J-C Health Care Ltd.

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אוגוסט 2022

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

ברצוננו להביא לידיעתכם את העדכונים בעלון לרופא ובעלון לצרכן של התכשיר Uptravi®
בעקבות מידע מצטבר ממחקר ה - TRITON.

Uptravi® film-coated Tablets
(Selexipag 200 microgram to 1600 microgram/Tab)

ההתוויה המאושרת בישראל:

Uptravi is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients with WHO functional class (FC) II-III, either as combination therapy in patients insufficiently controlled with an endothelin receptor antagonist (ERA) and/or a phosphodiesterase type 5 PDE-5) inhibitor, or as monotherapy in patients who are not candidates for these therapies.

Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with
connective tissue disorders, and PAH associated with corrected simple congenital heart disease.

בהודעה זו כלולים העידכונים המהותיים בלבד. להלן העידכונים:

עלון לרופא

4.8 Undesirable effects

Haemoglobin decrease
In a Phase 3 placebo-controlled study in patients with PAH, mean absolute changes in haemoglobin at regular visits compared to baseline ranged from –0.34 to –0.02 g/dL in the selexipag group compared to –0.05 to 0.25 g/dL in the placebo group. A decrease from baseline in haemoglobin concentration to below 10 g/dL was reported in 8.6% of selexipag-treated patients and 5.0% of placebo-treated patients.

In a phase 3 placebo-controlled study in patients newly diagnosed with PAH, mean absolute changes in haemoglobin at regular visits compared to baseline ranged from –1.77 to –1.26 g/dL in the triple therapy group (selexipag, macitentan, tadalafil) compared to –1.61 to –1.28 g/dL in the double therapy group (placebo, macitentan and tadalafil). A decrease from baseline in haemoglobin concentration to below 10 g/dL was reported in 19.0% of patients in the triple therapy group and 14.5% in the double therapy group. Anaemia was reported with very common frequency (13.4%) in the triple therapy group compared to common frequency (8.3%) in the double therapy group.

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Dyspepsia
In a phase 3 placebo-controlled study in patients newly diagnosed with PAH, dyspepsia was reported with very common frequency (16.8%) in patients receiving triple therapy (selexipag, macitentan, tadalafil) compared to common frequency (8.3%) in patients receiving double therapy (placebo, macitentan and tadalafil).

5.1 Pharmacodynamic properties

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Long-term data in PAH
Patients enrolled into the pivotal study (GRIPHON) were eligible to enter a long-term open-label extension study. A total of 574 patients were treated with selexipag in the GRIPHON study; of these, 330 patients continued selexipag treatment in the open-label extension study. The median follow-up duration was 4.5 years and the median exposure to selexipag was 3 years. During the follow-up, at least one other PAH medication was added to selexipag. in 28.4% of the patients. However, most of the treatment exposure (86.3%) in all of the 574 patients was accumulated without addition of any new PAH medication. Kaplan-Meier estimates of survival of these 574 patients across the GRIPHON and the long-term extension study at 1, 2, 5 and 7 years were 92%, 85%, 71%, and 63%, respectively. Survival at 1, 2, 5, and 7 years for 273 patients of WHO FC II at baseline of the pivotal study were 97%, 91%, 80 % and 70%, respectively, and for 294 patients of WHO FC III at baseline were 88%, 80%, 62% and 56%, respectively. Given that additional PAH treatment was initiated in a small proportion of patients and that there was no control group in the extension study, the survival benefit of selexipag cannot be confirmed from these data.

Initial triple combination treatment with selexipag, macitentan and tadalafil in newly diagnosed PAH patients

In a double blind, placebo-controlled study, a total of 247 newly diagnosed PAH patients were randomised to evaluate the treatment effect of initial triple (selexipag, macitentan and tadalafil) (N = 123) versus initial double (placebo, macitentan and tadalafil) (N = 124) therapy.
The primary endpoint, change from baseline in pulmonary vascular resistance (PVR) at Week 26, did not show a statistically significant difference between the groups, while showing an improvement from baseline in both treatment groups (relative reduction by 54% in the initial triple therapy group vs 52% in the initial double therapy group).
Over a median follow-up of 2 years, 4 (3.4%) patients in the triple therapy group and 12 (9.4%) patients in the double therapy group died.

עלון לצרכן

4. תופעות לוואי

עידכון תופעת לוואי ברשימת

תופעות לוואי שכיחות (תופעות שמופיעות ב- 1-10 משתמשים מתוך 100)

- כאב בטן, כולל בעיות בעיכול

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בנוסף נכללו בעלונים תיקוני הגהה וניסוח, ללא שינוי במהות הטקסט.

למידע מלא יש לעיין בעלון לרופא ובעלון לצרכן כמצ"ב.

<u>השינויים בעלונים מסומנים כלהלן:</u>
טקסט מסומן באדום - מידע מעודכן הנוסף לעלון
טקסט מסומן **בירוק** - הזזת מיקום הטקסט ללא שינוי בטקסט
טקסט עם קו ~~מחיקה~~ - טקסט שהושמט

העלון לרופא והעלון לצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://data.health.gov.il/drugs/index.html#!/byDrug

כמו כן, ניתן לקבל עותק מודפס על ידי פנייה לבעל הרישום לטלפון 09-9591111

בברכה,

רונית עקירב
רוקחת ממונה