Viltepso (viltolarsen)

NEW PRODUCT SLIDESHOW

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Introduction

- **Brand name:** Viltepso
- **Generic name:** Viltolarsen
- **Pharmacologic class:** Antisense oligonucleotide
- **Strength and Formulation:** 250mg/5mL; solution for IV infusion; preservative-free
- **Manufacturer:** NS Pharma, Inc.
- **How supplied:** Single-dose vial—1
- **Legal Classification:** Rx

Viltepso

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Indication

- Treatment of **Duchenne muscular dystrophy** (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping.
  - Approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with Viltepso.
  - Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

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Dosage and Administration

- Measure serum cystatin C, urine dipstick, urine protein-to-creatinine ratio before initiating therapy.
- Consider measurement of glomerular filtration rate prior to initiation.
- Give as IV infusion using a peripheral or central venous catheter.
- **80mg/kg infused over 60 minutes once weekly**.

Considerations for Special Populations

- **Pregnancy:** No available human or animal data.
- **Nursing mothers:** No available human or animal data.
- **Geriatrics**: No experience in patients 65 years of age or older as DMD is largely a disease of children and young adults.
- **Renal impairment**: Not studied; monitor closely in patients with known renal impairment.
- **Hepatic impairment**: Not studied.

Warnings and Precautions

- Measure serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio prior to initiation.
- During treatment, monitor urine dipstick monthly, and serum cystatin C and urine protein-to-creatinine ratio every 3 months.
- Refer to pediatric nephrologist if a persistent increase in serum cystatin C or proteinuria is detected.
- Consider measuring glomerular filtration rate prior to initiation.
- Monitor renal function during treatment.
- Because of the effect of reduced skeletal muscle mass on creatinine measurements, serum creatinine may not be a reliable measure of kidney function.

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Adverse Reactions

- **Most common (≥ 15%)**: Upper respiratory tract infection, injection site reaction, cough, pyrexia.
- **Others**: Contusion, arthralgia, diarrhea, vomiting, abdominal pain, decreased ejection fraction, urticaria.
- Potential for immunogenicity; data show viltolarsen is not highly immunogenic.

Mechanism of Action

- Viltolarsen is an antisense oligonucleotide of the phosphorodiamidate morpholino oligomer subclass.
- It is designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping.
- Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping.

Pharmacokinetics

- Viltolarsen is metabolically stable based on *in vitro* data.
- Excreted mainly unchanged in the urine.
- Half-life: 2.5 hours.
- Plasma clearance: 217mL/hr/kg.
- Pharmacokinetics have only been evaluated in male pediatric DMD patients.
- No marked differences observed between white and Asian patients.

Clinical Trials

- Efficacy of Viltepso was evaluated in a multicenter, 2-period, dose-finding study (NCT02740972) in 16 DMD patients with a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping.
- Patients were randomized to Viltepso or placebo during the initial 4 weeks.
- All patients then received 20 weeks of open-label Viltepso 40mg/kg (n=8) or 80mg/kg (n=8) once weekly.
- **The primary efficacy end point** was the change from baseline in dystrophin protein level (measured as % of the dystrophin level in healthy subjects, ie, % of normal) at week 25.

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Clinical Trials

- **Inclusion criteria**
  - Male patients 4 to <10 years of age (median age 7 years) with confirmed mutation in the dystrophin gene that is amenable to exon 53 skipping.
  - On a stable corticosteroid regimen for at least 3 months.
  - Able to walk independently without assistive devices.
  - Able to complete the time to stand, time to run/walk and time to climb assessments.

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Clinical Trials

- Results for Viltepso 80mg/kg once weekly
  - As assessed by **validated Western blot** (normalized to myosin heavy chain): Mean dystrophin levels increased from 0.6% (SD 0.8) of normal at baseline to 5.9% (SD 4.5) of normal by week 25 (mean change in dystrophin of 5.3% [SD 4.5] of normal levels [*P* =.01]); the median change from baseline was 3.8%.
  - As assessed by **mass spectrometry** (normalized to filamin C): Mean dystrophin levels increased from 0.6% (SD 0.2) of normal at baseline to 4.2% (SD 3.7) of normal by week 25 (mean change in dystrophin of 3.7% [SD 3.8] of normal levels [nominal *P* =.03, not adjusted for multiple comparisons]); the median change from baseline was 1.9%.

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New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/viltepso/