יולי 2019

הנדון: אפיביר 150 מ"ג, 300 מ"ג טבליות מצופות
Epivir 150 mg, 300 mg Film Coated Tablets

רופא/ה נכבד/ה
רוקח/ת נכבד/ה,

חברת גלקסוסמיתקליין ישראל בע"מ (GSK) מבקשת להודיע על עדכון העלון לרופא של התכשיר: **Epivir tablets** עבור שני מינוניו.
העדכונים בעלונים כללו שינוי במשטר המינון של התכשיר, על כן אנו ממליצים לקרוא את העלונים בעיון.

בהודעה זו כלולים השינויים המהותיים בעלון לרופא.

מרכיבים פעילים וחוזקם:

Epivir 150mg: Lamivudine - 150 mg
Epivir 300mg: Lamivudine - 300 mg

התוויה הרשומה לתכשיר בישראל:

Epivir is indicated as part of antiretroviral combination therapy for the treatment of Human Immunodeficiency Virus (HIV) infected adults and children.

עדכונים מהותיים נעשו בסעיף הבא בעלון לרופא :

4.2 Posology and method of administration

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

Epivir may be administered with or without food.
To ensure administration of the entire dose, the tablet(s) should ideally be swallowed without crushing.

Epivir is also available as an oral solution for children over three months of age and who weigh less than 14 kg or for patients who are unable to swallow tablets (see section 4.4).
Patients changing between lamivudine oral solution and lamivudine tablets should follow the dosing recommendations that are specific for the formulation (see section 5.2)

Alternatively, for patients who are unable to swallow tablets, the tablet(s) may be crushed and added to a small amount of semi-solid food or liquid, all of which should be consumed immediately (see section 5.2).

Adults, adolescents and children (weighing at least 25 kg):

The recommended dose of Epivir is 300 mg daily. This may be administered as either 150 mg twice daily or 300 mg once daily (see section 4.4).

The 300 mg tablet is only suitable for the once a day regimen.

Children (weighing less than 25 kg):

Dosing according to weight bands is recommended for Epivir tablets.

Children weighing ≥ 20 kg to <25 kg: The recommended dose is 225 mg daily. This may be administered as either 75 mg (one-half of a 150 mg tablet) taken in the morning and 150 mg (one whole 150 mg tablet) taken in the evening, or 225 mg (one and a half 150 mg tablets) taken once daily.

Children weighing 14 to < 20 kg: The recommended dose is 150 mg daily. This may be administered as 75 mg (one-half of a 150 mg tablet) taken twice daily, or 150 mg (one whole 150 mg tablet) taken once daily.

Children from three months of age: As an accurate dosage cannot be achieved with the 300 mg non-scored tablet formulation in this patient population, it is recommended that the Epivir 150 mg scored tablet formulation is used and the corresponding recommended dosage instructions are followed.

Children less than three months of age: The limited data available are insufficient to propose specific dosage recommendations (see section 5.2).

Patients changing from the twice daily dosing regimen to the once daily dosing regimen should take the recommended once daily dose (as described above) approximately 12 hours after the last twice daily dose, and then continue to take the recommended once daily dose (as described above) approximately every 24 hours. When changing back to a twice daily regimen, patients should take the recommended twice daily dose approximately 24 hours after the last once daily dose.

Special populations:

Older people: No specific data are available; however, special care is advised in this age group due to age-associated changes such as the decrease in renal function and alteration of haematological parameters.

Renal impairment: Lamivudine concentrations are increased in patients with moderate - severe renal impairment due to decreased clearance. The dose should therefore be adjusted, using oral solution presentation of Epivir for patients whose creatinine clearance falls below 30 ml/min (see tables).

Dosing recommendations – Adults, adolescents and children (weighing at least 25 kg):

Creatinine clearance (ml/min)	**First dose**	**Maintenance dose**
≥50	300 mg or 150 mg	300 mg once daily or 150 mg twice daily
30-<50	150 mg	150 mg once daily
<30 As doses below 150 mg are needed the use of the oral solution is recommended		
15 to <30	150 mg	100 mg once daily
5 to <15	150 mg	50 mg once daily
<5	50 mg	25 mg once daily

There are no data available on the use of lamivudine in children with renal impairment. Based on the assumption that creatinine clearance and lamivudine clearance are correlated similarly in children as in adults; it is recommended that the dosage in children with renal impairment be reduced according to their creatinine clearance by the same proportion as in adults. The Epivir 10 mg/~~ml~~mL oral solution may be the most appropriate formulation to achieve the recommended ~~maintenance~~ dose in ~~paediatric patients~~children with renal impairment aged at least 3 months and weighing less than 25kg.

Dosing recommendations – Children aged at least 3 months and weighing less than 25 kg:

Creatinine clearance (ml/min)	**First dose**	**Maintenance dose**
≥50	~~8~~10 mg/kg or ~~4~~5 mg/kg	~~8mg~~10 mg/kg once daily ~~4~~or 5 mg/kg twice daily
30 to<50	~~4~~5 mg/kg	~~4~~5 mg/kg once daily
15 to <30	~~4~~5 mg/kg	~~2.6~~3.3 mg/kg once daily
5 to <15	~~4~~5 mg/kg	1.~~3~~6 mg/kg once daily
<5	1.~~3~~6 mg/kg	0.~~7~~9 mg/kg once daily

Hepatic impairment: Data obtained in patients with moderate to severe hepatic impairment shows that lamivudine pharmacokinetics are not significantly affected by hepatic dysfunction. Based on these data, no dose adjustment is necessary in patients with moderate or severe hepatic impairment unless accompanied by renal impairment.

מקרא לעדכונים המסומנים :
מידע שהוסר – מסומן בקו אדום חוצה ~~XXX~~
תוספת – כתב **כחול**
תוספת החמרה - כתב **כחול** – מסומן בצהוב מרקר

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:
https://data.health.gov.il/drugs/index.html#/byDrug וניתן לקבלו מודפס על-ידי פניה לחברת גלקסוסמיתקליין רח' בזל 25 פתח תקוה בטלפון: 03-9297100.

בברכה,
טניה רשקובן
רוקחת ממונה