ינואר 2024

Myozyme (Powder for Concentrate for Infusion)

חומר פעיל:

Alglucosidase alfa 50 mg/vial

ההתוויה המאושרת:

Myozyme is indicated for long-term enzyme replacement therapy (ERT) in patients with a confirmed diagnosis of pompe disease (acid alfa-glucosidase deficiency). The benefits of Myozyme in patients with late-onset Pompe disease have not been established.

חברת סאנופי 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

Approximately half of the patients treated with Myozyme in infantile-onset clinical studies and 28% of the patients treated with Myozyme in a late-onset clinical study developed infusion associated reactions (IARs). IARs are defined as any related adverse event occurring during the infusion or during the hours following infusion. Some reactions were severe (see section 4.8). A tendency was observed in infantile patients treated with a higher dose (40 mg/kg) to experience more symptoms when developing IARs. Infantile onset patients who develop high IgG antibody titres appear to be at higher risk for developing more frequent IARs. However, IARs occurred regardless of antibody titres. Patients with an acute illness (e.g. pneumonia, sepsis) at the time of Myozyme infusion appear to be at greater risk for IARs. Careful consideration should be given to the patient's clinical status prior to administration of Myozyme. Patients should be closely monitored and all cases of IARs, delayed reactions and possible immunological reactions should be reported to the marketing authorisation holder.

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Immunogenicity

The effect of IgG antibody formation on safety and efficacy has been evaluated in clinical trials and post-marketing experience. In clinical studies, the majority of patients developed IgG antibodies to alglucosidase alfa and seroconversion typically occured within 3 months of treatment. Thus~~-~~, development of IgG antibodies ~~seroconversion~~ is expected to occur in most patients treated with Myozyme. Overall, a correlation was not observed between the onset of IARs and the time of IgG antibody formation. IARs can occur across all levels of antibody titres, however a trend was observed for more frequent IARs with higher titres of IgG antibody. The clinical impact on efficacy is multifactorial, however the development of high and sustained IgG antibody titres is a contributing factor.

With regard to IOPD, a ~~A~~ tendency was observed for ~~infantile-onset~~ patients treated with a higher dose (40 mg/kg) to develop higher titres of IgG antibodies. Furthermore, Cross Reactive Immunologic Material (CRIM) status has been shown~~There does not appear~~ to be associated with immunogenicity and patients' responses to enzyme replacement therapies. Negative CRIM status, indicating no endogenous enzyme is detected, is a risk factor to develop high and sustained IgG antibody titres. This risk is higher among CRIM negative patients versus CRIM~~-a~~

~~correlation between the onset of IARs and the time of IgG antibody formation. A limited number of the IgG~~ positive patients and is a contributing factor to~~evaluated tested positive for inhibitory effects on in vitro testing. Due to the rarity of the condition and the limited experience to date, the effect of IgG antibody formation on safety and efficacy is currently not fully established. The probability of~~ a poor outcome~~ and of developing high and sustained IgG antibody titres appears higher among CRIM-negative patients (Cross Reactive Immunologic Material- negative patients in whom no endogenous GAA protein was detected by Western blot analysis) than among CRIM-positive patients in whom endogenous GAA protein was detected by Western blot analysis and/or predicted based on genotype~~. However, high and sustained IgG antibody titres has also occurred in a limited number of ~~some~~ CRIM-positive patients, generally with very low endogenous enzyme.

With respect to LOPD patients, the majority showed either stabilizing or decreasing antibody titres over time. The development of~~cause of a poor clinical outcome and of developing~~ high and sustained IgG antibody titres is infrequent in LOPD patients. Thus, the impact of IgG antibodies is more limited for LOPD patients~~thought to be multi-factorial~~.

~~-~~IgG antibody titres should be monitored based on clinical phenotype. Baseline serum sample collection prior to the first infusion is strongly encouraged. For IOPD patients, regular monitoring during first year of treatment (example: every 3 months) is suggested and subsequent monitoring depending on clinical outcomes and antibody titres level. For LOPD patients, antibody development should be assessed within 6 months and subsequent monitoring as clinically warranted based on safety and efficacy considerations~~regularly monitored~~.

Patients who experience hypersensitivity reactions may also be tested for IgE antibodies to alglucosidase alfa and other mediators of anaphylaxis. Patients who develop IgE antibodies to alglucosidase alfa appear to be at a higher risk for the occurrence of IARs when Myozyme is re-administered (see section 4.8). Therefore, these patients should be monitored more closely during administration of Myozyme. Some IgE positive patients were successfully rechallenged with Myozyme using a slower infusion rate at lower initial doses and have continued to receive Myozyme under close clinical supervision.
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5.2. Pharmacokinetic properties

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There was limited~~no~~ evidence that IgG antibodies to alglucosidase alfa affected pharmacokinetics. Higher mean clearance, lower mean AUC_{∞}, and lower mean C_{max} were observed in 5 patients who tested positive for inhibition of cellular uptake of enzyme. However, there was no apparent association between inhibition of uptake and the co-primary efficacy endpoints (see section 4.4).

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://israeldrugs.health.gov.il/#!/byDrug

בברכה,

חברת סאנופי ישראל בע"מ