ספטמבר 2023

הודעה על עדכון העלון לרופא:

Veklury® 100 mg Powder for Concentrate for Solution for Infusion (remdesivir 100 mg/vial)

רופאים ורוקחים נכבדים,

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

נוסח ההתוויה המאושרת :

Veklury is indicated for the treatment of coronavirus disease 2019 (COVID-19) in adults and in adolescents (aged 12 to less than 18 years and weighing at least 40 kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen or other non-invasive ventilation at start of treatment).

השינויים מסומנים בעמוד הבא 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 מינוריים נוספים.

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות:

https://data.health.gov.il/drugs/index.html#/byDrug

כמו כן ,ניתן לקבלו מודפס על ידי פנייה לבעל הרישום:

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

בברכה,

הדר אוליאר

רוקחת ממונה

גיליאד סיאנסז ישראל בע"מ

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העדכונים המהותיים שבוצעו בעלון לרופא:

4.6 Fertility, pregnancy and lactation

Pregnancy

There ~~are no or~~ is a limited amount of data ~~(less than 300 pregnancy outcomes)~~ from the use of remdesivir in pregnant women (less than 300 pregnancy outcomes). Most of the exposures occurred in the second, third or an unknown trimester and available data do not indicate any risk.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity at exposures of the major metabolite of remdesivir that were around human therapeutic exposures (see section 5.3). ~~Remdesivir should not be used during pregnancy unless the clinical condition of the women requires treatment with it.~~

Due to very limited experience, remdesivir should not be used during first trimester in pregnancy unless the clinical condition of the woman requires treatment with it. Use in the second and third trimester of pregnancy may be considered.
~~Women of child-bearing potential have to use effective contraception during treatment.~~
~~treatment~~

Use of effective contraception during treatment should be considered in women of child-bearing potential.

Breast-feeding

Remdesivir and its major metabolite are excreted into breast milk in very small amounts after intravenous administration. No clinical effect on the infant is expected due to low breast milk transfer and poor oral bioavailability.

~~It is unknown whether remdesivir is excreted in human milk or the effects on the breast-fed infant, or the effects on milk production.~~

~~In animal studies, the nucleoside analog metabolite GS-441524 has been detected in the blood of nursing rat pups of mothers given remdesivir. Therefore, excretion of remdesivir and/or metabolites into the milk of lactating animals can be assumed.~~

~~Because of the potential for viral transmission to SARS-CoV-2-negative infants and adverse reactions from the drug in breast-feeding infants, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from remdesivir therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.~~

As the clinical experience is limited, a decision about breast-feeding during treatment should be made after a careful individual benefit-risk assessment.

[…]

5. PHARMACOLOGICAL PROPERTIES

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5.1 Pharmacodynamic properties

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Antiviral activity

[…]

Based on *in vitro* testing, remdesivir retained similar antiviral activity (< 2.5-fold change in EC_{50} value) against clinical isolates of SARS-CoV-2 variants ~~containing the P323L substitution in the viral polymerase~~ including Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Epsilon (B.1.429), Kappa (B.1.617.1), Lambda (C.37), Iota (B.1.526), ~~and~~ Zeta (P.2)~~-~~, and Delta (B.1.617.2) variants compared to earlier lineage SARS-CoV-2 (lineage A) isolates. Similarly, for ~~For~~ the clinical isolates of ~~the Delta (B.1.617.2) and~~ Omicron variant (including B.1.1.529, BA.1, BA.2, BA.2.12.1, BA.2.75, BA.4 ~~and~~ BA.4.6, BA.5, BF.5, BQ.1.1 and XBB) ~~variants~~, remdesivir also maintained antiviral activity (≤ 1.1 ~~< 0.7~~-fold change in EC_{50} value) relative to the lineage A SARS-CoV-2 isolate~~s~~. The antiviral activity of remdesivir against SARS-CoV-2 variants is presented in Table 4.

Table 4: Remdesivir antiviral activity against clinical isolates of SARS-CoV-2 variants

SARS-CoV-2 Lineage	~~Country First Identified~~	WHO Nomenclature	Key Substitutions	Remdesivir EC_{50} (nM)	Fold Change in Susceptibility	Change in Susceptibility
A	~~USA~~	-	-	110	1.0	
B.1.1.7	~~UK~~	Alpha	P323L	192	1.58	No change[a]
B.1.351	~~South Africa~~	Beta	P323L	141	1.19	No change[a]
P.1	~~Brazil~~	Gamma	P323L	97	0.82	No change[a]
B.1.617.2	~~India~~	Delta	P323L, G671S	70	0.59	No change[a]
B.1.429	~~USA~~	Epsilon	P323L	210	1.94	No change[a]
P.2	~~Brazil~~	Zeta	P323L	151	1.17	No change[a]
B.1.526	~~USA~~	Iota	P323L	258	2.33	No change[a]
B.1.617.1	~~India~~	Kappa	P323L	77	0.63	No change[a]
C.37	~~Peru~~	Lambda	P323L	175	1.37	No change[a]
B.1.1.529 / BA.1	~~South Africa~~	Omicron	P323L	44	0.45	No change[a]
BA.2			P323L	25	0.23	No change[a]
BA.2.12.1			P323L	33	0.20	No change[a]
BA.2.75			P323L, G671S	32	0.30	No change[a]
BA.4			P323L	25	0.15	No change[a]
BA.4.6			P323L	92	0.64	No change[a]
BA.5			P323L	106	0.66	No change[a]
BF.5			P323L	134	0.94	No change[a]
BQ.1.1			Y273H, P323L	90	1.12	No change[a]
XBB			P323L, G671S	86	1.07	No change[a]

a Fold-change: < 2.5- is not significant. All variants show no reduction in susceptibility.

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5.2 Pharmacokinetic properties

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Other special populations

[…]

Pregnancy

In CO-US-540-5961 (IMPAACT 2032) study, mean exposures (AUC_{tau}, C_{max}, and C_{tau}) of remdesivir and its metabolites (GS-441524 and GS-704277) were comparable between pregnant and non-pregnant women of child-bearing potential.

[…]

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