יולי 2024

רופא/ה נכבד/ה

רוקח/ת נכבד/ה שלום רב,

<u>פרסום עדכון בעלוני התכשיר:</u>

SAPHNELO

CONCENTRATE FOR SOLUTION FOR INFUSION

הרכב:

ANIFROLUMAB 300 MG

חברת אסטרהזניקה ישראל מבקשת להודיע על עדכון העלון לרופא והעלון לצרכן בהתאם להוראות משרד הבריאות בתאריך **יולי 2024.**

<u>התוויה:</u>

Saphnelo is indicated for the treatment of adult patients with moderate to severe systemic lupus erythematosus (SLE), who are receiving standard therapy.

Limitations of Use:

The efficacy of SAPHNELO has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. Use of SAPHNELO is not recommended in these situations.

<u>העדכונים המהותיים בעלון לרופא הינם:</u>

8.1 Clinical Trials Experience

<u>Long-term Safety</u>

<u>Patients who completed Trials 2 and 3 (Phase III feeder trials) were eligible to continue on treatment in a randomized, double-blind, placebo-controlled long-term extension (LTE) study, for an additional 3 years. The long-term safety of SAPHNELO was assessed in 257 patients who received anifrolumab 300 mg and 112 patients who received placebo in both a feeder trial and the LTE. Of these, 177 patients who received SAPHNELO (68.9%) and 52 patients who received placebo (46.4%) completed a total of 4 years on treatment. The overall long-term safety profile of SAPHNELO was consistent with Trials 1, 2 and 3.</u>

<u>Specific Adverse Reactions</u>

Infections

In the <u>52-week</u> controlled-clinical trials, infections were reported in a greater proportion of patients while on treatment with SAPHNELO compared to placebo (69.7% [320/459] versus 55.4% [258/466]), corresponding to exposure-adjusted incidence rates (EAIR) of 141.8 and 99.9 per 100 patient years (PY), respectively.

Serious Infections

In the 52-week controlled-clinical trials, the incidence of serious infections while on treatment was 4.8% (22/459) in patients treated with SAPHNELO compared with 5.6% (26/466) in patients receiving placebo, corresponding to EAIR of 5.4 and 6.6 per 100 PY, respectively. The most frequent serious infection was pneumonia.

In the 52-week controlled-clinical trials, fatal infections occurred in 0.4% of patients receiving SAPHNELO and 0.2% of the patients receiving placebo.

During the LTE study, the most common serious infections were COVID-19 and pneumonia.

Herpes Zoster

In the 52-week controlled-clinical trials, the incidence of herpes zoster in patients while on treatment with SAPHNELO was 6.1% (28/459) and 1.3% (6/466) in patients on placebo, corresponding to EAIRs of 6.9 and 1.5 per 100 PY, respectively. Cases with multidermatomal involvement and disseminated presentation have been reported. Of the 28 SAPHNELO-treated patients with herpes zoster, 2 experienced disseminated disease requiring hospitalization compared to none among patients who received placebo.

Hypersensitivity Reactions Including Anaphylaxis

During the ~~drug~~ SLE development program, there was one report of an anaphylactic reaction in a patient who received 150 mg anifrolumab, and ~~2~~ 4 reports of angioedema after 300 mg. In general, the hypersensitivity reactions were predominantly mild or moderate in intensity and did not lead to discontinuation of SAPHNELO.

In the 52-week controlled-clinical trials, hypersensitivity reactions occurred in 2.8% (13/459) of patients while on treatment with SAPHNELO and 0.6% (3/466) of patients on placebo, corresponding to EAIR of 3.2 and 0.7 per 100 PY, respectively. Serious hypersensitivity reactions were reported for 0.6% (3/459) of patients receiving SAPHNELO, including angioedema (n=2).

Infusion-related Reactions

Infusion-related reactions were mild to moderate in intensity; the most common symptoms were headache, nausea, vomiting, fatigue, and dizziness.

In the 52-week controlled-clinical trials, the incidence of infusion-related reactions while on treatment was 9.4% (43/459) in patients while on treatment with SAPHNELO and 7.1% (33/466) in patients on placebo, corresponding to EAIRs of 11.1 and 8.7 per 100 PY, respectively.

Malignancies

In 52-week controlled-clinical trials, malignancies (excluding non-melanoma skin cancers) were observed in 0.7% (3/459) and 0.6% (3/466) of patients receiving SAPHNELO and placebo, corresponding to EAIR of 0.7 and 0.7 per 100 PY, respectively. Malignant neoplasm (including non-melanoma skin cancers) was reported for 1.3% (6/459) patients receiving SAPHNELO, compared to 0.6% (3/466) patients receiving placebo (EAIR: 1.3 and 0.7 per 100 PY, respectively). The malignancies that were reported in more than one patient treated with SAPHNELO included breast cancer and squamous cell carcinoma.

~~**8.2 Immunogenicity**~~

~~As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to anifrolumab in the trials described below with the incidence of antibodies in other trials or to other products may be misleading.~~

~~In Trials 2 and 3, anti-anifrolumab antibodies were detected in 6 of 352 (1.7%) patients who received SAPHNELO at the recommended dosing regimen during the 60-week study period. The clinical relevance of the presence of anti-anifrolumab antibodies is not known.~~

8.2 Postmarketing Experience

The following adverse reaction has been identified during post-approval use of SAPHNELO. Because the 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.

Arthralgia.

12.3 Pharmacokinetics

Elimination

From population PK analysis, anifrolumab exhibited non-linear PK due to IFNAR1-mediated drug clearance.

Following the administration of anifrolumab at a dose of 300 mg via intravenous infusion every 4 weeks, the estimated systemic clearance (CL) for anifrolumab was 0.193 L/day.

Based on population PK analysis of patients who received SAPHNELO for one year, serum concentrations of anifrolumab were below detection in 95% of patients approximately 16 weeks after the last dose.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of anifrolumab.

In Trials 2, 3, and the long-term extension, treatment emergent anti-anifrolumab antibodies were detected in 9 of 350 (ADA incidence 2.6%) patients who received SAPHNELO at the recommended dosing regimen for up to 4 years.

Because of the low occurrence of anti-drug antibodies, the effect of these antibodies on the pharmacokinetics, pharmacodynamics, safety, and/or effectiveness of anifrolumab products is unknown.

עדכונים מהותיים בעלון לצרכן:

תופעות לוואי

סאפנלו עלול לגרום לתופעות לוואי חמורות הכוללות:

- **זיהומים חמורים:** סאפנלו יכול להוריד את יכולת מערכת החיסון שלך להילחם בזיהומים. אתה עלול להיות בסיכון גבוה יותר לפתח זיהומים בדרכי הנשימה ושלבקת חוגרת (הרפס זוסטר) בזמן הטיפול בסאפנלו. זיהומים (כולל קורונה [COVID-19]) עלולים להיות חמורים, להוביל לאשפוז או מוות. **יש לפנות מיד לרופא אם יש לך אחד או יותר מהתסמינים הבאים של זיהום:**
  - חום, הזעה או צמרמורות
  - כאבי שרירים
  - שיעול
  - קוצר נשימה
  - צריבה בעת מתן שתן
  - תכיפות במתן שתן
  - שלשול או כאב בטן
  - עור חמים, אדום או כואב או פצעים על הגוף

תופעות לוואי *ששכיחותן* אינה ידועה (תופעות *ששכיחותן* טרם נקבעה)

- כאב מפרקים (ארתרלגיה)

מקרא לעדכונים המסומנים:
תוספת טקסט מהותי מסומנת בצבע כחול.
מחיקת טקסט מסומנת בקו חוצה בצבע אדום.

העלונים מפורסמים במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום.

בכבוד רב,
קארין קנבל דובסון
רוקחת ממונה
אסטרהזניקה (ישראל) בע"מ

אסטרהזניקה (ישראל) בע"מ, רח' עתירי ידע 1 כפר סבא 4464301

טלפון 073-2226099 פקס 09-7406527