GENE AND CELLULAR THERAPY - Exon Skipping Agents

Eteplirsen (Exondys 51; Sarepta Therapeutics, Inc.**)**
FDA Approval Date: 9/19/2016

AHFS PHARMACOLOGIC THERAPEUTIC CLASS
92:92 - Other Miscellaneous Therapeutic Agents
LEXI-COMP PHARMACOLOGIC THERAPEUTIC CLASS
Antisense Oligonucleotide

CURRENT FORMULARY STATUS WITHIN ENTERPRISE
Formulary

AVAILABLE FORMULATIONS[1]
Solution, Intravenous [preservative free]: 50 mg/mL (2 mL, 10 mL)

INDICATIONS[1]
FDA Approved

- Treatment of Duchenne muscular dystrophy (DMD) in patients who have confirmed mutation of the DMD gene that is amenable to exon 51 skipping.

Off-Label uses

- None

DESCRIPTION AND CLINICAL PHARMACOLOGY[1]
Exondys 51 binds to exon 51 of dystrophin pre-messenger RNA (mRNA), excluding this exon during processing. Exon skipping allows for production of an internally truncated dystrophin protein.

PHARMACODYNAMICS AND PHARMACOKINETICS[2]

Distribution	V_{dss}: 600 mL/kg
Protein binding	6 to 17%
Half-life elimination	3 to 4 hours
Time to peak	1.1 to 1.2 hours
Excretion	Renal

DOSING AND ADMINISTRATION[1]

Indication	Dosing
DMD	IV: 30 mg/kg once weekly

Geriatric

- DMD is largely a disease of children and young adults, there is no geriatric experience with Exondys 51.

Pediatric

- Male children ≥ 7 years and adolescents: refer to adult dosing. In clinical trials, patients ranged in age from 7 to 13 years.

Renal impairment

- Has not been studied - there are no dosage adjustments provided in the manufacturer's labeling.

Hepatic impairment

- Has not been studied - there are no dosage adjustments provided in the manufacturer's labeling.

LITERATURE REVIEW AND CLINICAL EFFICACY[2,3]

Exondys 51 was evaluated in three clinical studies in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. Exondys 51 demonstrated an increase in dystrophin production that is reasonably likely to predict clinical benefit in patients with DMD who have confirmed mutation of the dystrophin gene amenable to exon 51 skipping. A clinical benefit, including improved motor function has not been established. An ongoing confirmatory trial is being conducted and is expected to conclude in 2026.

CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS[1]

Black Box Warnings

- N/A

Contraindications

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

Warnings and Precautions

- Hypersensitivity reactions
    - Including rash, urticaria, pyrexia, flushing, cough, dyspnea, bronchospasm, and hypotension.
    - Manage appropriately and consider slowing the infusion rate or interrupting therapy.

ADVERSE REACTIONS[4]

Common

- Dermatologic: Contact dermatitis (25%)
- Gastrointestinal: Vomiting (10 to 38%)
- Neurologic: Impairment of balance (38%)

Serious

- Immunologic: Hypersensitivity reaction

Dose Adjustments for Toxicity

- Hypersensitivity reactions
    - Consider slowing infusion or interrupting therapy.

RISK EVALUATION AND MITIGATION STRATEGIES

There is no REMS program associated with Exondys 51.

MAJOR INTERACTIONS[1]

There are no known significant interactions.

MONITORING REQUIREMENTS[2]

There are no monitoring parameters listed in the manufacturer's labeling.

PREGNANCY/BREASTFEEDING[1]

- Exondys 51 has not been studied in females. Animal reproduction studies have not been conducted.
- It is not known if Exondys 51 is excreted in breast milk.

MEDICATION SAFETY ISSUES[1]

Sound/Look Alike issues

- N/A

High Alert Medication

- N/A

SPECIAL STORAGE PRECAUTIONS[1]

- Store at 2 to 8°C (36 to 46°F). Do not freeze. Protect from light and store in the original carton until ready to use.
- The diluted solution may be stored at 2 to 8°C (36 to 46°F) for up to 24 hours. Do not freeze. Discard unused portions.

SPECIAL HANDLING/ADMINISTRATION[2]

- Allow vials to warm to room temperature prior to dilution. Mix contents of each vial by gently inverting 2 or 3 times; do not shake.
- Use a 21-gauge or smaller or non-coring needle to withdraw the calculated volume and dilute in NS to a total volume of 100 to 150 mL.
- Do not use if the solution in vial is cloudy, discolored, or contains extraneous particulate matter other than trace amounts of small, white to off-white, amorphous particles.
- Administer by IV infusion over 35 to 60 minutes through a 0.2-micron inline filter: complete infusion within 4 hours of dilution.
- Consider slowing the infusion or interrupting therapy for hypersensitivity reactions.
- Flush IV access line with NS prior to and after infusion.
- Do not mix with other medications or infuse other medications concomitantly via the same IV access line.
- If a dose is missed, administer as soon as possible after the scheduled time.

COST AND REIMBURSEMENT INFORMATION[2,5,6]

Cost (Estimated WAC)	Annual cost for 30-kg person: $748,800 (30 kg * 30 mg/kg per week = 90 mg weekly = 18 mL/week; WAC = 800/mL * 18 mL * 52 weeks)
Reimbursement Code	NDC 60923-0363-02: Single-dose vials containing 100mg/2mL NDC: 60923-0284-10: Single-dose vial containing 500 mg/10mL
NOC Code Billing Guide	See IPD COSESOURxCE

HCPS	Billing Unit	GPO Cost /Billing Unit	340 B Cost/ Billing Unit	Medicare	Traditional WV Medicaid	Aetna Better Health	BCBS	PEIA
J1428	10 mg	N/A	$121.65	Not separately reimbursable				

Patient Assistance Availability	Pass Through Status	NTAP	Charge Map/ Method	Charge/ Rev Cod	Bill by	Allow billing for waste?
Yes	No	No	N/A	0636	Admin amount	Yes

PATIENT ASSISTANCE AVAILABILITY[7]

- SareptAssist by Sarepta Therapeutics, Inc. offers free or low-cost drugs to individuals who are unable to pay for their medication.
- Patients must meet financial and other program specific criteria to be eligible for assistance.
- Care managers provide information on insurance benefits, financial assistance options, treatment logistics, options for weekly infusions, and ongoing education and support.
- Additional information available at sarepta.com/sareptassistcall; 1-888-SAREPTA, M-F 8:30AM-6:30PM ET.

REFERENCES

1. Eteplirsen. Lexi-Drugs [online database]. Lexi-Comp, Inc. Accessed 10/25/21.
2. Exondys 51 (eteplirsen) injection, for intravenous use [package insert]. Cambridge, MA. Sarepta Therapeutics, Inc. 2021.
3. New Drug Review: Vyondys 53 (golodirsen). IPD Analytics. 2021.
4. Eteplirsen [contained in: EXONDYS 51]. In: DRUGDEX ® System [Internet Database]. Greenwood Village, Colo. Thomson Micromedex. Updated periodically. Accessed 10/25/21.
5. Eteplirsen. Clinical Pharmacology [internet database]. Gold Standard, Inc., 2007. Available at: http://www.clinicalpharmacology.com. Accessed 11/18/21.
6. WVUHS Pharmacy Financial Services.
7. SAREPTASSIST. Available at: https://www.sarepta.com/sareptassist. Accessed 10/19/21.