ספטמבר 2024

הודעה על עדכון עלונים:

Sunlenca® film coated tablets

(lenacapavir)

רופאים ורוקחים נכבדים,

חברת גיליאד סיאנסז ישראל בע"מ מבקשת להודיעכם על עדכון בעלון לרופא של התכשיר בנדון.

ההתוויה הרשומה לתכשיר בישראל:

Sunlenca tablet, in combination with other antiretroviral(s), is indicated for the treatment of adults with multidrug resistant HIV-1 infection for whom it is otherwise not possible to construct a suppressive anti-viral regimen, for oral loading prior to administration of long-acting lenacapavir injection.

השינויים מסומנים בעלון המצורף כאשר הטקסט המודגש באדום הוסף לעלון ואילו הטקסט המחוק ~~בקו~~ ~~חוצה~~ נגרע ממנו. הסימונים בצהוב הינם החמרות במידע הבטיחותי.

העדכונים המשמעותיים ביותר מופיעים במכתב זה, קיימים עדכונים נוספים.

העלונים לרופא ולצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות:

https://israeldrugs.health.gov.il/#!/byDrug

כמו כן ,ניתן לקבלם מודפסים על ידי פנייה לבעל הרישום:

גיליאד סיאנסז ישראל בע"מ, רחוב החרש 4 ,ת.ד. 6090, פארק העסקים הוד השרון 4524075, ישראל.

התכשיר משווק ע"י סל"א.

בברכה,

מריה חורגין

רוקחת ממונה

גיליאד סיאנסז ישראל בע"מ

העדכונים המהותיים בעלון לרופא:

4.5 Interaction with other medicinal products and other forms of interaction

Effect of lenacapavir on the pharmacokinetics of other medicinal products

Lenacapavir is a moderate inhibitor of CYP3A and a P-gp inhibitor. Caution is advised if Sunlenca is co-administered with a sensitive CYP3A and/or P-gp substrate with a narrow therapeutic index. Lenacapavir is not a clinically meaningful inhibitor of ~~P-gp and~~ BCRP and does not inhibit OATP.

Table 2: Interactions between Sunlenca and other medicinal products

Medicinal product by therapeutic areas	Effects on concentrations. Mean percent change in AUC, C_{max}	Recommendation concerning co-administration with Sunlenca
CORTICOSTEROIDS (systemic)		
Dexamethasone Hydrocortisone/cortisone	Interaction not studied. Plasma concentrations of corticosteroids may be increased when co-administered with lenacapavir. Plasma concentrations of lenacapavir may decrease when co-administered with systemic dexamethasone, which may result in loss of therapeutic effect and development of resistance.	Co-administration of Sunlenca with corticosteroids whose exposures are significantly increased by CYP3A inhibitors can increase the risk for Cushing's syndrome and adrenal suppression. Initiate with the lowest starting dose and titrate carefully while monitoring for safety. Caution is warranted when systemic dexamethasone is co-administered with Sunlenca, particularly for long-term use. Alternative corticosteroids should be considered.
ANTICOAGULANTS		
Direct Oral Anticoagulants (DOACs) Rivaroxaban Dabigatran Edoxaban	Interaction not studied. Plasma concentration of DOAC may be increased when co-administered with lenacapavir.	Due to potential bleeding risk, dose adjustment of DOAC may be required. Consult the Summary of Product Characteristics of the DOAC for further information on use in combination with ~~combined~~ moderate CYP3A inhibitor and/or P-gp inhibitors.

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5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction and development.

Lenacapavir was not mutagenic or clastogenic in conventional genotoxicity assays.

Lenacapavir was not carcinogenic in a 6-month rasH2 transgenic mouse study at doses of up to 300 mg/kg/dose once every 13 weeks, which resulted in exposures approximately 60 times the exposure in humans at the recommended human dose (RHD). ~~A 2-year rat carcinogenicity study is ongoing.~~

In a 2-year rat carcinogenicity study, there were lenacapavir-treatment induced subcutaneous primary sarcomas associated with fibrosis and inflammation present at the injection sites in animals administered 927 mg/kg/dose once every 13 weeks. 11/110 animals manifested sarcomas at the high dose where each animal had up to 16 injection sites – corresponding to an incidence of <1% total injection sites across animals at the high dose. Drug concentrations in the injection depot sites are difficult to determine but systemically, the 927 mg/kg dose corresponds to 44 times the exposure in humans at the RHD. At the no-observed-adverse-effect level (NOAEL), the 309 mg/kg/dose corresponds to 25 times the exposure in humans at the RHD. Rats are prone to sarcoma formation at the subcutaneous injection site, but a clinical relevance cannot be excluded considering the long duration of the drug depot in humans. There were no neoplasms associated with systemic exposure to lenacapavir at any dose.

In offspring from rat and rabbit dams treated with lenacapavir during pregnancy, there were no toxicologically significant effects on developmental endpoints.

In rats, male and female fertility was not affected at lenacapavir exposures up to 8 times the human exposure at the ~~recommended human dose (~~RHD~~)~~. In rats and rabbits, embryofoetal development was not affected at exposures up to 21 and 172 times the human exposure, respectively, at the RHD. In rats, pre- and postnatal development was not affected at exposures up to 7 times the human exposure at the RHD.

Transfer of lenacapavir from maternal to neonatal rats was observed in a prenatal and postnatal development study, but it is not known whether the transport occurred via the placenta or the milk; therefore the potential for lenacapavir to pass into the placenta or be excreted into milk in humans is not known.