Viltepso®
(viltolarsen) injection

An exon-skipping treatment option for DMD patients with an exon 52 deletion

- Exon skipping is a genetic technique that assists in "skipping over" an exon
- An antisense oligonucleotide acts as a molecular repair to mask the exon next to the deleted exon(s) during the protein production process[1,2]
- Exon skipping can be used to treat specific exon deletions[3-6]
- VILTEPSO®, an exon-skipping treatment, can be used to treat patients with DMD with an exon 52 deletion[6,7]

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.

IMPORTANT SAFETY INFORMATION

- **Warnings and Precautions:** In clinical studies, no patients experienced kidney toxicity during treatment with VILTEPSO. However, kidney toxicity from drugs like VILTEPSO may be possible. Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting and during treatment with VILTEPSO. Consider measuring GFR before starting VILTEPSO.

Please see Important Safety Information throughout. For more information about VILTEPSO, see accompanying full Prescribing Information.

Specific exon deletions are amenable to specific exon-skipping therapies

There are common areas for mutations in the DMD gene; ***molecular repairs*** through exon skipping can treat some of the common deletion mutations

About **8% of patients with DMD** in the US would be amenable to treatment with exon 53 skipping[3]

The **most common deletions** amenable to exon 53 skipping include deletions of **exons 45-52, exons 47-52, exons 48-52, exons 49-52, exons 50-52, and exon 52**.[8] A complete list of exon 53 skip-amenable deletions is provided in the lower table on the right

VILTEPSO®: a proven exon-skipping therapy

- 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[6]
- Patients taking VILTEPSO (80 mg/kg/week; n=8) showed **a mean increase in dystrophin levels to 5.9%** of normal by Week 25 vs 0.6% of normal at baseline[6]
- **100% of patients** showed an increase in dystrophin levels[6]
- VILTEPSO can be used to treat patients with **DMD with an exon 52 deletion**[6,7]

INDICATION

VILTEPSO is for the treatment of DMD in patients amenable to exon 53 skipping. Accelerated approval is based on an increase in dystrophin. There is an ongoing study to confirm the clinical benefit of VILTEPSO.

IMPORTANT SAFETY INFORMATION (continued)

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

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Patients with an exon 52 deletion are amenable to two exon-skipping therapy options

- In the US, about **2% of patients** with DMD have **an exon 52 deletion**[7]
- For this cohort of patients, **either exon 51 OR exon 53 skipping therapy** can be used as treatment[3]

Exon 51 Skip-amenable Deletions (complete list)[3]									
3-50	4-50	5-50	6-50	9-50					
10-50	11-50	13-50	14-50	15-50	16-50	17-50	19-50		
21-50	23-50	24-50	25-50	26-50	27-50	28-50	29-50		
30-50	31-50	32-50	33-50	34-50	35-50	36-50	37-50	38-50	39-50
40-50	41-50	42-50	43-50	45-50	47-50	48-50	49-50		
50	52	52-58	52-61	52-63	52-64	52-66	52-76	52-77	

Amenable to exon 51 skipping therapy

Exon 52 deletion

Amenable to exon 51 or exon 53 skipping therapy

Exon 53 Skip-amenable Deletions (complete list)[3]									
3-52	4-52	5-52	6-52	9-52					
10-52	11-52	13-52	14-52	15-52	16-52	17-52	19-52		
21-52	23-52	24-52	25-52	26-52	27-52	28-52	29-52		
30-52	31-52	32-52	33-52	34-52	35-52	36-52	37-52	38-52	39-52
40-52	41-52	42-52	43-52	45-52	47-52	48-52	49-52		
50-52	52	54-58	54-61	54-63	54-64	54-66	54-76	54-77	

Amenable to exon 53 skipping therapy

Study 1 (Phase II) Study Design

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)[6,9]
24 weeks, followed by a 168-week extension study

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▲ **Prescribing Information for VILTEPSO®** ▲

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

Sign up for updates at VILTEPSO.com to learn more about treatment

References: 1. Nguyen Q, Yokota T. Antisense oligonucleotides for the treatment of cardiomyopathy in Duchenne muscular dystrophy. *Am J Transl Res.* 2019;11(3):1202-1218. **2.** Nakamura A. Mutation-based therapeutic strategies for Duchenne muscular dystrophy: from genetic diagnosis to therapy. *J Pers Med.* 2019;9(1). doi:10.3390/jpm9010016 **3.** Exon skipping. CureDuchenne.org. Accessed February 19, 2021. https://cureduchenne.org/cure/exon-skipping **4.** Exondys 51®. Prescribing information. Sarepta Therapeutics, Inc.; 2020. **5.** Vyondys 53™. Prescribing information. Sarepta Therapeutics, Inc.; 2020. **6.** VILTEPSO®. Prescribing information. NS Pharma, Inc.; 2020. **7.** Bladen CL, Salgado D, Monges S, et al. The TREAT-NMD DMD Global Database: analysis of more than 7,000 Duchenne muscular dystrophy mutations. *Human Mutat.* 2015;36(4):395-402. **8.** Clemens PR, Rao VK, Connolly AM, et al. Safety, tolerability, and efficacy of viltolarsen in boys with Duchenne muscular dystrophy amenable to exon 53 skipping: a phase 2 randomized clinical trial. 2020;77(8):982-991. *JAMA Neurol.* doi:10.1001/jamaneurol.2020.1264 **9.** U.S. National Library of Medicine. Extension study of NS-065/NCNP-01 in boys with Duchenne muscular dystrophy (DMD). Accessed February 19, 2021. https://clinicaltrials.gov/ct2/show/NCT03167255?term=NS-065&draw=2&rank=1

For more information about VILTEPSO, see accompanying full Prescribing Information.

NS Pharma

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