
## Indication

VILTEPSO is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. This indication is 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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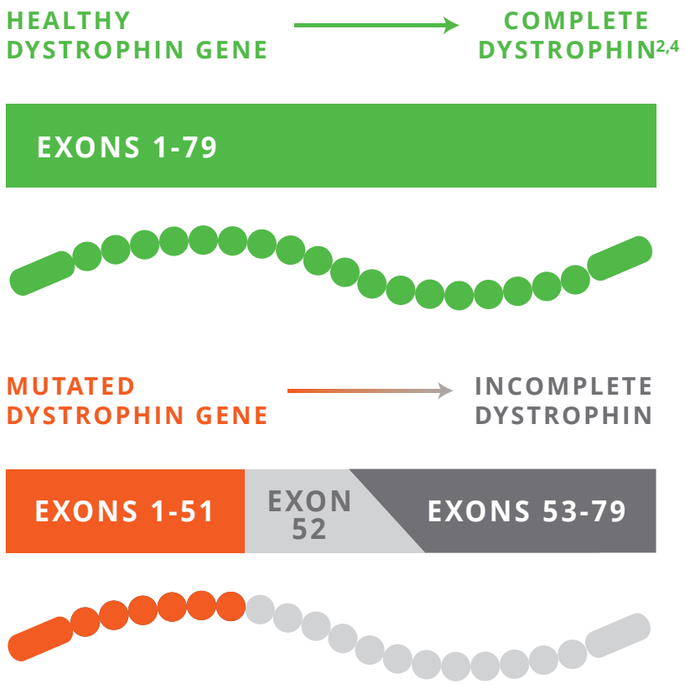
# Lack of dystrophin (dystrophinopathy) causes a progressive loss of muscle strength and motor function[1,2]

- DMD is caused by mutations in the dystrophin gene, which leads to a lack of dystrophin production[3]
- Patients with DMD experience progressive muscle weakness, with symptom onset as early as 2 years[5]




**EARLY DIAGNOSIS** is instrumental to inform the management of progressive muscle weakness and function decline in patients with DMD.[6,7]

## Important Safety Information

**Warnings and Precautions (continued):** Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting VILTEPSO. Consider also measuring glomerular filtration rate before starting VILTEPSO. During treatment, monitor urine dipstick every month, and serum cystatin C and urine protein-to-creatinine ratio every three months.



# VILTEPSO is for DMD patients with a confirmed mutation that is amenable to exon 53 skipping[8]

VILTEPSO is designed to bind to and induce **skipping of exon 53 of the dystrophin pre-mRNA,** resulting in the production of a shortened dystrophin protein that contains essential functional portions[8]

An estimated **10% of patients** with DMD would be amenable to treatment with an exon 53-skipping therapy[9]*

VILTEPSO was discovered through an **innovative triple-screening approach** designed to identify antisense oligonucleotides with the highest possible exon-skipping efficiency[10]

*Common deletions that can be treated with VILTEPSO include 45-52, 47-52, 48-52, 49-52, 50-52, and 52 of the dystrophin gene.[9]

mRNA=messenger RNA.

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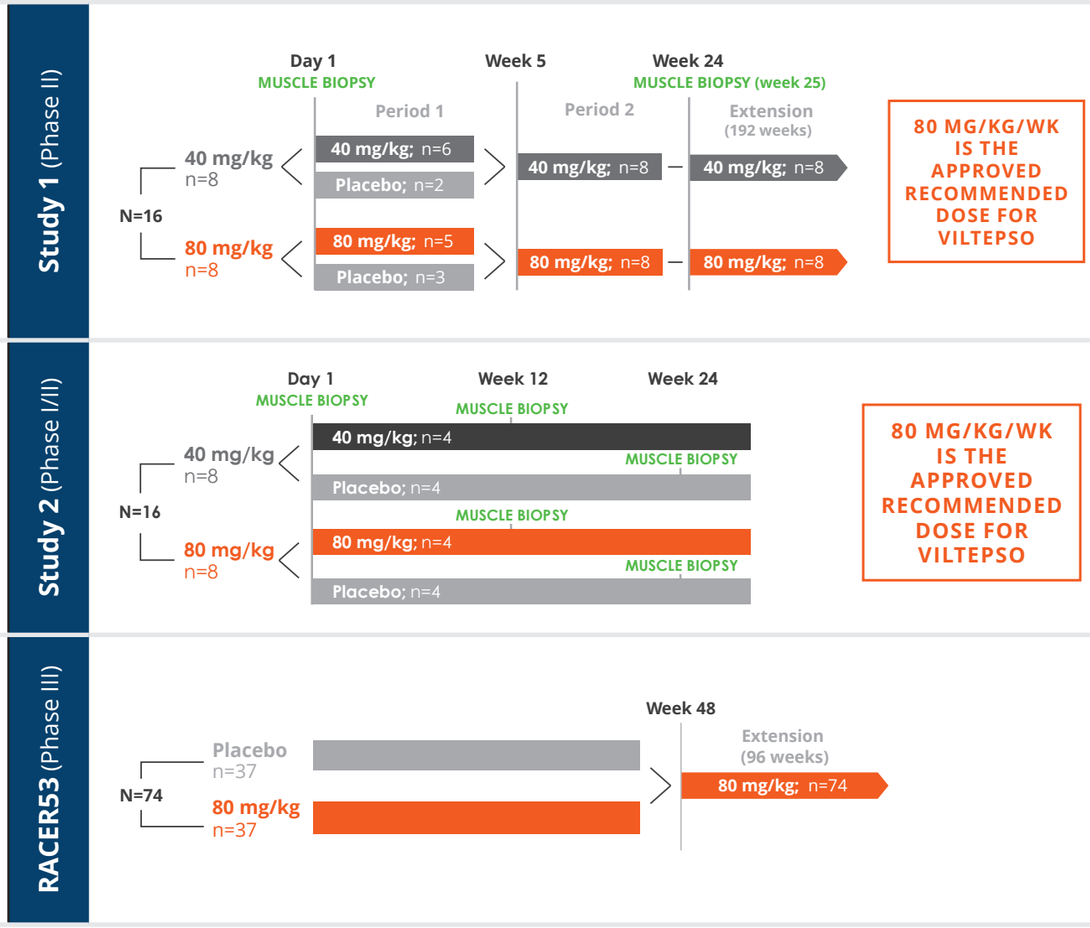
Viltepso® (viltolarsen) injection

# VILTEPSO safety and efficacy as studied in an ongoing clinical trial program[4,8,11-13]




**80 MG/KG/WK IS THE APPROVED RECOMMENDED DOSE FOR VILTEPSO**

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As part of the accelerated approval of VILTEPSO, NS Pharma is conducting a **CONFIRMATORY STUDY**, begun in October 2019, to further evaluate the functional benefit of treatment.

| | Study endpoints | Description |
|---|---|---|
| **Study 1** (Phase II) | **Primary:** Safety, tolerability, dystrophin protein production (Western blot)[4]<br>**Secondary:** Other dystrophin measures (RT-PCR, MS, and IFS), timed motor function tests (6MWT, TTCLIMB, TTRW, TTSTAND) and NSAA[4] | A 2-period, North American dose-finding study with ambulant males aged 4 to <10 years with a confirmed mutation of the DMD gene amenable to exon 53 skipping who were receiving a stable dose of corticosteroids for ≥3 months (N=16)[4,8,11]<br>**24 weeks**<br>**Open-label extension study up to 192 weeks** |
| **Study 2** (Phase I/II) | **Primary:** Dystrophin measures (Western blot, IFS, and RT-PCR)[4]<br>**Secondary:** Safety, pharmacokinetics, motor function tests (6MWT, TTRW, TTSTAND, and timed up & go test), muscle strength, and serum CK levels[4] | A multicenter, parallel-group, open-label, dose-finding study conducted in Japan in ambulant and nonambulant* males aged 5 to <18 years with a confirmed mutation of the DMD gene amenable to exon 53 skipping (N=16)[4,8]<br>**24 weeks** |
| **RACER53** (Phase III) | **Primary:** TTSTAND[12]<br>**Secondary:** TTRW, TTCLIMB, 6MWT, NSAA, and muscle strength[12] | A global, multicenter, randomized, double-blind, placebo-controlled study in ambulant males aged 4 to <8 years with a confirmed mutation of the DMD gene amenable to exon 53 skipping who were receiving a stable dose of corticosteroids for ≥3 months (N=74)[4,12,13]<br>**48 weeks**<br>**Open-label extension study up to 96 weeks** |

*Defined as patients with a 6MWT distance of <75 meters.

CK=creatine kinase; IFS=immunofluorescence staining; MS=mass spectrometry; NSAA=North Star Ambulatory Assessment; RT-PCR=reverse transcriptase-polymerase chain reaction; 6MWT=6-minute walk test; TTCLIMB=time to climb 4 stairs; TTRW=time to run/walk 10 meters; TTSTAND=time to stand from supine.

## Important Safety Information

**Warnings and Precautions (continued):** Urine should be free of excreted VILTEPSO for monitoring of urine protein. Obtain urine either prior to VILTEPSO infusion, or at least 48 hours after the most recent infusion. Alternatively, use a laboratory test that does not use the reagent pyrogallol red, which has the potential to generate a false positive result due to cross reaction with any VILTEPSO in the urine. If a persistent increase in serum cystatin C or proteinuria is detected, refer to a pediatric nephrologist for further evaluation.

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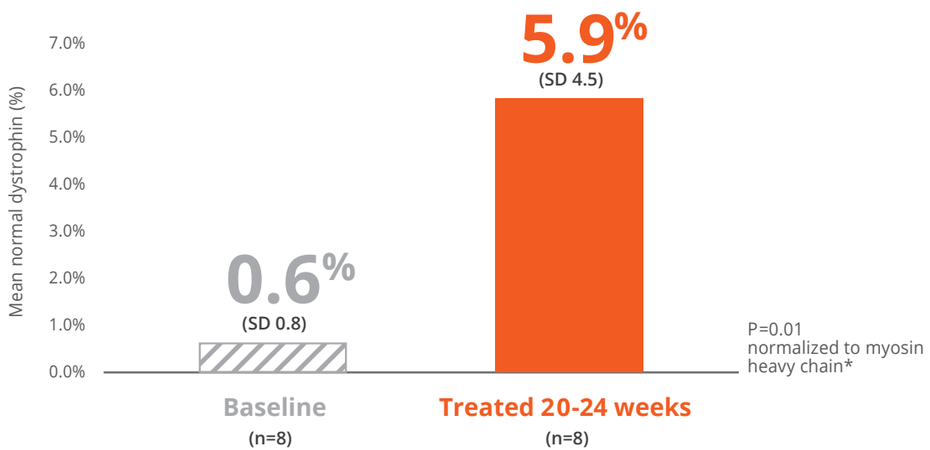
Viltepso® (viltolarsen) injection

# VILTEPSO provided significant improvements in dystrophin expression[8,9]

In Study 1, the efficacy of 20-24 weeks of VILTEPSO was evaluated in ambulant males aged 4 to <10 years.[8,9]

## Study 1: Mean increase in dystrophin expression to nearly 6% of normal with VILTEPSO (80 mg/kg/wk) vs 0.6% at baseline[8,9]




- Efficacy was assessed by validated Western blot (normalized to myosin heavy chain) based on the change from baseline in dystrophin protein level, measured as percentage of the dystrophin level in healthy subjects at week 25[8]
- Mean change in dystrophin was 5.3% (SD 4.5) of normal levels (*P*=0.01)[8]
  - Median change from baseline was 3.8%[8]

**DYSTROPHIN WHERE IT MATTERS:** Immunofluorescence staining showed VILTEPSO-induced increases in dystrophin levels were correctly localized to the muscle cell membrane.[8,9]

**P*-value for change from baseline at week 25 was statistically significant.[9]

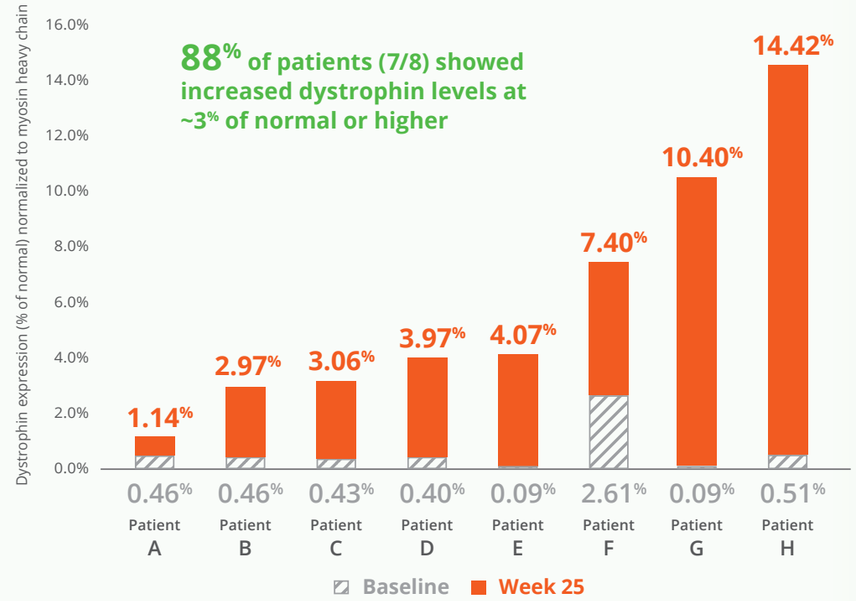
## Important Safety Information

**Adverse Reactions:** The most common adverse reactions include upper respiratory tract infection, injection site reaction, cough, and pyrexia.



# 100% of patients showed an increase in dystrophin levels with VILTEPSO[8]

## Study 1: Dystrophin levels at 25 weeks vs baseline[8]




- In a clinical study of patients aged 4 to <10 years, **100%** of patients showed an increase in dystrophin levels with VILTEPSO, with a mean increase in dystrophin expression to ~6% of normal vs 0.6% at baseline[8]
- Exon 53 skipping was observed, on average, in **43.9%** of dystrophin mRNA molecules in patients treated with VILTEPSO (80 mg/kg/wk), as measured by RT-PCR[4]
- The statistically significant increase in dystrophin expression was measured by Western blot analysis, which is a **validated**, **highly sensitive**, and **reproducible** methodology[4,8]

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Viltepso®
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# In the same 24-week study, secondary endpoint results provided additional evidence of dystrophin production[4]

| Secondary endpoint | Baseline (n=8) | Week 25 VILTEPSO (n=8) |
|---|---|---|
| Exon 53 skipping efficiency assessed by RT-PCR | 0.0% | **43.9%** ***P*=0.0001** |
| Dystrophin production assessed by MS* | 0.6% | **4.2%** ***P*=0.03** |
| Dystrophin localization by IFS | 1.8% | **34.8%** ***P*=0.0026** |

*Mean dystrophin levels as assessed by mass spectrometry (normalized to filamin C) increased from 0.6% (SD 0.2) of normal at baseline to 4.2% (SD 3.7) of normal by week 25, with a mean change in dystrophin of 3.7% (SD 3.8) of normal levels (nominal *P*=0.03, not adjusted for multiple comparisons); the median change from baseline was 1.9%.[8]

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# In the same 24-week study, secondary endpoints included several motor function tests[4]

**Functional tests were secondary endpoints of study 201 and were compared to Duchenne natural history data, which is not considered an adequate comparator arm. Functional data are not in the US Prescribing Information, and therefore definitive conclusions should not be drawn.**

| Secondary endpoint | DNHS—mean change from baseline at week 25 (n=65)† | VILTEPSO—mean change from baseline at week 25 (n=8) |
|---|---|---|
| **Time to stand** | | |
| velocity (rise/second)‡ | -0.01 | **0.02** |
| (seconds)§ | 0.66 | **-0.44** |
| **Time to climb 4 stairs** | | |
| velocity (task/second) | 0.01 | **0.00** |
| (seconds) | 0.15 | **0.00** |
| **Time to run/walk 10 meters** | | |
| velocity (meters/second)‡ | -0.04 | **0.24** |
| (seconds)§ | 0.08 | **-0.66** |
| **6-minute walk test**‖ (meters) | -65.3 | **44.0** |
| **North Star Ambulatory Assessment**¶ | -1.1 | **1.1** |

†The control subjects for this trial were matched for age and corticosteroids from the CINRG-DNHS registry.
‡Negative velocity means lower rate of velocity; positive velocity means higher rate of velocity.
§Negative time means less time; positive time means more time.
‖Negative number means less distance traveled; positive number means greater distance traveled.
¶Negative number means a lower score relative to baseline; positive number means a higher score relative to baseline.

CINRG=Cooperative International Neuromuscular Research Group; DNHS=Duchenne Natural History Study.

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Viltepso® (viltolarsen) injection

# Safety profile evaluated in two 24-week clinical studies[8]

**Adverse reactions** reported in ≥10% of DMD patients treated with VILTEPSO 80 mg/kg once weekly[8]

| Adverse reaction | VILTEPSO (80 mg/kg once weekly) (N=16); n (%) |
|---|---|
| Upper respiratory tract infection* | **10** (63%) |
| Injection site reaction† | **4** (25%) |
| Cough | **3** (19%) |
| Pyrexia | **3** (19%) |
| Contusion | **2** (13%) |
| Arthralgia | **2** (13%) |
| Diarrhea | **2** (13%) |
| Vomiting | **2** (13%) |
| Abdominal pain | **2** (13%) |
| Ejection fraction decreased | **2** (13%) |
| Urticaria | **2** (13%) |

No treatment-related SAEs, drug-related TEAEs, discontinuations, or deaths occurred.[9,14]

*Upper respiratory tract infection includes the following terms: upper respiratory tract infection, nasopharyngitis, and rhinorrhea.

†Injection site reaction includes the following terms: injection site bruising, injection site erythema, injection site reaction, and injection site swelling.



# Treatment choice: Get VILTEPSO at home or at a treatment center

VILTEPSO is given as an 80-mg/kg weekly **intravenous infusion**[8]

The **appropriate dose** of VILTEPSO is calculated based upon **patient weight**, at a recommended weekly dose of 80 mg/kg[8]

Please refer to the Pocket Dosing Guide for the weekly dosing chart.

VILTEPSO is infused over **60 minutes** by a healthcare professional at home or at a treatment center[8]

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Viltepso® (viltolarsen) injection

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NS PHARMA ACCESS SOLUTIONS

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- Insights about infusion site options for your patients
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*Program covers the cost of the medication only and does not cover the costs to administer the infusion. See full Eligibility Requirements & Terms and Conditions on back of brochure.



# Indication and Important Safety Information

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**References: 1.** Hoffman EP, Brown RH Jr, Kunkel LM. Dystrophin: the protein product of the Duchenne muscular dystrophy locus. *Cell*. 1987;51(6):919-928. doi:10.1016/0092-8674(87)90579-4 **2.** Niks EH, Aartsma-Rus A. Exon skipping: a first in class strategy for Duchenne muscular dystrophy. *Expert Opin Biol Ther*. 2017;17(2):225-236. doi:10.1080/14712598.2017.1271872 **3.** Birnkrant DJ, Bushby K, Bann CM, et al; for the DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *Lancet Neurol*. 2018;17(3):251-267. doi:10.1016/S1474-4422(18)30024-3 **4.** Data on file, NS Pharma, Inc. **5.** Blake DJ, Weir A, Newey SE, Davies KE. Function and genetics of dystrophin and dystrophin-related proteins in muscle. *Physiol Rev*. 2002;82(2):291-329. doi:10.1152/physrev.00028.2001 **6.** US Food and Drug Administration. Duchenne muscular dystrophy and related dystrophinopathies: developing drugs for treatment guidance for industry. Accessed May 27, 2020. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/duchenne-muscular-dystrophy-and-related-dystrophinopathies-developing-drugs-treatment-guidance. **7.** Institute for Clinical and Economic Review. Deflazacort, eteplirsen, and golodirsen for Duchenne muscular dystrophy: effectiveness and value. Accessed May 27, 2020. https://icer-review.org/wp-content/uploads/2018/12/ICER_DMD_Draft_Scope_011119-1.pdf. **8.** Viltepso [prescribing information]. Paramus, NJ: NS Pharma, Inc.; 2021. **9.** Clemens PR, Rao VK, Connolly AM, et al; for the CINRG DNHS Investigators. Safety, tolerability, and efficacy of viltolarsen in boys with Duchenne muscular dystrophy amenable to exon 53 skipping: a phase 2 randomized clinical trial. *JAMA Neurol*. 2020;77(8):982-991. doi:10.1001/jamaneurol.2020.1264 **10.** Watanabe N, Nagata T, Satou Y, et al. NS-065/NCNP-01: an antisense oligonucleotide for potential treatment of exon 53 skipping in Duchenne muscular dystrophy. *Mol Ther Nucleic Acids*. 2018;13:442-449. doi:10.1016/j.omtn.2018.09.017 **11.** US National Library of Medicine. Extension study of NS-065/NCNP-01 in boys with Duchenne muscular dystrophy (DMD). ClinicalTrials.gov Identifier: NCT03167255. **12.** US National Library of Medicine. Study to assess the efficacy and safety of viltolarsen in ambulant boys with DMD (RACER53). ClinicalTrials.gov Identifier: NCT04060199. **13.** US National Library of Medicine. Study to assess the safety and efficacy of viltolarsen in ambulant boys with DMD (RACER53-X). ClinicalTrials.gov Identifier: NCT04768062. **14.** Komaki H, Takeshima Y, Matsumura T, et al. Viltolarsen in Japanese Duchenne muscular dystrophy patients: a phase 1/2 study. *Ann Clin Transl Neurol*. 2020;7(12):2393-2408. doi:10.1002/acn3.51235

Viltepso®
(viltolarsen) injection

**For the treatment of DMD in patients amenable to exon 53 skipping**

# VILTEPSO provided a mean increase in dystrophin to nearly 6% of normal[8]

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**Safety profile** evaluated in two 24-week clinical studies[8]

Infused over 60 minutes by a healthcare professional **at home or at a treatment center**[8]

Sign up for updates at **VILTEPSO.com**

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