אוגוסט 2024

Nexviazyme

חומר פעיל:

Avalglucosidase alpha ..... 100 mg / vial

ההתוויה המאושרת:

Nexviazyme is indicated for long-term enzyme replacement therapy (ERT) for the treatment of patients with Pompe disease (acid α-glucosidase deficiency).

חברת סאנופי מבקשת להודיע על עדכון העלון לרופא.

העדכונים העיקריים הינם:

4.8 Undesirable effects

…..

During the open-label extension period ~~until at least 145 weeks~~, serious adverse reactions were reported by 3 (5.8%) patients continuing Nexviazyme treatment throughout the study and by 3 (6.8~~2 (4.5~~%) patients who switched to Nexviazyme. The most frequently reported adverse reactions (>5%) by patients continuing Nexviazyme treatment throughout the study were nausea, chills, erythema, pruritus, and urticaria. The most frequently reported adverse reactions (>5%) by patients who switched to Nexviazyme were pruritus, rash, headache, nausea, chills, fatigue, and~~pruritus~~, urticaria~~, and rash~~.

…..

During the open-label extension period ~~until at least 145 weeks~~, IARs were reported in 12 (23.5%) patients continuing Nexviazyme treatment throughout the study; IARs reported in more than 1 patient were nausea, chills~~, pyrexia~~, erythema, pruritus, pyrexia, urticaria, rash, and ocular hyperaemia. IARs were reported in ~~21~~ 22 (~~47.7~~50%) patients who switched to Nexviazyme; IARs reported in more than 1 patient were pruritus, headache, rash, nausea, chills,~~ feeling cold~~, fatigue, urticaria, respiratory distress, feeling cold, chest discomfort, erythema,~~ pruritus, urticaria, rash~~, rash erythematous, rash pruritic, skin plaque, ~~and~~ burning sensation, lip swelling, and swollen tongue. The number of IARs in both groups decreased over time.

Immunogenicity

The incidence of ADA response to avalglucosidase alfa in Nexviazyme -treated patients with Pompe disease is shown in Table 3. The median time to seroconversion was 8.3 weeks.

In treatment-naïve adult patients, the occurrence of IARs was observed in both ADA-positive and ADA-negative patients. Increase in the incidence of IARs and hypersensitivity were observed with higher IgG ADA titres. In treatment-naïve patients, a trend for increases in the incidence of IARs was observed with increasing ADA titres, with the highest incidence of IARs (69.2%) reported in the high ADA peak titre range ≥12,800, compared with an incidence of 33.3% in

Greenwork Park, Yakum, Building E, 1st floor, 6097600, Israel
Tel.: +972-9-8633081 - Fax: +972-9-8851444 - www.sanofi.co.il

patients with intermediate ADA titre 1,600-6,400, an incidence of 14.3% in those with low ADA titre 100-800 and an incidence of 33.3% in those who were ADA negative. In enzyme replacement therapy (ERT) experienced adult patients, the occurrences of IARs and hypersensitivity were higher in patients who developed treatment emergent ADA compared to patients who were ADA negative. One (1) treatment naïve patient and ~~1~~ 2 treatment-experienced patients developed anaphylaxis. The occurrences of IARs were similar between paediatric patients with ADA positive and negative status. One treatment-experienced paediatric patient developed anaphylaxis (see section 4.4).

In clinical study EFC14028/COMET, 81 of 96 (84.4%) patients developed treatment-emergent ADA. Majority of patients developed ADA titre in the low to intermediate range, with 7 ~~2~~ patients reported High Sustained Antibody Titres (HSAT) to Nexviazyme. Evaluation of~~but this was not associated with a loss of efficacy.~~ ADA cross-reactivity at week 49 showed that~~studies showed that the majority of~~ patients generate antibodies that are cross-reactive to alglucosidase alfa and~~. At week 49, in addition to cross-reactivity, antibodies specific to~~ Nexviazyme were detected in 3 (5.9%) patients. Variable impact on~~ADA did not impact measures of~~ PK, PD, and efficacy measures ~~while limited impacts on PK and PD~~ were observed among high titre patients, however, in most patients there was no clinically significant effect of ADA on efficacy~~primarily with high titre patients~~ (see section 5.2).

…..

5.1 Pharmacodynamic properties

…..

For patients who switched from alglucosidase alfa to Nexviazyme treatment after week 49, the LS mean change in FVC % predicted from week 49 to week 145 was 0.~~7~~ 81 (1.~~1~~08) (95% CI: -1.~~4~~32, 2.~~8~~95). A stabilization in FVC % predicted was maintained after the switch to Nexviazyme in the alglucosidase alfa group with similar values to the Nexviazyme group at week 145. Patients who continued in the Nexviazyme arm maintained an improvement in FVC % predicted compared with baseline.

…..

Table 5 – LS mean change from baseline to week 49 for additional secondary endpoints

Endpoint	Nexviazyme LS mean change (SE)	Alglucosidase Alfa LS mean change (SE)	LS mean difference (95% CI)
6-minute walk test (6MWT) distance (meters)[a,b]	32.21 (9.93)	2.19 (10.40)	30.01 (1.33, 58.69)
Maximum Inspiratory Pressure (MIP) (% predicted)[c]	8.~~70~~ 71 (2.09)	4.~~29~~ 33 (2.19)	4.~~40~~ 38 (-1.~~63~~64, 10.~~44~~39)
Maximum Expiratory Pressure (% predicted)[c]	10.~~89~~ 97 (2.84)	8.~~38~~ 35 (2.~~96~~97)	2.~~51~~ 61 (-5.~~70~~61, 10.~~73~~83)

Hand-held dynamometry (HHD) summary scores	260.69 (46.07)	153.72 (48.54)	106.97 (-26.56, 240.5)
Quick Motor function Test (QMFT) total score	3.98 (0.63)	1.89 (0.69)	2.08 (0.22, 3.95)
Health-related survey on quality of life (SF-12)	PCS[d] score: 2.37 (0.99) MCS[e] score: 2.88 (1.22)	1.60 (1.07) 0.76 (1.32)	0.77 (-2.13, 3.67) 2.12 (-1.46, 5.69)

…..

5.2 Pharmacokinetic properties

…..

Immunogenicity

In the study 1, EFC14028/COMET, 95.2% (59 of 62 patients) receiving Nexviazyme developed treatment-emergent ADA. Given the variability in ADA response, no clear trend of ADA peak titre and impact on PK was evident in patients at week 49.~~No clear trend of ADA impact on PK was observed.~~

…..

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