דצמבר 2018

<u>הנדון: עדכון עלונים של התכשיר Ofev</u>

Ofev 100 mg, soft capsules (nintedanib)
Ofev 150 mg, soft capsules (nintedanib)

רופא/ה יקר/ה, רוקח/ת יקר/ה,

חברת בורינגר אינגלהיים ישראל בע"מ מבקשת להודיעכם על עדכון בעלון לרופא ובעלון לצרכן של התכשיר בנדון.

ההתוויה הרשומה לתכשיר בישראל:

OFEV is indicated for the treatment of idiopathic pulmonary fibrosis (IPF) in adults.

השינויים המשמעותיים ביותר בעלונים סומנו מטה.

העלונים המעודכנים נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות.
כמו כן, ניתן לקבלם על-ידי פנייה לבעל הרישום:
בורינגר אינגלהיים ישראל בע"מ, רח' מדינת היהודים 89 הרצליה פיתוח, ובטלפון 09-9730500.

ב ב ר כ ה,

מירי חזן
רוקחת ממונה
בורינגר אינגלהיים ישראל

עדכונים בעלון לרופא:

9.2 Postmarketing Experience

…

- drug-induced liver injury *[see Warnings and Precautions (8.2)]*, non-serious and serious bleeding events, some of which were fatal *[see Warnings and Precautions (8.6)]*,
- pancreatitis,
- thrombocytopenia, rash, pruritus.

9.1 Clinical Trials Experience

Combination with Pirfenidone
Concomitant treatment with nintedanib and pirfenidone was investigated in an exploratory open-label, randomized (1:1) trial of nintedanib 150 mg twice daily with add-on pirfenidone (titrated to 801 mg three times a day) compared to nintedanib 150 mg twice daily alone in 105 randomized patients for 12 weeks. The primary endpoint was the percentage of patients with gastrointestinal adverse events from baseline to Week 12. Gastrointestinal adverse events were in line with the established safety profile of each component and were experienced in 37 (70%) patients treated with pirfenidone added to nintedanib versus 27 (53%) patients treated with nintedanib alone.

Diarrhea, nausea, vomiting, and abdominal pain (includes upper abdominal pain, abdominal discomfort, and abdominal pain) were the most frequent adverse events reported in 20 (38%) versus 16 (31%), in 22 (42%) versus 6 (12%), in 15 (28%) versus 6 (12%) patients, and in 15 (28%) versus 7 (14%) treated with pirfenidone added to nintedanib versus nintedanib alone, respectively. More subjects reported AST or ALT elevations (≥3x the upper limit of normal) when using pirfenidone in combination with nintedanib (n=3 (6%)) compared to nintedanib alone (n=0) *[see Warnings and Precautions (8.2, 8.3)]*.

10 DRUG INTERACTIONS

…

10.3 Pirfenidone

In a multiple-dose study conducted to assess the pharmacokinetic effects of concomitant treatment with nintedanib and pirfenidone, the coadministration of nintedanib with pirfenidone did not alter the exposure of either agent *[see Clinical Pharmacology (14.3)]*. Therefore, no dose adjustment is necessary during concomitant administration of nintedanib with pirfenidone.

…

14 CLINICAL PHARMACOLOGY

…

Boehringer Ingelheim Israel LTD
Medinat Ha-Yehudim St, 89, P.O. Box 4124, Hertzliya –Pituach, Israel 4676672
Phone +9729-9730515 Fax +9729-9730549

14.3 Pharmacokinetics

…

Drug Interaction Studies

Effect of pirfenidone coadministration on nintedanib AUC and Cmax was evaluated in a multiple-dose drug-drug interaction study. Pirfenidone did not have an effect on the exposure of nintedanib. Concomitant treatment with nintedanib and pirfenidone was also investigated in a separate trial, which was an exploratory open-label, randomized (1:1) trial of nintedanib 150 mg twice daily with add-on pirfenidone (titrated to 801 mg three times a day) compared to nintedanib 150 mg twice daily alone in 105 randomized patients for 12 weeks. Similar nintedanib trough plasma concentrations were observed when comparing patients receiving nintedanib alone with patients receiving nintedanib with add-on pirfenidone.

...

עדכונים בעלון לצרכן:

4. תופעות לוואי

...

תופעות לוואי שדווחו לאחר תחילת השיווק ולא ניתן להעריך את שכיחותן:

- פגיעה בתפקוד הכבד (DILI)
- דלקת בלבלב
- מיעוט טסיות בדם (טרומבוציטופניה)
- פריחה
- גרד

...

Boehringer Ingelheim Israel LTD
Medinat Ha-Yehudim St, 89, P.O. Box 4124, Hertzliya –Pituach, Israel 4676672
Phone +9729-9730515 Fax +9729-9730549