PAXOVIR™

Nirmatrelvir INN Tablets and Ritonavir USP Tablets

DESCRIPTION

Paxovir™ is a combined preparation of Nirmatrelvir and Ritonavir. Nirmatrelvir is a Peptidomimetic inhibitor of the SARS-CoV-2 main protease (Mpro), also referred to as 3C-like protease (3CLpro) or nsp5 protease. Inhibition of SARS-CoV-2 Mpro renders it incapable of processing polyprotein precursors, preventing viral replication. Nirmatrelvir inhibited the activity of recombinant SARS-CoV-2 Mpro in a biochemical assay with a k_i value of 3.1 nM and an IC_{50} value of 19.2 nM. Nirmatrelvir was found to bind directly to the SARS-CoV-2 Mpro active site by X-ray crystallography. Ritonavir is an HIV-1 protease inhibitor but is not active against SARS-CoV-2 Mpro. Ritonavir inhibits the CYP3A-mediated metabolism of Nirmatrelvir, resulting in increased plasma concentrations of Nirmatrelvir.

EMERGENCY USE AUTHORIZATION

EUA of Nirmatrelvir, a SARS-CoV-2 main protease (Mpro: also referred to as 3CLpro or nsp5 protease) inhibitor, and Ritonavir, an HIV-1 protease inhibitor and CYP3A inhibitor, 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 severe acute respiratory syndrome coronavirus 2 (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

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

DOSAGE AND ADMINISTRATION

- Initiate **Paxovir™** treatment as soon as possible after diagnosis of COVID-19 and within 5 days of symptom onset.
- Administer orally with or without food.
- Dosage: 300 mg Nirmatrelvir (two 150 mg tablets) with 100 mg Ritonavir (one 100 mg tablet), with all three tablets taken together twice daily for 5 days.
- Dose reduction for moderate renal impairment (eGFR ≥30 to <60 mL/min): 150 mg Nirmatrelvir (one 150 mg tablet) with 100 mg Ritonavir (one 100 mg tablet), with both tablets taken together twice daily for 5 days.
- **Paxovir™** is not recommended in patients with severe renal impairment (eGFR <30 mL/min).
- **Paxovir™** is not recommend in patients with severe hepatic impairment (Child-Pugh Class C).

CONTRAINDICATIONS

- History of clinically significant hypersensitivity reactions to the active ingredients (Nirmatrelvir or Ritonavir) or any other components.
- Co-administration with drugs highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions.
- Co-administration with 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.

SIDE EFFECTS

- Dysgeusia
- Diarrhea
- Hypertension
- Myalgia

PRECAUTION AND WARNING

- The concomitant use of Nirmatrelvir and Ritonavir with certain other drugs may result in potentially significant drug interactions. Consult the full prescribing information prior to and during treatment for potential drug interactions.
- Hepatotoxicity: Hepatic transaminase elevations, clinical hepatitis, and jaundice have occurred in patients receiving ritonavir.
- HIV-1 Drug Resistance: Nirmatrelvir and Ritonavir use may lead to a risk of HIV-1 developing resistance to HIV protease inhibitors in individuals with uncontrolled or undiagnosed HIV-1 infection.

USE IN PREGNANCY AND LACTATION

There are no available human data on the use of Nirmatrelvir during pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Published observational studies on Ritonavir use in pregnant women have not identified an increase in the risk of major birth defects. Published studies with Ritonavir are insufficient to identify a drug-associated risk of miscarriage. There are maternal and fetal risks associated with untreated COVID-19 in pregnancy. There are no available data on the presence of Nirmatrelvir in human or animal 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 Nirmatrelvir and Ritonavir and potential adverse effects on the breastfed infant from Nirmatrelvir and Ritonavir or from the underlying maternal condition. Breastfeeding individuals with COVID-19 should follow practices according to clinical guidelines to avoid exposing the infant to COVID-19.

DRUG INTERACTION

Co-administration of Nirmatrelvir and Ritonavir can alter the plasma concentrations of other drugs and other drugs may alter the plasma concentrations of Nirmatrelvir and Ritonavir. Consider the potential for drug interactions prior to and during Nirmatrelvir and Ritonavir therapy and review concomitant medications during Nirmatrelvir and Ritonavir therapy.

PHARMACEUTICAL PRECAUTION

Store below 25 °C temperature. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Paxovir™ Tablet : Combipack box containing 2 strips of 3 tablets each. Each strip contains 2 light pink color film coated tablets of Nirmatrelvir INN 150 mg and 1 white color film coated tablet of Ritonavir USP 100 mg.

SK+F
Manufactured by
ESKAYEF PHARMACEUTICALS LTD.
TONGI, GAZIPUR, BANGLADESH
TM TRADEMARK
PM08275 V02