	BCBS	PEIA
J1427	10 mg	N/A	$56.4	$28.43-$54.82 No ASP established	$28.43-$54.82	$30.42-$58.66	Not covered	$28.43-$54.82 Not listed on formulary

Patient Assistance Availability	Pass Through Status	NTAP	Charge Map/ Method	Charge/ Rev Cod	Bill by	Allow billing for waste?
Yes	Yes	No	IV charges over $1,000 Cost x 1.8	0636	Admin amount	Yes

PATIENT ASSISTANCE AVAILABILITY[7]

- NS Support by NS Pharma, Inc. provides optimal access support and resources for patients, their caregivers, and healthcare professionals.
- Co-Pay Assistance Program - eligible patients may qualify for savings on their deductible, co-pay, and coinsurance for their medication costs of VILTEPSO.
- Patient Assistance Program - help for uninsured patients in financial need.
- Additional information available at viltepso.com/support; 1-833-NSSUPRT (1-833-677-8778), M-F 8 AM-8 PM ET.

REFERENCES

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