מאי 2024

רופא/ה נכבד/ה,

רוקח/ת נכבד/ה,

הנדון:
Edurant® film-coated tablets

אדוראנט™ טבליות מצופות

חברת יאנסן ישראל (J-C Health Care Ltd.) מבקשת להודיעכם כי העלון לרופא של התכשיר בנדון התעדכנו באפריל 2024.

פרטי העדכון העיקריים מופיעים בהמשך *(טקסט שנוסף מסומן ב*אדום*, טקסט שהושמט מסומן כטקסט* ~~כחול עם קו חוצה~~*, טקסט המהווה החמרה מודגש (*ברקע צהוב*)*, אך קיימים עדכונים נוספים.

ההתוויה המאושרת לתכשיר בישראל:

EDURANT, in combination with other antiretroviral agents, is indicated for the treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-naïve adult patients with HIV-1 RNA less than or equal to 100,000 copies/mL at the start of therapy. EDURANT is not recommended for patients less than 18 years of age.

מרכיב פעיל: Rilpivirine (as hydrochloride) 25mg

העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://israeldrugs.health.gov.il/#!/byDrug.

כמו כן, מצורף לפרסום זה וניתן לקבל העתק מודפס שלו באמצעות פנייה לבעל הרישום:

ג'ויסי הלת' קר בע"מ - יאנסן ישראל , קיבוץ שפיים, 6099000, טל': 09-9591111.

בברכה,
ויקטוריה גוטליובר-הדדי
רוקחת ממונה
ג'ויסי הלת' קר בע"מ

העדכונים העיקריים בעלון לרופא הינם:

4.2 Posology and method of administration

Therapy should be initiated by a physician experienced in the management of HIV infection.

Posology

The recommended dose of EDURANT is one 25 mg tablet taken once daily. EDURANT **must be taken ~~orally~~ with a meal** [*see section 5.2 ~~Pharmacokinetic properties~~*].

Dose adjustment
For patients concomitantly receiving rifabutin, the EDURANT dose should be increased to 50 mg (two tablets of 25 mg each) taken once daily~~, taken with a meal~~. When rifabutin co-administration is stopped, the EDURANT dose should be decreased to 25 mg once daily~~, taken with a meal~~ ~~*[see section 4.5 Interaction with other medicinal products and other forms of interaction]*~~ (see section 4.5).

...

Special populations

...

Pregnancy
Lower exposures of rilpivirine were observed during pregnancy, therefore viral load should be monitored closely. Alternatively, switching to another ART regimen could be considered (see sections 4.4, 4.6, 5.1 and 5.2).

...

4.4 Special warnings and precautions for use

…

Pregnancy
Edurant should be used during pregnancy only if the potential benefit justifies the potential risk. Lower exposures of rilpivirine were observed when rilpivirine 25 mg once daily was taken during pregnancy. In the Phase III studies, lower rilpivirine exposure, similar to that seen during pregnancy, has been associated with an increased risk of virological failure, therefore viral load should be monitored closely (see sections 4.6, 5.1 and 5.2). Alternatively, switching to another ART regimen could be considered.

4.6 Fertility, pregnancy and lactation

Pregnancy

A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) indicate no malformative or feto/neonatal toxicity of rilpivirine (see sections 4.4, 5.1 and 5.2). Lower exposures of rilpivirine were observed during pregnancy, therefore viral load should be monitored closely.

Animal studies do not indicate reproductive toxicity (see section 5.3).

The use of rilpivirine may be considered during pregnancy, if necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pregnancy

Rilpivirine in combination with a background regimen was evaluated in a clinical trial of 19 pregnant women during the second and third trimesters, and postpartum.

The pharmacokinetic data demonstrate that total exposure (AUC) to rilpivirine as a part of an antiretroviral regimen was approximately 30% lower during pregnancy compared with postpartum (6-12 weeks). The virologic response was generally preserved throughout the study: of the 12 subjects that completed the study, 10 subjects were suppressed at the end of the study; in the other 2 subjects an increase in viral load was observed only postpartum, for at least 1 subject due to suspected suboptimal adherence. No mother to child transmission occurred in all 10 infants born to the mothers who completed the trial and for whom the HIV status was available. Rilpivirine was well tolerated during pregnancy and postpartum. There were no new safety findings compared with the known safety profile of rilpivirine in HIV-1 infected adults (see sections 4.2, 4.4 and 5.2).

..

5.2 Pharmacokinetic properties

Pregnancy and Postpartum

The exposure to total rilpivirine after intake of rilpivirine 25 mg once daily as part of an antiretroviral regimen was lower during pregnancy (similar for the 2nd and 3rd trimester) compared with postpartum (see table 7). The decrease in unbound (ie, active) rilpivirine pharmacokinetic parameters during pregnancy compared to postpartum was less pronounced than for total rilpivirine.

In women receiving rilpivirine 25 mg once daily during the 2nd trimester of pregnancy, mean intra-individual values for total rilpivirine C_{max}, AUC_{24h} and C_{min} values were, respectively, 21%, 29% and 35% lower as compared to postpartum; during the 3rd trimester of pregnancy, C_{max}, AUC_{24h} and C_{min} values were, respectively, 20%, 31% and 42% lower as compared to postpartum.

Table 7: Pharmacokinetic Results of Total Rilpivirine After Administration of Rilpivirine 25 mg Once Daily as Part of an Antiretroviral Regimen, During the 2nd Trimester of Pregnancy, the 3rd Trimester of Pregnancy and Postpartum

Pharmacokinetics of total rilpivirine (mean ± SD, t_{max}: median [range])	**Postpartum (6-12 Weeks) (n=11)**	**2nd Trimester of pregnancy (n=15)**	**3rd Trimester of pregnancy (n=13)**
C_{min}, ng/ml	84.0 ± 58.8	54.3 ± 25.8	52.9 ± 24.4
C_{max}, ng/ml	167 ± 101	121 ± 45.9	123 ± 47.5
t_{max}, h	4.00 (2.03-25.08)	4.00 (1.00-9.00)	4.00 (2.00-24.93)
AUC_{24h}, ng.h/ml	2714 ± 1535	1792 ± 711	1762 ± 662