יולי 2019

רופא/ה נכבד/ה
רוקח/ת נכבד/ה שלום רב,

Fasenra 30 mg solution for injection : פרסום עדכון בעלון התכשיר

הרכב:

Each pre-filled syringe contains 30 mg benralizumab* in 1 ml.
*Benralizumab is a humanised monoclonal antibody produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.
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התוויה:

Fasenra is indicated as an add-on maintenance treatment in adult patients with severe eosinophilic asthma inadequately controlled despite high-dose inhaled corticosteroids plus long-acting β-agonists.

חברת אסטרהזניקה ישראל מבקשת להודיע על עדכון עלון בהתאם להוראות משרד הבריאות בתאריך **יוני 2019.**

העדכון העיקרי בעלון לרופא הוא:

4.5 Interaction with other medicinal products and other forms of interaction

In a randomized, double blind parallel group study of 103 patients aged between 12 and 21 years with severe asthma, the humoral antibody responses induced by seasonal influenza virus vaccination do not ~~No formal drug interaction studies have been conducted. An effect of benralizumab on the pharmacokinetics of co-administered medicinal products is not expected~~ appear to be affected by benralizumab treatment. An effect of benralizumab on the pharmacokinetics of co-administered medicinal products is not expected (see section 5.2).

Cytochrome P450 enzymes, efflux pumps and protein-binding mechanisms are not involved in the clearance of benralizumab. There is no evidence of IL-5Rα expression on hepatocytes. Eosinophil depletion does not produce chronic systemic alterations of proinflammatory cytokines.

4.8 Undesirable effects

Long-term safety

In a 56-week extension trial in patients with asthma from Trials 1, 2 and 3, 842 patients were treated with Fasenra at the recommended dose and remained in the trial. The overall adverse event profile was similar to the asthma trials described above.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Long-term extension trial

The long-term efficacy and safety of Fasenra was evaluated in a phase 3, 56-week extension trial BORA (Trial 4). The trial enrolled 2123 patients, 2037 adults and 86 adolescent patients (aged 12 years and older) from Trials 1, 2 and 3. Trial 4 assessed the long-term effect of Fasenra on annual exacerbation rate, lung function, ACQ-6, AQLQ(S)+12 and maintenance of OCS reduction at the 2 dosing regimens studied in the predecessor studies.

At the recommended dosing regimen, the reduction in annual rate of exacerbations observed in the placebo-controlled predecessor Trials 1 and 2 (in patients with baseline blood eosinophil counts ≥300 cells/μL who were taking high-dose ICS) was maintained over the second year of treatment (Table 6). In patients who received Fasenra in predecessor Trials 1 and 2, 73% were exacerbation-free in the extension Trial 4.

Table 6. Exacerbations over an extended treatment period

	Placebo[b] (N=338)	Fasenra (N=318)		
	Trial1&2	Trial1&2	Trial4	Trial1,2&4[c]
Rate	1.23	0.65	0.48	0.56

a. Patients that entered Trial 4 from predecessor Trials 1 and 2 with baseline blood eosinophil counts ≥300 cells/μL who were taking high-dose ICS.

b. Placebo patients in Trials 1 and 2 are included up to the end of the predecessor trial (Week 48 in

Trial 1, Week 56 in Trial 2).

c. Total duration of treatment: 104 - 112 weeks

Similar maintenance of effect was observed throughout Trial 4 in lung function, ACQ-6 and AQLQ(S)+12 (Table 7).

Table 7. Change from baseline for lung function, ACQ-6, and AQLQ(S)+12[a]

	Trial 1&2 Baseline[b]	Trial 1&2 EOT[c]	Trial 4 EOT[d]
Pre-bronchodilator FEV1 (L)			
n	318	305	290
Mean baseline (SD)	1.741 (0.621)	--	--
Change from baseline (SD)[e]	--	0.343 (0.507)	0.404 (0.555)
ACQ-6			
n	318	315	296
Mean baseline (SD)	2.74 (0.90)	--	--
Change from baseline (SD)[e]	--	-1.44 (1.13)	-1.47 (1.05)
AQLQ(S)+12			
n	307	306	287
Mean baseline	3.90 (0.99)	--	--
Change from baseline (SD)[e]	--	1.58 (1.23)	1.61 (1.21)

n= number of patients with data at timepoint. SD = standard deviation

a. Baseline blood eosinophil counts ≥300 cells/μL and taking high-dose ICS: Fasenra administered at the recommended dosage regimen.

b. Integrated analysis of Trial 1 and 2 baseline includes adults and adolescents.

c. Integrated analysis at End of Treatment (EOT) of Trial 1(Week 48) and Trial 2 (Week 56).

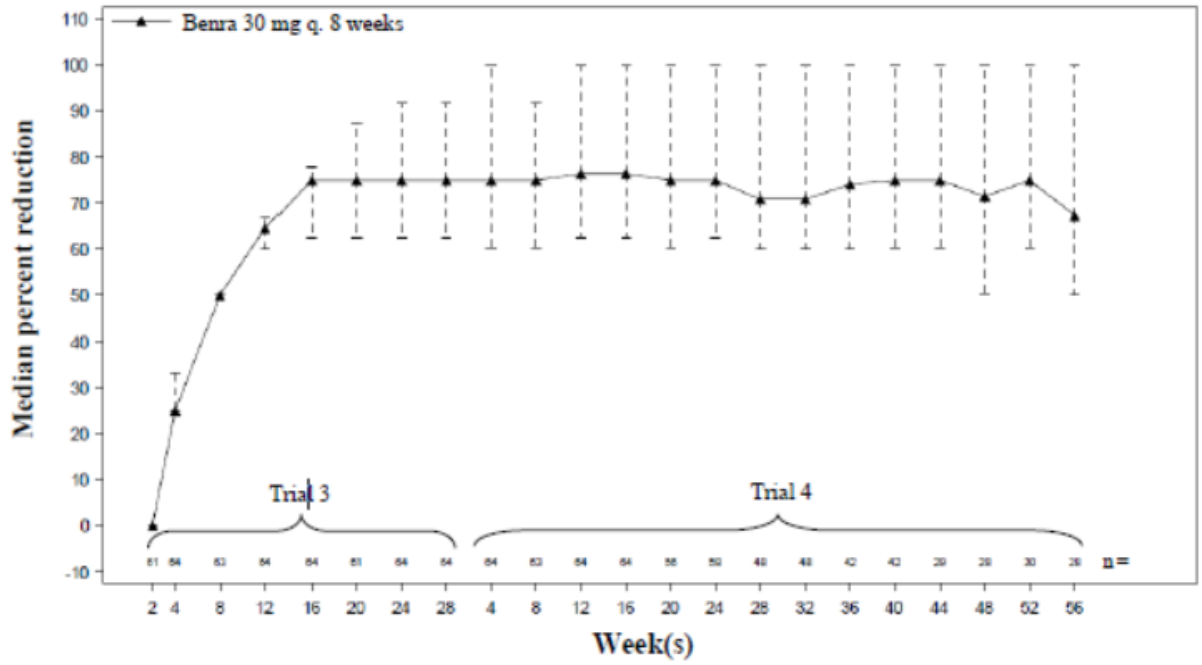
d. EOT for Trial 4 was Week 48 (the last timepoint for adults and adolescent data).

e. Baseline is prior to Fasenra treatment in Trial 1 and 2.

Efficacy in Trial 4 was also evaluated in patients with baseline blood eosinophil counts <300 cells/μl and was consistent with Trials 1 and 2.

Maintenance of the reduction in daily OCS dose was also observed over the extension trial in patients enrolled from Trial 3 (Figure 1).

Figure 1. Median percent reductions in daily OCS over time (Trial 3 and 4)[a]



a. Predecessor Trial 3 patients who continued Fasenra treatment into Trial 4. Patients were permitted to enter a second extension trial after a minimum of 8 weeks in Trial 4 without completing the 56-week extension period.

Immunogenicity

Overall, treatment-emergent anti-drug antibody response developed in 107 out of 809 (13%) patients treated with Fasenra at the recommended dosing regimen during the 48 to 56 week treatment period of the phase 3 placebo-controlled exacerbation trials. Most antibodies were neutralising and persistent. Anti-benralizumab antibodies were associated with increased clearance of benralizumab and increased blood eosinophil levels in patients with high anti-drug antibody titres compared to antibody negative patients; in rare cases, blood eosinophil levels returned to pre-treatment levels. Based on current patient follow-up, no evidence of an association of anti-drug antibodies with efficacy or safety was observed.

Following a second year of treatment of these patients from the phase 3 placebo-controlled trials, an additional 18 out of 510 (4%) had newly developed treatment-emergent antibodies. Overall, in patients who were anti-drug antibody positive in the predecessor trials, titres remained stable or declined in the second year of treatment.

No evidence of an association of anti-drug antibodies with efficacy or safety was observed.

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

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