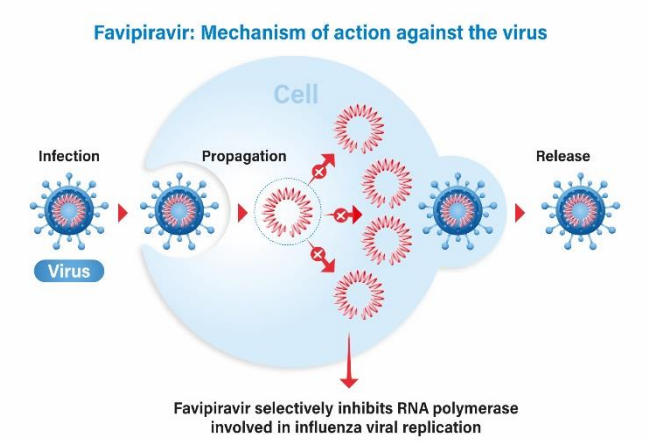
Favivent FAQ booklet

1. What is Favipiravir?

- Favipiravir is a pyrazine carboxamide derivative (6-fluoro-3-hydroxy-2-pyrazinecarboxamide).[1]
- It is a broad-spectrum antiviral agent.[1]
- It has proven efficacy against a wide range of influenza viruses, including strains resistant to existing anti-influenza drugs.[1]
- It is also found to be effective against other RNA viruses.[1]
- It is approved in some countries, including Japan and China, for novel and re-emerging strains of the Influenza virus.[2]

2. What is the mechanism of action of Favipiravir in COVID-19?

- After entering the infected cells, prodrug Favipiravir gets converted into its active form.[3,4]
- The antiviral activity disturbs the nucleotide incorporation process during viral RNA replication.[3,4]
- The dysregulation in viral RNA replication leads to increased number and frequency of transition mutations, potentially inhibiting the RdRp of RNA viruses.[3,4]



RdRp, RNA-dependent RNA polymerase

3. What is the current approval status of Favipiravir in India for COVID-19?

In India, Favipiravir has been approved for restricted emergency use for mild-to-moderate COVID-19 subject to various conditions and restrictions.[5,*]

4. In what formulation Favipiravir is available?

Available [6]

- As a tablet of 200 mg

5. What is the recommended dosage and method of administration of Favipiravir in the management of COVID-19?

	Day 1	Day 2 to max 14 days
Total daily dose [6]	1800 mg BID	800 mg BID
Morning	200 mg x 9 tabs	200 mg x 4 tabs
Evening	200 mg x 9 tabs	200 mg x 4 tabs

6. What are the possible contraindications for the use of Favipiravir?

The possible contraindications for Favipiravir are as follows[6]:

- Women known or suspected to be pregnant (early embryonic deaths and teratogenicity have been reported in animal studies)
- Lactating women
- Severe renal impairment
- Severe hepatic impairment
- Hypersensitivity to the active substance or to any of the excipients

7. What are the undesirable effects of Favipiravir?

The major undesirable effects of Favipiravir that have been observed in clinical studies include[6]:

- Increased blood uric acid level
- Diarrhea
- Decrease of neutrophil count
- Increased AST (SGOT)
- Increased ALT (SGPT)

8. What are the pharmacokinetic properties of Favipiravir?

The pharmacokinetic properties of Favipiravir are mentioned below[6]:

Absorption: Favipiravir demonstrates quick oral absorption, with $t_{1/2}$ = 2.5 to 5 hours and T_{max} = 2 hours.

Distribution: Plasma protein binding = 54%, V_d = 15-20 Liters.

Metabolism: Favipiravir is not metabolized by cytochrome P-450. It is mostly metabolized by aldehyde oxidase and partly metabolized to a hydroxylated form by xanthine oxidase.

Excretion: Favipiravir is excreted as a hydroxylated form into the urine, and a little amount of the unchanged drug was observed.

9. What are the common drug-drug interactions of Favipiravir?

- Favipiravir is not metabolized by cytochrome P-450, but it is mostly metabolized by aldehyde oxidase and partly metabolized by xanthine oxidase.[6]

- Certain medication, when co-administered with Favipiravir, can cause undesirable effects as shown in the Table below. Therefore, precaution should be taken while administrating these drugs along with Favipiravir.[6]

Medications	Unwanted effects
Pyrazinamide	Blood uric acid level rises.
Repaglinide	The blood level of repaglinide may rise, and adverse reactions to repaglinide may be seen.
Theophylline	The blood level of Favipiravir may rise, and adverse reactions to Favipiravir may be seen.
Famciclovir, Sulindac	The efficacy of these drugs may be decreased.

10. What precautions should be taken while administering Favipiravir in a special population?

Types of special population and precautions to be taken in the particular population are shown in the Table below.[6]

Type of special population	Precautions to be taken
Pregnancy, delivery, or lactation	• Avoid administering Favipiravir to women known or suspected to be pregnant. • When administering Favipiravir to lactating women, instruct to stop lactating.
Pediatric	• Favipiravir has not been administered to children.
Elderly	• Favipiravir is administered with care by monitoring their general conditions.
Liver function impairment	• An increase in the plasma level of Favipiravir has been reported.
Renal impairment	• The use of Favipiravir is not studied in this population.

11. What precautions should be taken considering the teratogenic potential of Favipiravir?

- When administering Favipiravir to women of childbearing potential, it is important to confirm a negative pregnancy test prior to initiation of therapy.[6]
- Explain the risk fully, and instruct thoroughly to use the most effective contraceptive methods for up to 7 days post completion of the treatment.[6]
- As Favipiravir is also distributed in the sperm, explain the risk fully and instruct thoroughly to use the most effective contraceptive methods (men must wear a condom) for up to 7 days post completion of the treatment.[6]
- Instruct the male patient undergoing treatment to refrain from sexual intercourse with a pregnant woman.[6]
- If pregnancy is suspected during the treatment, the treatment should be discontinued immediately and the woman should consult the doctor.[6]

12. Which other conditions necessitate precautions while administering Favipiravir?

- In patients suffering from gout or a history of gout and those with hyperuricemia, the blood uric acid level may rise and the symptoms may be aggravated with the administration of Favipiravir.[6]
- Although the causal relationship is not known, psychoneurotic symptoms, eg, abnormal behavior, after administration of anti-influenza virus agents including Favipiravir have been reported.[6]

13. What is the clinical evidence to support the use of Favipiravir in COVID-19?

Around 3–4 published studies of Favipiravir in the treatment of COVID-19 conducted in limited patients at China, Russia, and Japan support the use of Favipiravir.[6]

Japanese study[7] conducted by Doi *et al*.

- This was an observational study conducted in Japan, where Favipiravir was administered to hospitalized patients with COVID-19 in addition to other medications.
- Overall, 2,141 subjects were administered Favipiravir.
- Ninety-three percent of the patients were administered two doses of 1,800 mg on the first day, followed by 800 mg twice a day on the subsequent days.
- The rates of clinical improvement at 7 days were 73.8% and 66.6% for mild and moderate disease, respectively.
- The rates of clinical improvement at 14 days were 87.8% and 84.5% for mild and moderate disease, respectively, which were better compared with those reported on day 7.
- The outcomes suggested that the majority of patients with mild and moderate COVID-19 receiving Favipiravir recovered from the illness.

Study[8] conducted by Chen *et al*.

- This was a prospective, multicenter, open-label, randomized superiority trial conducted to compare the efficacy and safety of Favipiravir with Umifenovir in the treatment of patients with COVID-19.
- Patients with confirmed COVID-19 admitted to three hospitals were given conventional therapy + Favipiravir (n = 116) or Umifenovir (n = 120).
- The primary outcome was clinical recovery rate by day 7, whereas the duration of fever, cough relief latency, and auxiliary oxygen therapy or non-invasive mechanical ventilation rate were the secondary outcomes.
- Clinical recovery rate at day 7 was found to be significantly higher in the Favipiravir group (71.43%) compared with that in the Umifenovir group (55.86%) [$P = 0.0199$].
- For subjects with moderate COVID-19 and patients with COVID-19 having hypertension and/or diabetes, the latency to fever reduction and cough relief in the Favipiravir group was found to be considerably shorter compared with that in the Umifenovir group.
- No statistical difference was observed in auxiliary oxygen therapy or non-invasive mechanical ventilation rate (both $P > 0.05$).
- The study concluded that in patients with moderate COVID-19 (untreated with antiviral previously), Favipiravir can be considered a preferred choice of treatment, which can be

attributed to superior clinical recovery rate after 7 days and effective reduction in the incidence of fever and cough.

Abbreviations

Vd: Volume of distribution

ALT: Alanine aminotransferase

AST: Aspartate transaminase

SGOT: Serum glutamic oxaloacetic transaminase

SGPT: Serum glutamic pyruvic transaminase

*** For restricted emergency use and for the use only of medical practitioners or a hospital or a laboratory.**

Please read full prescribing information and consult your doctor for further information and clarification prior to taking any medication.

References

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