

**FACT SHEET FOR HEALTH CARE PROVIDERS EMERGENCY USE AUTHORIZATION (EUA)  
OF FAVIPRAVIR FOR TREATMENT OF COVID-19 PATIENTS**

Badan POM, The Indonesian Food and Drug Administration, has issued an Emergency Use Authorization (EUA) to permit the emergency use of favipiravir for the management of adult patients (aged 18 years and older) with mild to moderate COVID-19, combined with standard supportive care.

**The Emergency Use Authorization of favipiravir is for the management of adult patients (aged 18 years and older) with mild to moderate COVID-19, combined with standard supportive care.**

**ADMINISTRATION:**

**Favipiravir must be administered by a healthcare professional pursuant to a valid prescription of a licensed practitioner.**

**Favipiravir must be administered orally.**

The Optimal dosing and duration of treatment is unknown.

The suggested dose under this EUA for favipiravir to treat adults patients with mild to moderate COVID-19 is in accordance with the available clinical trials and current available guideline on the procedure for the treatment of COVID-19, which is: **1600 mg orally twice daily for first day followed by 600 mg orally twice daily on subsequent days until 7 to 14 days, based on clinical consideration by prescriber. The total administration period should not be more than 14 days.** The suggested dose and duration may be updated as data from clinical trials becomes available

**Health care providers must submit a report on all medication errors and ALL SERIOUS ADVERSE EVENTS related to favipiravir, See specific reporting instructions below.**

**WARNING**

1. Since early embryonic death and teratogenicity have been observed in animal studies for favipiravir, **DO NOT** administer the drug to women known or suspected to be pregnant (See Contraindication Section).
2. When administering favipiravir 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, discontinue treatment immediately and consult to Doctor.
3. Favipiravir is distributed in sperm. When administering the drug to male patients, explain fully the risk of the drug and instructed thoroughly to use most effective contraception method in sexual intercourse during the treatment and for 7 days after treatment (men must wear a condom). In addition, instruct not to have sexual intercourse with pregnant woman.
4. Prior to the treatment, explain thoroughly the efficacy and the risk (including the risk of exposure to fetus) of favipiravir written to patient and his/her family members and informed consent should be obtained prior to the start of the treatment.
5. Examine carefully the necessity of Favipiravir before use.

For information on clinical trials that are testing the use of favipiravir in COVID-19, please see [www.clinicaltrials.go.id](http://www.clinicaltrials.go.id).

### **INSTRUCTIONS FOR ADMINISTRATION**

This section provides essential information on the use of favipiravir under this EUA for the management of adult patients (aged 18 years and older) with mild to moderate COVID-19, combined with standard supportive care.

Please refer to this fact sheet for information on use of favipiravir under the EUA.

### **COMPOSITION**

Each tablet contains favipiravir 200 mg.

### **CONTRAINDICATIONS**

- Favipiravir should not be used in a pregnant woman or women may possibly be pregnant.
- Hypersensitivity to the any of the excipients in favipiravir tablet.

### **DOSING**

The optimal dosing and duration of treatment is unknown.

#### **Favipiravir must be administrated by orally.**

The optimal dosing and duration of treatment is unknown.

The suggested dose under this EUA for favipiravir to treat adults patients with mild to moderate COVID-19 is in accordance with the available clinical trials and current available guideline on the procedure for the treatment of COVID-19, which is: **1600 mg orally twice daily for first day followed by 600 mg orally twice daily on subsequent days until 7 to 14 days, based on clinical consideration by prescriber. The total administration period should not be more than 14 days.**

The suggested dose and duration may be updated as data from clinical trials becomes available.

### **WARNINGS**

Administration of favipiravir should be careful for patients, such as:

- Woman of childbearing potential should have negative result test of pregnancy before the treatment started. If pregnancy occur during the treatment, the treatment should be stopped.
- When favipiravir is going to be used in breastfeeding women, breast-feeding must be stopped due to active metabolite of favipiravir distributed in human milk.
- Favipiravir is distributed in sperm. When the drug is going to be used in man, give thorough explanation about the risk and instructs:
  - to use most effective contraception method in sexual intercourse during the treatment and for 7 days after treatment (men must wear a condom),
  - not to have sexual intercourse with pregnant woman.
- Although causal effect correlation have not known, psychoneurotic symptoms, such as abnormal behaviors, were reported after administering favipiravir. Their families must be made aware of the following precautionary points to avoid rare accidents such as falls due to abnormal behaviour. Patients or their families should be informed to take preventive measures after favipiravir administration such as to look after for at least 2 days after patients if they are treated at home.

- Favipiravir should be given with caution in gout patients or patients who has a history of gout hyperuricemia patients since uric acid can be increased and worsening the symptoms.
- Favipiravir should be given with caution to elderly patients and monitored regularly.
- The administration favipiravir in children have not been established.
- In *in-vitro* study, favipiravir inhibited the current hERG at the C<sub>max</sub> which 3 times higher than C<sub>max</sub> in human dose, so that the risk of QT interval prolongation of favipiravir at therapeutic dose considered to be low.

## DRUG INTERACTIONS

Favipiravir is mostly metabolized by aldehyde oxidase (AO), and partly metabolized by xanthine oxidase (XO). Favipiravir is not metabolized by cytochrome P-450 (CYP).

Favipiravir inhibits AO and CYP2C8, but does not induce CYP. According the *in-vitro* studies, Favipiravir inhibited irreversibly aldehyde oxidase (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.

Favipiravir should use with caution if given concomitantly with the drug below:

Drug	Signs and symptoms	Mechanism and risk factors
Pyrazinamide	Increase uric acid in blood. At dose 1500 mg once daily and favipiravir 1200 mg/400 mg twice daily, uric acid concentration in blood reach 11.6 mg/dl when administer pyrazinamide alone, and become 13.9 mg/dl when administered in combination.	Increasing of reabsorption of uric acid in renal tubular.
Repaglinide	Blood concentration of repaglinide may increase, and adverse reaction towards repaglinide may occur.	Inhibition of CYP2C8 cause increasing of repaglinide concentration in blood.
Theophylline	Blood favipiravir concentration may increase, and adverse reaction towards favipiravir may occur.	Interaction with xantin oksidase (XO) can increase favipiravir concentration in blood.
Famciclovir, Sulindac	Efficacy of these drugs may be reduced.	Inhibition of AO by favipiravir may decrease blood level of active forms of these drugs.
Chloroquine (Substrate of CYP2C8)	Potential interaction	Clinically significance have not known.
Oseltamivir	Potential interaction	Clinically significance have not known.

## ADVERSE EFFECTS

In Japanese clinical studies and the global phase III study (studies conducted with dose levels lower than the approved dosage), adverse reactions were observed in 100 of 501 subjects (19.96%) evaluated for the safety (including abnormal laboratory test values). Major adverse reactions included increase of blood uric acid level in 24 subjects (4.79%), diarrhoea in 24 subjects (4.79%), decrease of neutrophil count in 9 subjects (1.80%), increase of AST (GOT) in 9 subjects (1,80%), increase of ALT (GPT) in 8 subjects (1,60%).

Others adverse event are shock, pneumonia, hepatitis fulminant, liver dysfunction, jaundice, toxic epidermal necrolysis (TEN), oculomucocutaneous syndrome (Stevens-Johnson syndrome), acute renal disturbance, decrease in white blood cell, neutrophil, and trombocyte, neurologic symptoms, psychiatric, duodenum bleeding.

The adverse effect were reported after administration favipiravir in lower dose than stated in Dosing section, such as:

	≥ 1 %	0,5 - < 1%	< 0,5 %
Hypersensitivity		Rash	Eczeina. pcuritus
Hepatic	AST (GOT) increased, ALT (GPT) increased, y-GTP increased		Blood ALP increased, blood bilirubin increased
Gastrointestinal	Diarrhoea (4.79%)	Nausea. vomiting. abdominal pain	Abdominal discormfort, duodenal ulcer, haematochezia, gastritis
Hematologic	Neutrophill count decreased, white blood cell count decreased		White blood cell count increased, reticulocyte count decreased, monocyte increased
Metabolic disorder	Blood uric acid increased (4,79%). Blood triglycerides increased	Glucose urine present	Blood potassium decreased
Respiratory			Asthma, oropharyngeal pain, rhinitis, nasopharyngitis
Others			Blood CK (CPK) increased, blood urine present, Tonsil polyp. pigmentation, dysgeusia, bruise, vision blurred, eye pain, vertigo, Supraventricular, Extrasystoles

### Storage Condition :

Store at room temperature (below 30 °C).

## **INSTRUCTIONS FOR HEALTH CARE PROVIDERS**

As the health care provider administering favipiravir, you should, provide your patients with the Fact Sheet titled "Emergency Use Authorization (EUA) of favipiravir **Informasi Produk untuk Pasien** (Fact Sheet for Patients and Parent/Caregivers)" and communicate the following information to the patient:

1. That the Badan POM has authorized emergency use favipiravir.
2. That the patient has the option to accept or refuse administration of favipiravir.
3. The potential consequences of refusing favipiravir.
4. The significant known and potential risks and benefits of favipiravir, as supplied under this EUA.
5. The alternative products that are available and their benefits and risks, including clinical trials.

If providing this information will delay the administration of Favipiravir to a degree that would endanger the lives of patients, the information must be provided to the patients as soon as practicable after favipiravir is administered.

If the drug is dispensed separate from the pack for inpatient use, the dispensing container should clearly identify the drug and dosage strength.

## **MANDATORY REQUIREMENTS FOR FAVIPIRAVIR ADMINISTRATION UNDER EMERGENCY USE AUTHORIZATION:**

In order to mitigate the risks of using this approved product for an unapproved use under EUA and to optimize the potential benefit of favipiravir, the following items are required. Use of favipiravir under this EUA is limited to the following (all requirements must be met):

1. Adult patients with COVID-19.
2. As the health care provider, communicate to your patient or parent/caregiver information consistent with the "**Informasi Produk untuk Pasien**" prior to the patient receiving favipiravir. Health care providers (to the extent practicable given the circumstances of the emergency) must document in the patient's medical record that the patient/caregiver has been:
  - Given the "**Informasi Produk untuk Pasien**"
  - Informed of alternatives to receiving authorized favipiravir and
  - Informed that favipiravir is authorized for the use of treatment of adult patients with COVID-19 under this Emergency Use Authorization.
3. The prescribing health care provider and/or the provider's designee are/is to provide responses to requests from Badan POM for information about adverse events and medication errors following receipt of favipiravir.
4. The prescribing health care provider and/or the provider's designee are/is responsible for reporting medication errors and adverse events (death, serious adverse events\*) occurring during favipiravir treatment within 7 calendar days from the onset of the event. The reports should include unique identifiers and the words "**Favipiravir Treatment under Emergency Use Authorization (EUA).**" in the description section of the report.
  - Submit adverse event reports to:  
Pusat Farmakovigilans/MESO Nasional

Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif

Badan Pengawas Obat dan Makanan <https://e-meso.pom.go.id/ADR>

- Submitted reports should include in the field name, "Describe Event, Problem, or Product Use/Medication Error" the statement "**Favipiravir Treatment under EUA**"

\*Serious Adverse Events are defined as:

- death;
- a life-threatening adverse event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
- a congenital anomaly/birth defect;
- a medical or surgical intervention to prevent death, a life-threatening event, hospitalization, disability, or congenital anomaly

#### **Additional Requirement for Use Under this UEA**

5. Additional requirements for reporting of patient outcomes, in addition to safety, may be required as a condition of use under this EUA.

#### **APPROVED AVAILABLE ALTERNATIVES**

There are no approved available alternative products. There is an EUA for treatment of the same population with favipiravir. The health care provider should visit <https://clinicaltrials.gov/> to determine whether enrollment of the patient(s) in a clinical trial is more appropriate than product use under this EUA.

#### **AUTHORITY FOR ISSUANCE OF THE EUA**

Indonesia Government has declared an emergency situation as a result of pandemic outbreak of COVID-19 that justifies the emergency need of using favipiravir as an treatment option in this situation. In response to that situation, the Badan POM has issued an Emergency Use Authorization (EUA) for the use of the Badan POM-approved product favipiravir for treatment of adult patients with COVID-19. As a health care provider, you must comply with the mandatory requirements of the EUA listed above.

Although limited scientific information is available, it is reasonable to believe that favipiravir may be effective for treatment of adult patients with COVID-19, as specified in this Fact Sheet. You may be contacted and asked to provide information to help with the assessment of the use of the product during this emergency. Serious adverse events related to the use of favipiravir must be reported to Badan POM through Pusat Farmakovigilans/MESO Nasional, Badan Pengawas Obat dan Makanan online <http://e-meso.pom.go.id/ADR>. Please include in the field name, "Describe Event, Problem, or Product Use/Medication Error" the following statement: **Favipiravir Treatment under Emergency Use Authorization (EUA)**.

This EUA for favipiravir will end when the Badan POM determines that the circumstances justifying the EUA no longer exist or when there is a change in the approval status of the product such that an EUA is no longer needed.

#### **PACKAGING**

Box, 10 Blisters @ 10 Film Coated Tablet

**HARUS DENGAN RESEP DOKTER  
ON MEDICAL PRESCRIPTION ONLY**

**EMERGENCY USE ONLY**

**PRODUCED BY:**

PT. Kimia Farma Tbk.,  
Banjaran, Bandung - Indonesia