J-C Health Care Ltd.

Kibbutz Shefayim 6099000, ISRAEL
tel +972-9-959-1111
fax +972-9-958-3636

מאי 2021

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

ברצוננו להביא לידיעתכם את העדכונים בעלון לרופא של התכשיר:

158-52-35072-00 - סטלרה 130 מ"ג/Stelara 130mg
Concentrate for solution for infusion
Ustekinumab 5mg/1ml vial

המאושר להתוויות הבאות:

Crohn's Disease
STELARA is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNFα antagonist or have medical contraindications to such therapies.

Ulcerative colitis
STELARA is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies

השינויים המהותיים בעלון לרופא מופיעים בסעיפים הבאים:

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC05.

Mechanism of action
Ustekinumab is a fully human IgG1κ monoclonal antibody that binds with specificity to the shared p40 protein subunit of human cytokines interleukin (IL)-12 and IL-23. Ustekinumab inhibits the bioactivity of human IL-12 and IL-23 by preventing p40 from binding to the IL-12Rβ1 receptor protein expressed on the surface of immune cells. Ustekinumab cannot bind to IL-12 or IL-23 that is already bound to IL-12Rβ1 cell surface receptors. Thus, ustekinumab is not likely to contribute to complement- or antibody-mediated cytotoxicity of cells with IL-12 and/or IL-23 receptors. IL-12 and IL-23 are heterodimeric cytokines secreted by activated antigen presenting cells, such as macrophages and dendritic cells, and both cytokines participate in immune functions; IL-12 stimulates natural killer (NK) cells and drives the differentiation of CD4+ T cells toward the T helper 1 (Th1) phenotype, IL-23 induces the T helper 17 (Th17) pathway. However, abnormal regulation of IL 12 and IL 23 has been associated with immune mediated diseases, such as psoriasis, psoriatic arthritis, Crohn's disease and ulcerative colitis.

By binding the shared p40 subunit of IL-12 and IL-23, ustekinumab may exert its clinical effects in psoriasis, psoriatic arthritis, Crohn's disease and ulcerative colitis through interruption of the Th1 and Th17 cytokine pathways, which are central to the pathology of these diseases.

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In patients with Crohn's disease ~~and ulcerative colitis~~, treatment with ustekinumab resulted in a decrease in inflammatory markers including C-Reactive Protein (CRP) and fecal calprotectin during the induction phase, which were then maintained throughout the maintenance phase. CRP was assessed during the study extension and the reductions observed during maintenance were generally sustained through week 252.

In patients with ulcerative colitis, treatment with ustekinumab resulted in a decrease in inflammatory markers including CRP and fecal calprotectin during the induction phase, which was maintained throughout the maintenance phase and study extension through week 92.

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Clinical efficacy

Crohn's Disease
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In IM-UNITI, patients who completed the study through week 44 were eligible to continue treatment in a study extension. Among the 718 patients who entered and were treated in the study extension, clinical remission and response were generally maintained through week ~~92~~ 252 for both patients who failed TNF-therapies and those who failed conventional therapies.

No new safety concerns were identified in this study extension with up to ~~2~~5 years of treatment in patients with Crohn's Disease.
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Health-related quality of life
Health-related quality of life was assessed by Inflammatory Bowel Disease Questionnaire (IBDQ) and SF-36 questionnaires. At week 8, patients receiving ustekinumab showed statistically significantly greater and clinically meaningful improvements on IBDQ total score and SF-36 Mental Component Summary Score in both UNITI-1 and UNITI-2, and SF-36 Physical Component Summary Score in UNITI-2, when compared to placebo. These improvements were generally better maintained in ustekinumab-treated patients in the IM-UNITI study through week 44 when compared to placebo. Improvement in health-related quality of life was generally maintained during the extension through week ~~92~~252.
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Ulcerative colitis
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Week 16 Responders to Ustekinumab Induction
Ustekinumab treated patients who were not in response at week 8 of UNIFI-I received an administration of 90 mg SC ustekinumab at week 8 (36% of patients). Of those patients, 9% of patients who were initially randomized to the recommended induction dose achieved clinical remission and 58% achieved clinical response at Week 16.

Patients who were not in clinical response to ustekinumab induction at week 8 of the UNFI-I study but were in response at week 16 (157 patients) entered into the non-randomized portion of UNIFI-M and continued to receive maintenance dosing every 8 weeks; among these patients, a majority (62%) maintained response and 30% achieved remission at week 44.

Study Extension
In UNIFI, patients who completed the study through week 44 were eligible to continue treatment in a study extension. Among the 588 patients who entered and were treated in the

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study extension, symptomatic remission was generally maintained through week 92 for patients who failed conventional therapy (but not a biologic therapy) and those who failed biologic therapy, including those who failed both anti-TNF and vedolizumab.

No new safety concerns were identified in this study extension with up to 2 years of treatment in patients with ulcerative colitis.

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Health-related quality of life
Health-related quality of life was assessed by Inflammatory Bowel Disease Questionnaire (IBDQ), SF-36 and EuroQoL-5D (EQ-5D) questionnaires.

At week 8 of UNIFI-I, patients receiving ustekinumab showed significantly greater and clinically meaningful improvements on IBDQ total score, EQ-5D and EQ-5D VAS, and SF-36 Mental Component Summary Score and SF-36 Physical Component Summary Score when compared to placebo. These improvements were maintained in ustekinumab-treated patients in UNIFI-M through week 44. Improvement in health-related quality of life as measured by IBDQ and SF-36 was generally maintained during the extension through week 92.

Patients receiving ustekinumab experienced significantly more improvements in work productivity as assessed by greater reductions in overall work impairment and in activity impairment as assessed by the WPAI-GH questionnaire than patients receiving placebo.

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העלון לרופא נשלח לפרסום במלואו למאגר התרופות שבאתר משרד הבריאות. כמו כן, ניתן לקבלו מודפס בפניה אלינו לטלפון 09-9591111 .

בברכה,
צפריר כהן
רוקח ממונה