Revipir Tablets
(Favipiraviر) 200mg

ریویپر ٹیبلٹس ۲۰۰ ملی گرام
(فیوی پیراویر)

QUALITATIVE AND QUANTITATIVE COMPOSITION
Revipir Tablet 200mg
Each film-coated tablet contains:
Favipiravir.....200mg
Innovator's Specification

WARNING: (1) When administering REVIPIR to women of child-bearing potential, confirm a negative pregnancy test result before starting the treatment. Explain fully the risks and instruct thoroughly to use most effective contraceptive methods with her partner during and for 7 days after the end of the treatment. If pregnancy is suspected during the treatment, instruct to discontinue the treatment immediately and to consult a doctor. (2) REVIPIR is distributed in sperm. When administering the drug to male patients, explain fully the risks and instruct thoroughly to use most effective contraceptive methods in sexual intercourse during and for 7 days after the end of the treatment (men must wear a condom). In addition, instruct not to have sexual intercourse with pregnant women. (3) Prior to the treatment, explain thoroughly the efficacy and risks (including the risk of exposure to fetus) in writing to patients or their family members and obtain their written consent. 5) Examine carefully the necessity of REVIPIR before use.

DESCRIPTION: Favipiravir which is a new antiviral drug that selectively and potently inhibits the RNA-dependent RNA polymerase (RdRp) of RNA viruses. Chemically, Favipiravir is6-Fluoro-3-hydroxypyrazine-2-carboxamide. **CLINICAL PHARMACOLOGY:** ***Mechanism of Action:*** It is considered that favipiravir is metabolized in cells to a ribosyl triphosphate form (favipiravir RTP) and that favipiravir RTP selectively inhibits RNA polymerase involved in influenza viral replication. With regards to the activity against human DNA polymerases α, β and γ, favipiravir RTP (1000 μmol/L) showed no inhibitory effect on α, 9.1-13.5% inhibitory effect on β and 11.7-41.2% inhibitory effect on γ. Inhibitory concentration (IC50) of favipiravir RTP on human RNA polymerase II was 905 μmol/L. **PHARMACOKINETICS:** ***Absorption:*** The following table shows pharmacokinetic parameters of favipiravir after an oral administration in adults at 1600 mg twice daily for 1 day, then 600 mg twice daily for 4 days followed by 600 mg once daily for 1 day (1600 mg/600 mg BID).

Dosage		Cmax (μg/mL)	AUC (μg·hr/mL)	Tmax (hr)	T1/2 (hr)
1600mg/ 600mg BID	Day 1	64.56 (17.2)	446.09 (28.1)	1.5 (0.75, 4)	4.8±1.1
	Day 6	64.69 (24.1)	553.98 (31.2)	1.5 (0.75, 2)	5.6±2.3

Distribution: When favipiravir was orally administered to an adult male subjects at 1200 mg twice daily for 1 day followed by 800mg twice daily for 4 days (1200 mg/800 mg BID), the geometric mean concentration of the drug in semen was 18.341 μg/mL on Day 3, and 0.053 μg/mL on the second day after the treatment. The semen levels became below the limit of quantification (0.02 μg/mL) in all subjects in 7 days after the end of the treatment. The mean ratio of the drug concentration in semen to that in plasma was 0.53 on Day 3 and 0.45 on the second day after the treatment. ***Metabolism:*** Favipiravir was not metabolized by cytochrome P-450 (CYP), mostly metabolized by aldehyde oxidase (AO), and partly metabolized to a hydroxylated form by xanthine oxidase (XO). A glucuronate conjugate was observed in human plasma and urine as a metabolite other than the hydroxylated form. ***Excretion:*** Favipiravir was mainly excreted as a hydroxylated form into the urine, and little amount unchanged drug was observed. In an oral 7-day multiple dose study with 6 healthy adults, cumulative urinary excretion ratio of the unchanged drug and the hydroxylated form was 0.8% and 53.1%, respectively, during 48 hours after the last administration.

INDICATIONS: Revipir (Favipiravir) is indicated for treatment of novel or re-emerging pandemic influenza virus infections (limited to cases in which other influenza antiviral drugs are ineffective or not sufficiently effective).

CONTRAINDICATIONS:
Favipiravir is contraindicated in,
- Women known or suspected to be pregnant
- Patients with a history of hypersensitivity to any ingredient of the drug

SPECIAL POPULATION: ***Patients with liver function:*** When favipiravir was orally administered to subjects with mild and moderate liver function impairment (Child-Pugh classification A and B, 6 subjects each) at 1200 mg twice daily for 1 day followed by 800 mg twice daily for 4 days (1200 mg/800 mg BID) compared to healthy adult subjects, Cmax and AUC at day 5 were approximately 1.6 fold and 1.7 fold, respectively in subjects with mild liver function impairment, and 1.4 fold and 1.8 fold, respectively in subjects with moderate liver function impairment. when favipiravir was orally administered to subjects with severe liver function impairment (Child-Pugh classification C, 4 subjects) at 800 mg twice daily for 1 day followed by 400 mg twice daily for 2 days (800 mg/400 mg BID), compared to healthy adult subjects, Cmax and AUC at day 3 were approximately 2.1 fold and 6.3 fold, respectively. ***Elderly:*** Elderly often have reduced physiological functions, AVIGAN should be administered with care to them by monitoring their general conditions. ***Pregnancy:*** Do not administer favipiravir, to women known or suspected to be pregnant. ***Nursing Mothers:*** The major metabolite of favipiravir, a hydroxylated form, was found to be distributed in breast milk. when administering favipiravir to lactating women, instruct to stop lactating.

DRUG INTERACTIONS: In vitro: Favipiravir inhibited irreversibly AO in a dose and time dependent manner, and inhibited CYP2C8 in a dose dependent manner. There were no inhibitory activity to XO, and weak inhibitory activity to CYP1A2, 2C9, 2C19, 2D6, 2E1 and 3A4. The hydroxylated metabolite showed weak inhibitory activity to CYP1A2, 2C8, 2C9, 2C19, 2D6, 2E1 and 3A4. Inductive effect of favipiravir on CYP was not observed.

Revipir should be administered with care when co-administered with the following drugs

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Pyrazinamide	Blood uric acid level increases.	Reabsorption of
Repaglinide	Blood level of repaglinide may increase, and adverse reactions to repaglinide may occur.	Inhibition of CYP2C8 increases blood level of repaglinide.
Theophylline5	Blood level of AVIGAN may increase, and adverse reactions to AVIGAN may occur.	Interaction with XO may increase blood level of AVIGAN.
Famciclovir Sulindac	Efficacy of these drugs may be reduced.	Inhibition of AO by Revipir3 may decrease blood level of active forms of these drugs

WARNINGS:
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• Favipiravir is distributed in sperm. When administering the drug to male patients, explain fully the risks and instruct thoroughly to use most effective contraceptive methods in sexual intercourse during and for 7 days after the end of the treatment (men must wear a condom). In addition, instruct not to have sexual intercourse with pregnant women.
• Prior to the treatment, explain thoroughly the efficacy and risks (including the risk of exposure to fetus) in writing to patients or their family members and obtain their written consent.
• Examine carefully the necessity of REVIPIR before use.

PRECAUTIONS:
• Patients with gout or a history of gout, and patients with hyperuricaemia (Blood uric acid level may increase, and symptoms may be aggravated
• Increase of plasma level of favipiravir has been reported in patients with liver function impairment
• Psychoneurotic symptoms such as abnormal behavior after administration of anti-influenza virus agents including Favipiravir have been reported. For the
treatment of children and minors, patients/their family should be instructed that, after the start of treatment with anti-influenza virus agents, abnormal behavior may be developed, and guardians and others should make an arrangement so that children/minors are not left alone for at least 2 days when they are treated at home. Since similar symptoms associated with influenza encephalopathy have been reported, the same instruction as above should be given.
• Influenza virus infection may be complicated with bacterial infections or may be confused with influenza-like symptoms. In case of bacterial infection or suspected to be bacterial infection, appropriate measures should be taken, such as administration of anti-bacterial agents

ADVERSE REACTIONS:
The following clinically significant adverse reactions have been reported with other anti-influenza virus agents. Patients should be carefully monitored, and if any abnormality is observed, the treatment should be discontinued and appropriate measures should be taken.
• Shock, anaphylaxis
• Pneumonia
• Hepatitis fulminant, hepatic dysfunction, jaundice
• Toxic epidermal necrolysis (TEN), oculomucocutaneous syndrome (Stevens-Johnson syndrome)
• Acute kidney injury
• White blood cell count decreased, neutrophil count decreased, platelet count decreased
• Neurological and psychiatric symptoms (consciousness disturbed, abnormal behavior, deliria, hallucination, delusion, convulsion, etc.)
• Colitis haemorrhagic
DOSAGE AND ADMINISTRATION
The usual dosage of favipiravir for adults is 1600 mg orally twice daily for 1 day followed by 600 mg orally twice daily for 4 days. The total administration period should be 5 days.

INSTRUCTIONS: Dosage as directed by the physician. Store below 30°C. Protect from heat, light and moisture.

PRESENTATION: Revipir (Favipiravir) 200mg tablets available in Alu/Alu Blister of 3 X 10's, Packed in carton box with leaf insert.

ہدایات: خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
۳۰ ڈگری سینٹی گریڈ سے کم پر رکھیں، گرمی، روشنی اور نمی سے محفوظ رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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