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אפריל 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 העלונים לרופא ולצרכן.

העדכונים העיקריים הינם:

בעלון לרופא:

1. NAME OF THE MEDICINAL PRODUCT

Nexviazyme

The marketing of Nexviazyme is subject to a risk management plan (RMP) and it is marketed with a healthcare professional guide providing important safety information. Please ensure you are familiar with this material as it contains important safety information.

4.2 Posology and method of administration

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Dose modification for IOPD (infantile-onset Pompe disease) *patients*

For IOPD (infantile-onset Pompe disease) patients who experience lack of improvement or insufficient response in cardiac, respiratory, and/or motor function while receiving 20 mg/kg, a dose increase to 40 mg/kg every other week should be considered in the absence of safety concerns (e.g., severe hypersensitivity, anaphylactic reactions, or risk of fluid overload).

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Table 1 – Infusion rate schedule

~~Patient~~Recommended Dose		Infusion rate (mg/kg/hour)					Approximate duration (h)
		step 1	step 2	step 3	step 4	step 5	
~~LOPD~~20 mg/kg		1	3	5[a]	7[a]	NA	4 to 5
	4-step process	1	3	5	7	NA	7

~~IOPD~~40 mg/kg	5-step process[b]	1	3	6	8	10[b]	5

[a] For ~~LOPD~~ patients with a recommended dose of 20mg/kg and body weight of 1.25-5 kg a maximum infusion rate of 4.8 mg/kg/hour can be applied.

[b] For IOPD patients ~~with~~ who experience lack of improvement a dose increase to 40 mg/kg every other week is recommended. For a body weight of 1.25-5 kg a maximum infusion rate of 9.6 mg/kg/hour can be applied.

4.4 Special warnings and precautions for use

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Immunogenicity

Treatment emergent anti-drug antibodies (ADA) were reported in both treatment naïve (95%) and treatment-experienced patients (~~49~~62%) (see section 4.8).

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Contact your local Sanofi ~~Genzyme~~ representative or Sanofi ~~Genzyme~~ EU Medical Services for information on the Sanofi ~~Genzyme~~ Speciality Care testing services.

4.8 Undesirable effects

Summary of the safety profile

Serious adverse reactions reported in patients treated with Nexviazyme were respiratory distress and chills in 1.4% of patients and in 0.7% of patients each were headache, dyspnoea, hypoxia, tongue oedema~~respiratory distress~~, nausea, pruritis, urticaria, skin discoloration, chest discomfort, pyrexia, blood pressure increased or decreased, body temperature increased, heart rate increased, and oxygen saturation decreased. Hypersensitivity reactions were reported in 60.6~~43.5~~% of patients, anaphylaxis in 2.8~~1.4~~%, and IARs in 39.4~~26.1~~% in patients. A total of 24.9% of patients receiving Nexviazyme in clinical studies permanently discontinued treatment; 2.8% of ~~0.7%~~ patients each discontinued the treatment because of the following events considered to be related to Nexviazyme : respiratory distress, chest discomfort, dizziness, cough, nausea, flushing, ocular hyperaemia, urticaria, and erythema.

The most frequently reported adverse drug reactions (ADRs) (>5%) were pruritus (13~~9~~.4%), nausea (12~~rash (8~~%), headache (10.6%), rash (10.6~~7.2~~%), urticaria (8~~6~~.5%), chills (7.7%), fatigue (7.7~~6.5~~%~~), nausea (5.8%~~), and erythema~~chills~~ (5.~~1~~6%).

The pooled safety analysis from 4 clinical studies (EFC14028/COMET, ACT14132/mini-COMET, TDR12857/NEO, and LTS13769/NEO-EXT) included a total of 142~~138~~ patients (118 adult and 24~~20~~ paediatric patients (1 paediatric patient directly enrolled in the open-label extension period of Study 1))~~)~~ treated with Nexviazyme. ADRs reported in

patients treated with Nexviazyme in the pooled analysis of clinical studies are listed in Table 2.

Tabulated list of adverse reactions

Adverse reactions ~~(reported in at least 3 patients)~~ per System Organ Class, presented by frequency categories: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data).

Due to the small patient population, an adverse reaction reported in 2 patients is classified as common. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

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Table 2 – Adverse reactions occurring in patients treated with Nexviazyme in a pooled analysis of clinical studies (N=142~~138~~)

System organ class	Frequency	Preferred term
Infections and infestations	Uncommon	Conjunctivitis
Immune Disorders	Very common Common	Hypersensitivity Anaphylaxis
Nervous system disorders	Very ~~Common~~common Common Common Common Common Uncommon ~~Uncommon~~	Headache Dizziness Tremor Somnolence Burning sensation Paraesthesia ~~Somnolence~~
Eye Disorders	Common ~~Uncommon~~Common ~~Uncommon~~Common Common Uncommon	Ocular hyperaemia Conjunctival hyperaemia Eye pruritus Eyelid oedema Lacrimation increased
Cardiac Disorders	~~Uncommon~~Common Uncommon	Tachycardia Ventricular extrasystoles
Vascular Disorders	Common ~~Uncommon~~Common ~~Uncommon~~Common Common Common Common	Hypertension Flushing Hypotension Cyanosis Hot flush Pallor
Respiratory, thoracic, and mediastinal disorders	Common Common ~~Uncommon~~Common ~~Uncommon~~Common ~~Uncommon~~Common Uncommon Uncommon	Cough Dyspnoea Respiratory distress Throat irritation Oropharyngeal pain Tachypnoea Laryngeal oedema ~~Respiratory distress~~ ~~Throat irritation~~
Gastrointestinal disorders	Very ~~Common~~ common Common Common Common Common ~~Uncommon~~Common Common Common Uncommon Uncommon Uncommon ~~Uncommon~~	Nausea Diarrhoea Vomiting Lip swelling Swollen tongue Abdominal pain Abdominal pain upper Dyspepsia Hypoaesthesia oral Paraesthesia oral Dysphagia ~~Dyspepsia~~

System organ class	Frequency	Preferred term
Skin and subcutaneous tissue disorders	Very ~~Common~~ common	Pruritus
	~~Common~~Very common	Rash
	Common	Urticaria
	Common	Erythema
	Common	Palmer erythema
	Common	Hyperhidrosis
	Common	Rash erythematous
	Common	Rash pruritic
	Common	Skin plaque
	Uncommon	Angioedema
	~~Uncommon~~	~~Hyperhidrosis~~
	Uncommon	Skin discolouration
Musculoskeletal and connective tissue disorders	Common	Muscle spasms
	Common	Myalgia
	C~~Unc~~ommon	Pain in extremity
	Common	Flank pain
General disorders and administration site conditions	Common	Fatigue
	Common	Chills
	Common	Chest discomfort
	Common	Pain
	Common	Influenza-like illness
	Common	Infusion site pain
	Common	Pyrexia
	Common	Asthenia
	Common	Face oedema
	Common	Feeling cold
	Common	Feeling hot
	Common	Sluggishness
	Uncommon	Facial pain
	Uncommon	Hyperthermia
	Uncommon	Infusion site extravasation
	Uncommon	Infusion site joint pain
	Uncommon	Infusion site rash
	Uncommon	Infusion site reaction
	Uncommon	Infusion site urticaria
	Uncommon	Localized oedema
	Uncommon	Peripheral swelling
	~~Uncommon~~	~~Pyrexia~~
	~~Uncommon~~	~~Asthenia~~
Investigation	Common	Blood pressure increased
	Common	Oxygen saturation decreased
	~~Uncommon~~Common	Body temperature increase
	Uncommon	Heart rate increased
	Uncommon	Breath sounds abnormal
	Uncommon	Complement factor increased
	Uncommon	Immune complex level increased

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Table 2 includes treatment related adverse events that are considered biologically plausibly related to avalglucosidase alfa based on the alglucosidase alfa SmPC.

In a comparative study, EFC14028/COMET, 100 LOPD (late-onset Pompe disease) patients aged 16 to 78 naïve to enzyme replacement therapy were treated either with 20 mg/kg of Nexviazyme (n=51) or 20 mg/kg of alglucosidase alfa (n=49). During the double-blind active-controlled period of 49 weeks, serious ~~Serious~~ adverse reactions were reported in 2% of patients treated with Nexviazyme and 6.1% of those treated with alglucosidase alfa. A total of 8.2% patients receiving alglucosidase alfa in the study permanently discontinued treatment due to adverse reactions; none of the patients from the Nexviazyme group permanently discontinued the treatment. The most frequently reported ADRs (>5%) in patients treated with Nexviazyme were headache, nausea, pruritus, urticaria, and fatigue.

The 95 patients who entered open-label extension period of EFC14028/COMET consisted of 51 patients who continued treatment with Nexviazyme and 44 patients who switched from alglucosidase alfa to Nexviazyme.

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 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 headache, nausea, chills, fatigue, pruritus, urticaria, and rash.

No adverse reaction or IAR was reported by the additional paediatric patient directly enrolled in the open-label extension period.

Description of selected adverse reactions

Hypersensitivity (including anaphylaxis)
In a pooled safety analysis, 86/142 (60.6~~/138 (43.5~~%) patients experienced hypersensitivity reactions including 7/142~~6/138~~ (4.39%) patients who reported severe hypersensitivity reactions and 4/142 (~~2/138~~ (~~1.4~~2.8%) patients who experienced anaphylaxis. Some of the hypersensitivity reactions were IgE mediated. Anaphylaxis signs and symptoms included tongue oedema, hypotension, hypoxia, respiratory distress, chest pressure, generalised oedema, generalised flushing, feeling hot, cough, dizziness, dysarthria, throat tightness, dysphagia nausea, redness on palms, swollen lower lip, decreased breath sounds, redness on feet, swollen tongue, itchy palms and feet, and oxygen desaturation. Symptoms of severe hypersensitivity reactions included tongue

oedema, respiratory failure, respiratory distress, generalized oedema, erythema, urticaria, and rash.

Infusion-associated reactions (IARs)
In a pooled safety analysis, IARs were reported in approximately 56/142 (39~~42/138 (30~~.4%) of patients treated with avalglucosidase alfa in clinical studies. Severe IARs were reported in 6/142 (4~~3/138 (2~~.2%) of patients including symptoms of respiratory distress, hypoxia, chest discomfort, generalized oedema, tongue oedema, dysphagia, nausea, erythema, urticaria, and increased or decreased blood pressure. IARs reported in more than 1 patient included respiratory distress, chest discomfort, dyspnoea, ~~chills,~~ cough, oxygen saturation decreased, throat irritation, dyspepsia, nausea, vomiting, diarrhoea, lip swelling, swollen tongue, erythema, palmar erythema, rash, rash erythematous, pruritus, urticaria, hyperhidrosis, skin plaque, ocular hyperaemia, eyelid oedema, face oedema, increased or decreased blood pressure, tachycardia, ~~erythema, fatigue,~~ headache, dizziness, tremor, burning sensation, pain (including pain in extremity, abdominal pain upper, oropharyngeal pain, and flank pain), somnolence, sluggishness, fatigue, pyrexia, influenza~~-~~ like illness, chills, flushing, feeling hot or cold, cyanosis, and pallor~~nausea, ocular hyperaemia, pain in extremity, pruritus, rash, rash erythematous, tachycardia, urticaria, vomiting, chest discomfort, dizziness, hyperhidrosis, lip swelling, oxygen saturation decreased, pain, palmar erythema, swollen tongue and tremor~~. The majority of IARs were assessed as mild to moderate.

In the comparative study EFC14028/COMET study, fewer LOPD patients in the avalglucosidase alfa group reported at least 1 IAR (13/51 [25.5%]) in comparison to the alglucosidase alfa group (16/49 [32.7%]). Severe IARs were not reported in patients in the avalglucosidase alfa group and reported in 2 patients in the alglucosidase alfa group (dizziness, visual impairment, hypotension, dyspnoea, cold sweat, and chills). The most frequently reported treatment-emergent IARs ~~TEAEs~~ (>2 patients) in the avalglucosidase alfa group were pruritus (7.8%) and urticaria (5.9%) and in the alglucosidase alfa group were nausea (8.2%), pruritus (8.2%), and flushing (6.1%). The majority of IARs reported in 7 (13.7%) patients were of mild severity in the avalglucosidase alfa group and 10 ~~[~~(20.4~~%]~~ %) patients in the alglucosidase alfa group~~)~~.

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, urticaria, rash, and ocular hyperaemia. IARs were reported in 21 (47.7%) patients who switched to Nexviazyme; IARs reported in more than 1 patient were headache, nausea, chills, feeling cold, fatigue, respiratory distress, chest discomfort, erythema, pruritus, urticaria, rash, rash erythematous, skin plaque, and burning sensation. 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 (69.261.5%) reported in the high ADA peak titre range ≥12,800, compared with an incidence of 33.317.2% in patients with intermediate ADA titre 1,600-6,400, an incidence of 14.37.1% 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 treatment-experienced patient developed anaphylaxis. The occurrences of IARs were similar between paediatric patients with ADA positive and negative status. One treatment-experienced ~~There were no~~ paediatric patient ~~patients who~~ developed anaphylaxis~~anaphylactic reactions~~ (see section 4.4).

In clinical study EFC14028/COMET, 2 patients reported High Sustained Antibody Titres (HSAT) to Nexviazyme but this was not associated with a loss of efficacy. ADA cross-reactivity studies showed that the majority of patients generate antibodies that are cross-reactive to alglucosidase alfa. At week 49, in addition to cross-reactivity, antibodies specific to Nexviazyme were detected in 3 (5.9%) patients. ADA did not impact measures of efficacy while limited impacts on PK and PD were observed primarily with high titre patients (see section 5.2).

Table 3 – Treatment emergent ADA incidence in LOPD and IOPD patient population

	Nexviazyme				~~Alglucosidase alfa~~	
	Treatment-naïve patients Avalglucosidase alfa ADA[a]	**Treatment-experienced patients[b] Avalglucosidase alfa ADA**			~~In primary analysis period – Alglucosidase alfa ADA~~	
	Adults 20 mg/kg every other week	**Adults 20 mg/kg every other week**	**Paediatric 20 mg/kg every other week**	**Paediatric 40 mg/kg every other week**	~~Adults 20 mg/kg every other week~~	~~Paediatric 20 mg/kg every other week to 40 mg/kg every week~~
	(N=~~61~~62) N (%)	**(N=~~55~~58) N (%)**	**(N=6) N (%)**	**(N=~~10~~16) N (%)**	~~(N=48) N (%)~~	~~(N=6) N (%)~~
ADA at baseline	2 (3.3)	~~40~~ 43 (7~~2~~.74.1)	1 (16.7)	~~1~~ 2 (~~10~~12.5)	~~2 (4.2)~~	~~3 (50)~~
Treatment emergent ADA	~~58~~ 59 (95.~~1~~2)	~~27~~ 36 (~~49~~62.1)	1 (16.~~7~~6)	~~5~~ 9 (~~50~~56.3)	~~46 (95.8)~~	~~3 (50)~~
Neutralizing antibody						
Both NAb types	~~13~~ 14 (2~~1.1~~2.6)	~~2~~ 5 (~~3~~8.6)	0	0	~~ND[c]~~	~~ND[c]~~
Inhibition enzyme activity, only	~~4~~ 5 (~~6.6~~8.1)	~~8~~ 6 (1~~4.5~~0.3)	0	0	~~4 (8.3)~~	~~2 (33.3)~~
Inhibition of enzyme uptake, only	~~10~~ 12 (~~16~~19.4)	~~8~~ 15 (25.9~~14.5~~)	0	~~0~~2 (12.5%)	~~19 (39.6)~~	~~0~~

[a] Includes two~~one~~ paediatric patients

[b] Treatment-experienced patients received alglucosidase alfa treatment before or during the clinical study within a range of 0.9-9.9 years for adult patients and 0.6~~5~~-11.~~7~~8 years for paediatric patients.

[c] Not determined

Paediatric population

Adverse drug reactions reported from clinical studies in the paediatric population (19 paediatric patients with IOPD between 1-12 years of age (mean age of 6.8) and two~~one 16-year-old~~ paediatric patients (9 and 16 years old) ~~patient~~ with LOPD) were similar to those reported in adults.

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5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Alimentary tract and metabolism products - enzymes, ~~<not yet assigned>~~, ATC code: A16AB22. ~~<not yet assigned>~~

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Clinical efficacy and safety

Clinical studies in patients with LOPD

Study 1, EFC14028/COMET, was a multinational, multicentre, randomised, double-blinded study comparing the efficacy and safety of Nexviazyme and alglucosidase alfa in 100 treatment-naïve LOPD patients aged 16 to 78 years of age at the initiation of treatment. Patients were randomised in a 1:1 ratio based on baseline forced vital capacity (FVC), gender, age, and country to receive 20 mg/kg of Nexviazyme or alglucosidase alfa once every other week for 12 months (49 weeks). ~~The study included an open-label, long-term, follow-up phase of up to 5 years for all patients, in which patients in the alglucosidase alfa arm were switched to treatment with Nexviazyme.~~

Study 1 included an open-label extension treatment period where all patients in the alglucosidase alfa arm were switched to Nexviazyme and continued treatment up to at least week 145. Overall, 95 patients entered the open-label period (51 from the Nexviazyme arm and 44 from the alglucosidase alfa arm). An additional paediatric patient was enrolled directly into the extension treatment period with Nexviazyme.

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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 (1.1) (95% CI: -1.4, 2.8). 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.

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The key secondary endpoint of study 1 was change in total distance walked in 6 minutes (6-Minute Walk Test, 6MWT) from baseline to 12 months (week 49). At week 49, the LS mean change from baseline (SE) in 6MWT for patients treated with Nexviazyme and alglucosidase alfa was 32.21 m (9.93) and 2.19 m (10.40) respectively. The LS mean difference of 30.01 m (95% CI: 1.33,58.69) showed numerical improvement with Nexviazyme compared with alglucosidase alfa. The results for the 6MWT are detailed in Table 5. ~~Additional secondary endpoints of the study were maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), Hand-held dynamometry (HHD) summary score, quick motor function test (QMFT) total score, and SF-12 (health-related survey on quality of life, both physical and mental component scores). The results for these endpoints are detailed in Table 5.~~

For patients who switched from alglucosidase alfa to Nexviazyme treatment after week 49, the LS mean change in 6MWT (distance walked in meters) from week 49 to week 145 was -2.3 m (10.6), 95% CI: -23.2, 18.7. At Week 145, a stabilization in 6MWT was observed after the switch from the alglucosidase alfa group to Nexviazyme. The Nexviazyme arm participants sustained the improvement compared with baseline.

Additional secondary endpoints of the study were maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), Hand-held dynamometry (HHD) summary score, quick motor function test (QMFT) total score, and SF-12 (health-related survey on quality of life, both physical and mental component scores). The results for these endpoints are detailed in Table 5.

In treatment-naïve LOPD patients aged 16 to 78, who started on Nexviazyme 20 mg/kg every other week, the mean percentage (SD) change in urinary hexose tetrasaccharides from baseline to week 49 was -53.90% (24.03), which was maintained at week 145 at -53.35% (72.73) in ~~for~~ patients who continued treatment ~~treated~~ with Nexviazyme . In patients who started on~~20 mg/kg every other week and~~ alglucosidase alfa 20 mg/kg every other week , the mean percentage (SD) change in urinary hexose tetrasaccharides from baseline to week 49 was~~was -53.90% (24.03) and~~ -10.8% (32.33), further decreased to -48.04% (41.97) at week 145 after switching from alglucosidase alfa to Nexviazyme.~~respectively, in week 49.~~

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~~In the EFC14028/COMET study, efficacy data were available in 24 patients at week 97, 17 patients at week 121, and 11 patients at week 145. Additionally, 9 patients randomised to alglucosidase alfa who switched the treatment to avalglucosidase alfa after week 49 continued the treatment for up to 2 years. FVC % predicted values remained elevated over baseline throughout dosing with avalglucosidase alfa for as long as 97 weeks in 24 patients who had reached this timepoint. Efficacy data in EFC14028/COMET study at week 97 for patients who switched from alglucosidase alfa to avalglucosidase alfa at week 49 showed numerical improvement for FVC % predicted and 6MWT. In the same study, the observed mean 6MWT distance remained elevated over baseline throughout dosing with avalglucosidase alfa for as long as 145 weeks in 10 patients who had reached this timepoint.~~

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בעלון לצרכן:

4. תופעות לוואי

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תופעות לוואי נוספות

תופעות לוואי שכיחות מאוד – תופעות שמופיעות ביותר ממשתמש אחד מתוך עשרה

- רגישות יתר
- כאב ראש
- בחילות
- גרד בעור
- פריחה

תופעות לוואי שכיחות – תופעות שמופיעות בעד משתמש אחד מתוך עשרה

- תגובה אנפילקטית (תגובה אלרגית חמורה)
- סחרחורת
- ישנוניות
- רעד
- תחושת צריבה
- עיניים אדומות
- גרד בעיניים
- נפיחות של העפעפיים
- פעימות לב מהירות
- סומק
- לחץ דם מוגבר
- לחץ דם נמוך
- הכחלה של העור והשפתיים

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- ~~סחרחורת~~
- שיעול
- קושי בנשימה
- גירוי בגרון
- ~~בחילות~~
- כאב בפה ובגרון
- שלשול
- הקאות
- נפיחות בשפתיים
- נפיחות בלשון
- כאב בטן
- כאב בבטן העליונה
- קשיי עיכול
- ~~גרד בעור~~
- סרפדת
- ~~פריחה~~
- אודם בכפות הידיים
- אודם בעור
- פריחה אדמומית
- הזעת יתר
- פריחה מגרדת
- נגעים בעור
- עוויתות שרירים
- כאבי שרירים
- כאב בזרוע או ברגל
- כאב בצד אחד של הגוף או בגב התחתון (flank pain)
- תשישות
- צמרמורת
- חום
- אי נוחות בחזה
- כאב
- מחלה דמוית שפעת
- כאב באתר ההזרקה
- רמת חמצן נמוכה בדם
- חולשה
- נפיחות בפנים
- תחושת קור או חום

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- דלקת עיניים
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- עיניים דומעות
- ~~פעימות לב מהירות~~
- פעימות לב עודפות
- ~~סומק~~
- ~~לחץ דם נמוך~~
- נשימה מהירה
- נפיחות בגרון
- חוסר תחושה בפה, בלשון או בשפה
- עקצוץ בפה, בלשון או בשפה
- קושי בבליעה
- ~~גירוי בגרון~~
- ~~כאב בטן~~
- נפיחות בעור
- ~~הזעה~~
- שינוי בצבע העור
- כאב בפנים
- עלייה בחום הגוף
- דליפה לרקמה במקום העירוי
- כאב במפרק במקום העירוי
- פריחה במקום העירוי
- תגובה במקום העירוי
- גרד במקום העירוי
- בצקת מקומית
- נפיחות בזרועות וברגליים
- ~~חום~~
- קולות נשימה חריגים (צפצופים)
- ~~תחושת עייפות~~
- ~~כאב בזרוע או ברגל~~
- ~~עור חיוור~~
- הופעת סמני דלקת בבדיקת דם
- ~~חולשה~~
- ~~קשיי עיכול~~
- ירידה בתחושה למגע, לכאב ולטמפרטורה
- ~~חוסר תחושה בפה, בלשון או בשפה~~
- ~~עקצוץ בפה, בלשון או בשפה~~
- ~~קושי בבליעה~~
- ~~כאב בצד אחד של הגוף או בגב התחתון (flank pain)~~
- ~~תחושת קור~~
- אי נוחות בפה (לרבות תחושת צריבה בשפתיים)

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~~תחושת צריבה~~
~~כאב בבטן העליונה~~

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים 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

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