מרץ 2022

רופא/ה , רוקח/ת נכבד/ה,

הנדון: **<u>עדכון העלון לרופא לתכשיר EXONDYS 51</u>**

חברת תרומד בע"מ מבקשת ליידע על עדכון העלון לרופא לתכשיר שבנדון.

<u>ההתוויה הרשומה:</u>

EXONDYS 51 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 51 skipping.

<u>חומר פעיל:</u> ETEPLIRSEN 50 MG / 1 ML

בהודעה זו מצוינים העדכונים המהותיים בלבד (טקסט עם קו תחתי מציין טקסט שהוסף לעלון ואילו טקסט עם קו חוצה מסמן טקסט שהורד מהעלון). נא לעיין בעלון המצורף להודעה זו המכיל את כלל העדכונים.

<u>עלון לרופא</u>

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions, including <u>bronchospasm, chest pain, cough, tachycardia,</u>~~rash~~ and urticaria ~~pyrexia, flushing, cough, dyspnea, bronchospasm, and hypotension,~~ have occurred in patients who were treated with EXONDYS 51.

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6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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~~In the EXONDYS 51 clinical development program, 107 patients received at least one intravenous dose of EXONDYS 51, ranging between 0.5 mg/kg (0.017 times the recommended dosage) and 50 mg/kg (1.7 times the recommended dosage). All patients were male and had~~

~~genetically confirmed Duchenne muscular dystrophy. Age at study entry was 4 to 19 years. Most (89%) patients were Caucasian.~~

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~~In~~ Adverse Reactions from Observational Clinical Studies

The following adverse reactions have been identified during observational studies that were conducted as part of the ~~88~~ clinical development program and continued post approval.

In open-label observational studies, 163 patients ~~who~~ received ~~≥30 mg/kg/week~~ at least one intravenous dose of EXONDYS 51, with doses ranging between 0.5 mg/kg (0.017 times the recommended dosage) and 50 mg/kg (1.7 times the recommended dosage).

All patients were male and had genetically confirmed Duchenne muscular dystrophy. Age at study entry was ~~for up~~ 6 months to ~~208 weeks~~ 19 years. Most (85%) patients were Caucasian.

The most common adverse reactions seen in ~~clinical studies, the following events were reported in ≥~~ greater than 10% of ~~patients and occurred more frequently than on the same dose in Study 1:~~the study population were headache, cough, rash, and vomiting~~, contusion, excoriation, arthralgia, rash, catheter site pain, and upper respiratory tract infection~~.

Hypersensitivity reactions have occurred in patients treated with EXONDYS 51 *[see Warnings and Precautions (5.1)]*.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of EXONDYS 51. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Postmarketing adverse reactions that occurred during infusion include bronchospasm, cyanosis of the lips, and malaise. The following adverse reactions have also been reported in patients receiving EXONDYS 51: pyrexia, flushing, protein urine present, and dehydration.

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12 CLINICAL PHARMACOLOGY

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12.2 Pharmacodynamics

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Dystrophin levels assessed by western blot can be meaningfully influenced by differences in sample processing, analytical technique, reference materials, and quantitation methodologies.

Therefore, comparing dystrophin results from different assay protocols will require a standardized reference material and additional bridging studies.

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13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Administration of eteplirsen to male transgenic (Tg.rasH2) mice (0, 200, 500, or 960 mg/kg) weekly for 26 weeks (intravenous [IV] injection for 15 weeks, followed by subcutaneous injection for 11 weeks) and to male rats (0, 60, 180, or 600 mg/kg IV) weekly for 96 weeks resulted in no increase in neoplasms.

~~Carcinogenicity studies have not been conducted with eteplirsen.~~

העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס ע"י פניה לחברת תרומד בע"מ
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