

Aldurazyme

CONCENTRATE FOR SOLUTION FOR INFUSION

חומר פעיל:

Laronidase 500 units / 5 mL

ההתוויה המאושרת:

Aldurazyme is indicated for long-term enzyme replacement therapy in patients with a confirmed diagnosis of mucopolysaccharidosis I (MPS I alfa-I-iduronidase deficiency) to treat the non-neurological manifestations of the disease.

חברת סאנופי ישראל בע"מ מבקשת להודיע על עדכון העלון לצרכן במתכונת עלון לרופא.

העדכונים העיקריים הינם:

4.4 Special warnings and precautions for use

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Infusion-associated reactions (IARs)

IARs, defined as any related adverse event occurring during the infusion or until the end of the infusion day were reported in patients treated with Aldurazyme (see section 4.8).

~~Some of these IARs may be severe (see below).~~

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Immunogenicity

In patients with clinical decline, assessing urinary GAGs, ADA and neutralising antibodies should be considered (see section 4.8).

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4.8 Undesirable effects

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Description of selected adverse reactions

Immunogenicity

Almost all patients developed IgG antibodies to laronidase. Most patients seroconverted within 3 months of initiation of treatment; although seroconversion in patients under 5 years old with a more severe phenotype occurred mostly within 1 month (mean 26 days versus 45 days in patients 5 years and older). By the end of the Phase 3 study (or at time of early study withdrawal), 13/45 patients had no detectable antibodies by radioimmunoprecipitation (RIP) assay, including 3 patients that had never seroconverted. Patients with absent to low antibody levels showed a robust reduction in urinary GAG level, whereas patients with high antibody ~~titers~~ titres showed variable reduction in urinary GAG. **In addition, higher ADA titres** ~~The clinical significance of this finding is unknown since there~~ **also observed in MPS I Registry patients with**



severe disease. Patients with persistently high ADA titres tended to have less reduction in urinary GAG. ~~no consistent relationships between IgG antibody level and clinical efficacy endpoints.~~

In ~~addition 60 patients in~~ the Phase 2 and 3 studies, 60 patients were tested for in-vitro neutralising effects. Four patients (three in the Phase 3 study and one in the Phase 2 study) showed marginal to low level in vitro inhibition of laronidase enzymatic activity, which did not appear to impact clinical efficacy and/or urinary GAG reduction.

In patients with clinical decline, assessing urinary GAGs, ADA and neutralising antibodies should be considered.

The presence of antibodies ~~was did~~ not ~~consistently appear to be~~ related to the incidence of IARs, although the onset of IARs typically coincided with the formation of IgG antibodies. Clinical trials and observational studies show only a small number of patients have tested positive for IgE antibodies. The development of IgE antibodies may be associated with hypersensitivity or anaphylactic reactions. ~~The occurrence of IgE antibodies was not fully explored.~~

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7. MARKETING AUTHORISATION HOLDER AND IMPORTER AND ITS ADDRESS

Sanofi ~~aventis~~ Israel Ltd, ~~10 Beni Gaon, P.O.B 8090, Netanya 4250499~~ Greenwork Park, P.O box 47, Yakum.

העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס על ידי פנייה לבעל הרישום - סאנופי ישראל בע"מ, Greenwork Park, מתחם העסקים בקיבוץ יקום, בניין E (קומה 1), 6097600, יקום או בטלפון: 09-8633081.

להלן הקישור לאתר משרד הבריאות: <https://www.gov.il/he/service/israeli-drug-index>

בברכה,
חברת סאנופי ישראל בע"מ