Nevirax®

Nirmatrelvir INN tablet & Ritonavir USP tablet

Composition

Nevirax®: Combipack of 2 strips. Each strip contains
2 Nirmatrelvir tablet: Each film coated tablet contains Nirmatrelvir INN 150 mg.
1 Ritonavir tablet: Each film coated tablet contains Ritonavir USP 100 mg.

Pharmacology

Nevirax® contains Nirmatrelvir and Ritonavir. Nirmatrelvir is a SARS-CoV-2 main protease inhibitor that has demonstrated activity against SARS-CoV-2 Mpro. Ritonavir is an HIV-1 protease inhibitor and is not active against SARS-CoV-2 Mpro. Ritonavir inhibits the CYP3A-mediated metabolism of Nirmatrelvir, thereby providing increased plasma concentrations of Nirmatrelvir.

Indication

Nevirax® is indicated for the treatment of mild to moderate coronavirus disease 2019 (COVID-19) in adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progression to severe COVID-19 including hospitalization or death.

Limitations of authorized use

- **Nevirax®** is not authorized for initiation of treatment in patients requiring hospitalization due to severe or critical COVID-19.
- **Nevirax®** is not authorized for pre-exposure or post-exposure prophylaxis for prevention of COVID-19.
- **Nevirax®** is not authorized for use longer than 5 consecutive days.

Dose and administration

Route of administration: **Nevirax®** should be taken in oral route with or without food. It should be swallowed whole and not chewed, broken or crushed.
Nevirax® treatment should be initiated as soon as possible after a diagnosis of COVID-19 has been made and within 5 days of symptom onset.

Adults and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progression to severe COVID-19 including hospitalization or death:

300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet), all three tablets taken together twice daily for 5 days. Nirmatrelvir must be co-administered with ritonavir.

Missed dose: If the patient misses a dose of **Nevirax®** within 8 hours of the time it is usually taken, the patient should take it as soon as possible and resume the normal dosing schedule. If the patient misses a dose by more than 8 hours, the patient should not take the missed dose and instead take the next dose at the regularly scheduled time. The patient should not double the dose to make up for a missed dose.

Renal Impairment

No dosage adjustment is needed in patients with mild renal impairment. In patients with moderate renal impairment (eGFR ≥30 to <60 mL/min), reduce the dose of **Nevirax®** to 150 mg nirmatrelvir and 100 mg ritonavir twice daily for 5 days. **Nevirax®** is not recommended in patients with severe renal impairment (eGFR <30 mL/min).

Hepatic Impairment

No dosage adjustment of **Nevirax®** is needed for patients with either mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment. **Nevirax®** is not recommended in patients with severe hepatic impairment (Child-Pugh Class C).

Contraindication

This combination is contraindicated in patients with a history of clinically significant hypersensitivity reactions (e.g., toxic epidermal necrolysis or Stevens-Johnson syndrome) to nirmatrelvir or ritonavir or any of its components. This combination is also contraindicated with drugs that are potent CYP3A inducers where significantly reduced nirmatrelvir or ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance.

Warning and precaution

Hepatotoxicity: Hepatic transaminase elevations, clinical hepatitis and jaundice have occurred in patients receiving ritonavir.
HIV-1 Drug Resistance: This combination use may lead to a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.

Side effects

The most common side effects are dysgeusia, diarrhea, hypertension and myalgia.

Use in pregnancy and lactation

Pregnancy: There are no available data on the use of this combination during pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

Lactation: There are no available data on the presence of nirmatrelvir in human milk, the effects on the breastfed infant or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for this combination and any potential adverse effects on the breastfed infant from this combination or from the underlying maternal condition.

Use in children and adolescents

Safety and efficacy in pediatric patients younger than 12 years of age or weighing less than 40 kg have not been established.

Drug interaction

Drug interaction with medication: Co-administration of this combination can alter the plasma concentrations of other drugs (alfuzosin, pethidine, ranolazine, amiodarone, colchicine, lurasidone, dihydroergotamine, lovastatin, sildenafil, triazolam) and other drugs may alter the plasma concentrations of it. Consider the potential for drug interactions prior to and during this combination therapy and review concomitant medications during nirmatrelvir & ritonavir therapy.

Drug interaction with food and others: Not applicable.

Overdose

Treatment of overdose with nirmatrelvir & ritonavir should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. There is no specific antidote for overdose with this combination.

Storage

Store in a cool (below 25ºC) and dry place protected from light. Keep away from the reach of children.

Packing

Nevirax®: Each combipack contains 2 strips in blister pack. Each strip contain 2 film coated tablets of Nirmatrelvir INN 150 mg & 1 film coated tablet of Ritonavir USP 100 mg.

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