To be sold by retail only under prescription of medical specialists

Molnupiravir Capsules 200 mg

1. GENERIC NAME

Molnupiravir capsules 200 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard cellulose capsule contains:

Molnupiravir……200 mg

Excipients…… q.s.

Approved colours (Titanium Dioxide I.P., Carmoisine, Ponceau 4R, Sunset Yellow FCF) are used in capsule shell.

The excipients used are microcrystalline cellulose, hydroxy propyl cellulose, croscarmellose sodium, magnesium stearate, HPMC shell size 0 and purified water.

3. DOSAGE FORM AND STRENGTH

Oral, capsule, 200 mg

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For treatment of adult patients with COVID-19, with $Sp0_2$ >93% and who have high risk of progression of the disease including hospitalization or death.

Molnupiravir is not authorized -

i. for use in patients less than 18 years of age.
ii. for initiation of treatment in patients requiring immediate hospitalization due to COVID-19 at that stage, (however, if it was initiated before hospitalization due to COVID 19, it may be continued).
iii. for use for longer than 5 consecutive days.
iv. for pre-exposure or post-exposure prophylaxis for prevention of COVID-19.
v. for pregnant women
vi. Females of childbearing potential should use a reliable method of contraception correctly and consistently, as applicable, for the duration of treatment and for 4 days after the last dose of molnupiravir.
vii. Males of reproductive potential who are sexually active with females of child bearing potential should use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose.

4.2 Posology and method of administration

Posology

Adults

The recommended dose of Molnupiravir is 800 mg (four 200 mg capsules) taken orally every 12 hours for 5 days.

The safety and efficacy of molnupiravir when administered for periods longer than 5 days have not been established.

Molnupiravir should be administered as soon as possible after a diagnosis of COVID-19 has been made and within 5 days of symptom onset.

Missed dose

If the patient misses a dose of Molnupiravir within 10 hours of the time it is usually taken, the patient should take as soon as possible and resume the normal dosing schedule. If a patient misses a dose by more than 10 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.

Special populations

Elderly

No dose adjustment of Molnupiravir is required based on age.

Renal impairment

No dose adjustment is required for patients with renal impairment.

Hepatic impairment

No dose adjustment is required for patients with hepatic impairment.

Pediatric population

The safety and efficacy of Molnupiravir in patients below 18 years of age have not been established. No data are available.

Method of administration

For oral use.

Molnupiravir 200 mg capsules can be taken with or without food.

The capsules should be swallowed whole with a sufficient amount of fluid (e.g., a glass of water). The capsules should not be opened, crushed or chewed.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per dose of 4 capsules, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions have been identified based on the limited available data. No clinical interaction studies have been performed withmolnupiravir. Molnupiravir is hydrolysed to n-hydroxycytidine (NHC) prior to reaching systemic circulation. Uptake of NHC and metabolism to NHC-TP are mediated by the same pathways involved in endogenous pyrimidine metabolism. NHC is not a substrate of major drug metabolising enzymes or transporters. Based on in vitro studies, neither molnupiravir nor NHC are inhibitors or inducers of major drug metabolising enzymes or inhibitors of major drug transporters. Therefore, the potential for molnupiravir or NHC to interact with concomitant medications is considered unlikely.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from the use of Molnupiravir in pregnant women. Studies in animals have shown reproductive toxicity.

Molnupiravir is not recommended during pregnancy. Women of childbearing potential should use effective contraception for the duration of treatment and for 4 days after the last dose of Molnupiravir (molnupiravir).

Breast-feeding

It is unknown whether molnupiravir or any of the components of molnupiravir are present in human milk, affect human milk production, or have effect on the breastfed infant. Animal lactation studies with molnupiravir have not been conducted.

Based on the potential for adverse reactions on the infant from Molnupiravir, breast-feeding is not recommended during treatment and for 4 days after the last dose of Molnupiravir.

Fertility

There were no effects on female or male fertility in rats at NHC exposures approximately 2 and 6 times respectively, the exposure in humans at the recommended human dose (RHD).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Summary of safety profile

In an interim analysis of a Phase 3 trial of subjects with mild to moderate COVID-19 treated with molnupiravir (n=386), the most common adverse reactions (≥1% of subjects) reported during treatment and during 14 days after the last dose were diarrhoea (3%), nausea (2%), dizziness (1%) and headache (1%) all of which were Grade 1 (mild) or Grade 2 (moderate).

Tabulated list of adverse reactions

The adverse reactions are listed below by system organ class and frequency. Frequencies are defined as follows: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000).

Table 1: Tabulated list of adverse reactions

Frequency	Adverse Reaction
Nervous system disorders	
Common	dizziness, headache
Gastrointestinal disorders	
Common	diarrhoea, nausea
Uncommon	Vomiting
Skin and subcutaneous tissue disorders	
Uncommon	rash, urticaria

Phase 3 DRL-MOL-002 study

Safety profile in the interim analysis of the ongoing phase 3 clinical study titled 'A Prospective, Randomized, Multicenter, open label, Parallel Group, Phase III Trial to Evaluate Safety and Efficacy of Oral Molnupiravir as add on to Standard supportive Care for treatment of Mild Patients with COVID-19 Disease in a subset of 823 subjects was as follows:

- Molnupiravir 800 mg orally twice daily for 5 days was generally well tolerated
- Incidence of AE and drug related AE was comparable between Molnupiravir and Placebo arm
- Only one SAE (in the placebo arm) was considered drug-related by the investigator and most SAEs were COVID-19 related

Table 2: Treatment Emergent Adverse Events

Parameter, n (%)	Molnupiravir + SOC (N = 363)	SOC (N = 367)
Abdominal pain	1 (0.3%)	0
Diarrhea	1 (0.3%)	0
Gastritis	3 (0.8%)	0
Nausea	4 (1.1%)	0
Chills	0	1 (0.3%)
Fatigue	1 (0.3%)	0
Malaise	2 (0.6%)	0

Parameter, n (%)	Molnupiravir + SOC (N = 363)	SOC (N = 367)
Pyrexia	3 (0.8%)	3 (0.8%)
COVID Pneumonia	0	**1 (0.3%)**
Sinusitis	1 (0.3%)	0
Muscle Spasm	0	2 (0.6%)
Myalgia	3 (0.8%)	0
Aguesia	1 (0.3%)	0
Headache	2 (0.6%)	1 (0.3%)
Sleep deficit	1 (0.3%)	0
Nephrolithiasis	0	1 (0.3%)
Cough	1 (0.3%)	0
Erythema	0	1 (0.3%)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

There is no human experience of overdosage with Molnupiravir. Treatment of overdose with Molnupiravir should consist of general supportive measures including the monitoring of the clinical status of the patient. Haemodialysis is not expected to result in effective elimination of NHC.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antivirals for systemic use, direct acting antivirals, ATC code: not yet assigned.

Mechanism of action

Molnupiravir is a prodrug that is metabolised to the ribonucleoside analogue N-hydroxycytidine (NHC) which distributes into cells where it is phosphorylated to form the pharmacologically active ribonucleoside triphosphate (NHC-TP). NHC-TP acts by a

mechanism known as viral error catastrophe. NHC-TP incorporation into viral RNA by the viral RNA polymerase, results in an accumulation of errors in the viral genome leading to inhibition of replication.

Antiviral Activity

NHC was active in cell culture assays against SARS-CoV-2 with 50% effective concentrations (EC50) ranging between 0.67 to 2.66 µM in A-549 cells and 0.32 to 2.03 µM in Vero E6 cells. NHC had similar activity against SARS-CoV-2 variants B.1.1.7 (Alpha), B.1351 (Beta), P.1 (Gamma), and B.1.617.2 (Delta) with EC50 values of 1.59, 1.77 and 1.32 and 1.68 µM, respectively. No impact was observed on the in vitro antiviral activity of NHC against SARS-CoV-2 when NHC was tested in combination with abacavir, emtricitabine, hydroxychloroquine, lamivudine, nelfinavir, remdesivir, ribavirin, sofosbuvir, or tenofovir.

Pharmacodynamic effects

The relationship between NHC and intracellular NHC-TP with antiviral efficacy has not been evaluated clinically.

Resistance

No amino acid substitutions in SARS-CoV-2 associated with resistance to NHC have been identified in Phase 2 clinical trials evaluating molnupiravir for the treatment of COVID-19. Studies to evaluate selection of resistance to NHC with SARS-CoV-2 in cell culture have not been completed.

Clinical efficacy and safety

Clinical data are based on an interim analysis of data from 775 randomised subjects in the Phase 3 MOVe-OUT trial. MOVe-OUT was a randomised, placebo-controlled, double-blind clinical trial studying molnupiravir for the treatment of non-hospitalised patients with mild to moderate COVID-19 who were at risk for progressing to severe COVID-19 and/or hospitalisation. Eligible subjects were 18 years of age and older and had one or more pre-defined risk factors for disease progression: 60 years of age or older, diabetes, obesity (BMI >30), chronic kidney disease, serious heart conditions, chronic obstructive pulmonary disease, or active cancer. The study included symptomatic subjects not vaccinated against SARS-CoV-2 and who had laboratory confirmed SARS-CoV-2 infection and symptom onset within 5 days of enrolment. Subjects were randomised 1:1 to receive 800 mg of Molnupiravir or placebo orally twice daily for 5 days.

At baseline, in all randomised subjects, the median age was 44 years (range: 18 to 88 years); 14% of subjects were 60 years of age or older and 3% were over 75 years of age; 52% of subjects were male; 52% were White, 6% Black or African American, 2% Asian; 58% were Hispanic or Latino. Forty-nine percent of subjects received Molnupiravir or placebo within 3 days of COVID-19 symptom onset. The most common risk factors were obesity (77%), 60 years of age or older (14%), and diabetes (14%). Overall, baseline demographic and disease characteristics were well balanced between the treatment arms.

<u>Clinical outcome summary</u>

- Molnupiravir significantly reduces the risk of hospitalization or death through Day 29
- All 8 subjects who died through Day 29 were in the placebo group and were hospitalised prior to their death.Molnupiravir was associated with improved clinical outcomes based on self-reported COVID-19 signs/symptoms and WHO 11-point ordinal scale

Virological response

Molnupiravir was associated with lower mean SARS-CoV-2 RNA at Days 3 and 5 compared with placebo.

Phase 2 study results demonstrated molnupiravir reduces percentage of participants with infectious virus compared to placebo and lead to increase in viral substitution consistent with proposed mechanism of action.

Table 3 provides the results of the primary endpoint (the percentage of subjects who were hospitalised or died through Day 29 due to any cause). Treatment with Molnupiravir resulted in a 6.8 percentage point reduction in the risk of hospitalisation or death (approximately 50% relative risk reduction). All 8 subjects who died through Day 29 were in the placebo group and were hospitalised prior to their death.

Table 3: Interim Efficacy Results in Non-Hospitalised Adults with COVID-19

	Molnupiravir (N=385) n (%)	**Placebo (N=377) n (%)**	***Risk difference* (95% CI)***	***p-value***
All-cause hospitalisation or death through Day 29†	28 (7.3%)	53 (14.1%)	-6.8 (-11.3, -2.4)	0.0012
Hospitalisation	28 (7.3%)	52 (13.8%)		
Death	0 (0%)	8 (2.1%)		
Unknown‡	0 (0%)	1 (0.3%)		

* Risk difference of molnupiravir-placebo based on Miettinen and Nurminen method stratified by time of COVID-19 symptom onset (≤3 days vs. >3 [4-5] days).
† Defined as ≥24 hours of acute care in a hospital or an acute care facility (e.g., emergency room).
‡ Subjects with unknown status at Day 29 are counted as having an outcome of all-cause hospitalisation or death in the efficacy analysis.
Note: All subjects who died through Day 29 were hospitalised prior to death.

Efficacy results were consistent across sub-groups including age (>60 years), at risk medical conditions (e.g., obesity, diabetes) and SARS-CoV-2 variants.

<u>Phase 3 DRL-MOL-002 study</u>

A Prospective, Randomized, Multicenter, open label, Parallel Group, compared to standard of care Phase III Trial to Evaluate Safety and Efficacy of Oral Molnupiravir as add on to Standard supportive Care for treatment in Mild Patients with COVID-19 Disease. This study plans to enroll 1218 patients.

Interim analysis was conducted when 75% subjects (411 in test arm vs. 412 in SOC arm) were enrolled. Analysis of 800 subjects is presented-

Interim results of 800 (app 75%) subjects till day 14 indicate significantly faster clinical improvement: Faster RT-PCR negativity, Better symptomatic reduction per WHO scale, higher reduction in viral load, and reduction in inflammatory marker (CRP) e and with faster as well as higher reductions in the SARS-Cov-2 viral load, which is expected to translate into better clinical outcomes in due course of follow-up.

Primary endpoint; only 1 patient hospitalized in SOC arm

Secondary endpoints: RT-PCR Negativity-No Significant Difference was observed in High Risk Population except for D5 where 83.5% vs 77.8% subjects showed improvement with Molnupiravir

Time to Clinical Improvement-Statistically significant difference at Day 5 and 10 was observed in both 1 point improvement and 2 point improvement on WHO cardinal scale in Molnupiravir arm.

Time to achieve at least one-point improvement in 11-Point ordinal scale by WHO			**Time to achieve at least two-point improvement in 11-Point ordinal scale by WHO**	
Parameter	**Molnupiravir 800 mg +SOC (N=406)**	**SOC (N=405)**	**Molnupiravir 800 mg +SOC (N=406)**	**SOC (N=405)**
N	401	398	383	383
N1	5	7	23	22
Median time [1]	5	5	6	9
95% CI for Median	(NE:NE)	(5:6)	(5:6)	(NE:NE)
Q1:Q3	5:9	5:10	5:10	5:13
p-value [2]	<.0001		<.0001	

- Molnupiravir addition to SOC significantly reduces the viral load at D5 and D10 in overall population. In high risk group it shows numerical improvement
- Relief of Specific Symptoms(fever, cough, loss of smell and loss of taste-Overall)-India study shows improvements in line with Merck Study
- Molnupiravir Leads to Greater Reduction in the CRP values in Patients with High Baseline CRP

Pediatric population

This medicine is not recommended for children and adolescents under 18 years due to the lack of data in these patients.

5.2 Pharmacokinetic properties

Molnupiravir is a 5´-isobutyrate prodrug that is hydrolysed to NHC prior to reaching systemic circulation. The pharmacokinetics of NHC are similar in healthy subjects and patients with COVID-19.

The pharmacokinetics of NHC at steady-state following administration of 800 mg molnupiravir every 12 hours are provided below in Table 4.

Table 4: Pharmacokinetics of NHC after administration of 800mg Molnupiravir every 12 hours

NHC Geometric Mean (%CV)		
$AUC_{0\text{-}12hr}$ (ng×hr/mL)*	C_{max} (ng/mL) †	C_{12hr} (ng/mL)*
8260 (41.0)	2970 (16.8)	31.1 (124)
%CV: Geometric coefficient of variation. * Values were obtained from population PK analysis. †Values were obtained from a Phase 1 study of healthy subjects.		

Absorption

Following twice daily oral administration of 800 mg molnupiravir, the median time to peak plasma NHC concentrations (Tmax) was 1.5 hours.

Effect of Food on Oral Absorption

In healthy subjects, the administration of a single 200 mg dose of molnupiravir with a high-fat meal resulted in a 35% reduction in NHC peak concentrations (Cmax), AUC was not significantly affected.

Distribution

NHC does not bind to plasma proteins.

Elimination

The effective half-life of NHC is approximately 3.3 hours. The fraction of dose excreted as NHC in the urine was ≤3% in healthy participants.

Other special populations

Gender, Race, Age

Population pharmacokinetic analysis showed that age, gender, race and ethnicity do not meaningfully influence the pharmacokinetics of NHC.

Pediatric Patients

Molnupiravir has not been studied in pediatric patients.

Renal Impairment

Renal clearance is not a meaningful route of elimination for NHC. No dose adjustment in patients with any degree of renal impairment is needed. In a population PK analysis, mild or moderate renal impairment did not have a meaningful impact on the pharmacokinetics of NHC. The pharmacokinetics of molnupiravir and NHC has not been evaluated in patients with eGFR less than 30 mL/min or on dialysis.

Hepatic Impairment

The pharmacokinetics of molnupiravir and NHC has not been evaluated in patients with hepatic impairment. Preclinical data indicate that hepatic elimination is not expected to be a major route of NHC elimination therefore hepatic impairment is unlikely to affect NHC exposure. No dose adjustment in patients with hepatic impairment is needed.

6. NON-CLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology

Reversible, dose-related bone marrow toxicity affecting all haematopoietic cell lines was observed in dogs at ≥17 mg/kg/day (0.4 times the human NHC exposure at the recommended human dose (RHD)). Mild decreases in peripheral blood cell and platelet counts were seen after 7 days of molnupiravir treatment progressing to more severe haematological changes after 14 days of treatment. Neither bone marrow nor haematological toxicity was observed in a 1-month toxicity study in mice up to 2,000 mg/kg/day (19 times the human NHC exposure at the RHD) and a 3-month toxicity study

in rats up to 1,000 mg/kg/day (9.3 and 15 times the human NHC exposure at the RHD in females and males, respectively).

Bone and cartilage toxicity, consisting of an increase in the thickness of physeal and epiphyseal growth cartilage with decreases in trabecular bone was observed in the femur and tibia of rapidly growing rats in a 3-month toxicity study at ≥ 500 mg/kg/day (5.4 times the human NHC exposure at the RHD). There was no bone or cartilage toxicity in a 1-month toxicity study in rapidly growing rats up to 500 mg/kg/day (4.2 and 7.8 times the human NHC exposure at the RHD in females and males, respectively), in dogs dosed for 14 days up to 50 mg/kg/day (1.6 times the human NHC exposure at the RHD), or in a 1-month toxicity study in mice up to 2,000 mg/kg/day (19 times the human NHC exposure at the RHD). Growth cartilage is not present in mature skeletons; therefore the bone and cartilage findings are not relevant for adult humans. The clinical significance of these findings for pediatric patients is unknown.

Carcinogenesis

Carcinogenicity studies with molnupiravir have not been conducted.

Mutagenesis

Molnupiravir and NHC were positive in the in vitro bacterial reverse mutation assay (Ames assay) with and without metabolic activation. In 2 distinct in vivo rodent mutagenicity models (Pig-a mutagenicity assay and Big Blue® (cII Locus) transgenic rodent assay) molnupiravir did not induce increased mutation rates relative to untreated historical control animals, and therefore is not mutagenic in vivo. Molnupiravir was negative for induction of chromosomal damage in in vitro micronucleus (with and without metabolic activation) and in vivo rat micronucleus assays. Based on the totality of the genotoxicity data, molnupiravir is of low risk for genotoxicity or mutagenicity in clinical use.

Impairment of Fertility

There were no effects on fertility, mating performance or early embryonic development when molnupiravir was administered to female or male rats at NHC exposures approximately 2 and 6 times, respectively, the human NHC exposure at the recommended human dose (RHD).

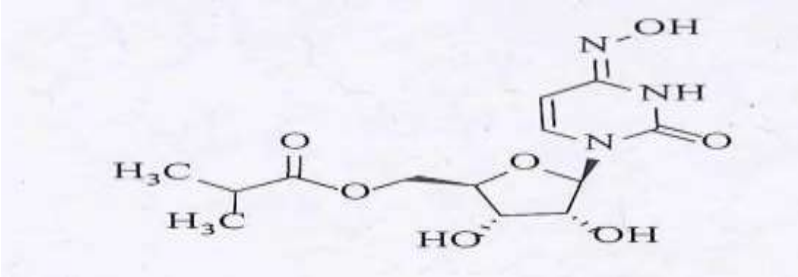
Development

In an embryofoetal development (EFD) study in rats, molnupiravir was administered orally to pregnant rats at 0, 100, 250, or 500 mg/kg/day from gestation days (GDs) 6 to 17. Molnupiravir was also administered orally to pregnant rats at up to 1,000 mg/kg/day from GDs 6 to 17 in a preliminary EFD study. Developmental toxicities included post-implantation losses, malformations of the eye, kidney, and axial skeleton, and rib variations at 1,000 mg/kg/day (8 times the human NHC exposure at the RHD) and decreased foetal body weights and delayed ossification at ≥500 mg/kg/day (2.9 times the human NHC exposure at the RHD). There were no developmental toxicities at ≤250 mg/kg/day (0.8 times the human NHC exposure at the RHD). Maternal toxicities included decreased food consumption and body weight losses, resulting in the early sacrifice of individual animals at 1,000 mg/kg/day, and decreased body weight gain at 500 mg/kg/day.

In an EFD study in rabbits, molnupiravir was administered orally to pregnant rabbits at 0, 125, 400, or 750 mg/kg/day from GDs 7 to 19. Developmental toxicity was limited to reduced foetal body weights at 750 mg/kg/day (18 times the human NHC exposures at the RHD). There was no developmental toxicity at ≤400 mg/kg/day (7 times the human NHC

exposures at the RHD). Maternal toxicities included reduced food consumption and body weight gains, and abnormal faecal output at 750 mg/kg/day.

7. DESCRIPTION



Molecular Formula: $C_{13}H_{19}N_3O_7$

Molecular Weight: 329.31 g/mol

Chemical name: ((2R,3S,4R,5R)-3,4-dihydroxy-5-(4-(hydroxyimino)-2-oxo-3,4-dihydropyrimidin-1(2H)-yl) tetrahydrofuran-2-yl) methyl isobutyrate / Uridine, 4-oxime, 5 ' -(2-methylpropanoate) / (2R,3 S,4 R,SR)-3 ,4-dihydroxy-5-((Z)-4-(hydroxyimino)-2-oxo-3 ,4-dihydropyrimidin-1 (2H)yl) tetrahydrofuran-2-yl) methyl isobutyrate**.**

A white to off white powder.

Molnupiravir capsules 200 mg

Red coloured cap and red coloured body (size '0'), opaque, hard vegetarian capsule contains a white to off-white powder.

The excipients used are microcrystalline cellulose, hydroxy propyl cellulose, croscarmellose sodium, magnesium stearate, HPMC shell size 0 and purified water.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

Not applicable

8.2 Shelf Life

09 month

Do not use later than date of expiry.

8.3 Packaging Information

Molnupiravir capsules 200 mg is available in blister strips of 10 capsules.

8.4 Storage and handling instructions

Store below 30°C. Keep out of reach of children.

9. PATIENT COUNSELLING INFORMATION

This medicine is intended for adult patients only

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or health care provider
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms of illness are the same as yours.
- If you get any side effects, talk to your doctor or health care provider. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?

9.1. What Molnupiravir is and what it is used for

Molnupiravir is an investigational oral antiviral agent and is used for treatment of adult patients with COVID-19, with $Sp0_2$ >93% and who have high risk of progression of the disease including hospitalization or death.

9.2. What you need to know before you use Molnupiravir

Do not take Molnupiravir:

- If you are allergic to Molnupiravir or any of the ingredients.
- If you are less than 18 years of age.
- If you are requiring immediate hospitalization due to COVID-19 at that stage for initiation of treatment, (however, if it was initiated before hospitalization due to COVID 19, it may be continued).
- For longer than 5 consecutive days.
- For pre-exposure or post-exposure prophylaxis for prevention of COVID-19.
- If you are pregnant women
- Females of childbearing potential should use a reliable method of contraception correctly and consistently, as applicable, for the duration of treatment and for 4 days after the last dose of molnupiravir.
- Males of reproductive potential who are sexually active with females of child bearing potential should use a reliable method of contraception correctly and consistently during treatment and for at least 3 months after the last dose.

Before taking Molnupiravir, tell your healthcare provider about all of your medical conditions, including if you:

- If you are pregnant,
- Tell your healthcare provider if you become pregnant or think you are pregnant during treatment with Molnupiravir.
- Are breastfeeding or plan to breastfeed. It is not known if Molnupiravir passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby during treatment with Molnupiravir.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Molnupiravir and other medicines may affect each other causing possible serious side effects. Molnupiravir may affect the way other medicines work, and other medicines may affect how Molnupiravir works.

Your healthcare provider can tell you if it is safe to take Molnupiravir with your other medicines. Do not start or stop any other medicines during treatment with Molnupiravir without talking to your healthcare provider first.

Know the medicines you take. Keep a list of your medicines to show your healthcare provider and pharmacist when you get a new medicine.

Children and adolescents

This medicine is not recommended for children and adolescents under 18 years due to the lack of data in these patients.

Driving and using machines

Do not drive or use any tools or machines until you know that this medicine does not affect you in a negative way.

9.3. How to take Molnupiravir

Always take this medicine exactly as your doctor has told you. Do not change the dose or stop taking Molnupiravir without first talking to your healthcare provider. Check with your doctor or health care provider if you are not sure.

How much to take

Your dose will be decided by your doctor and may depend on:

- How well you respond to a dose
- If you are taking some other medicines

The recommended dose of Molnupiravir is 800 mg (administered as 4 capsules of 200 mg) orally every 12 hours for 5 days as add on to standard supportive care

Taking this medicine

The capsules should be swallowed whole with a sufficient amount of fluid (e.g., a glass of water). The capsules should not be opened, crushed or chewed. You should take your dose regularly every day at the same time of the day, so that it is easier to remember it.

If you take more Molnupiravir than you should

If you take more of this medicine than you should, contact your doctor immediately. Overdose with Molnupiravir has not been observed in the clinical trial setting.

If you forget to take Molnupiravir

If you miss a dose within 10 hours of the time it is usually taken, then you should take as soon as possible and resume the normal dosing schedule. If you miss a dose by more than 10 hours, you should not take the missed dose and instead take the next dose at the regularly scheduled time. Do not take a double dose to make up for a forgotten dose. If you miss two or more doses, contact your doctor.

If you stop taking Molnupiravir

If you stop taking this medicine you will lose the effects of the medicine. You should not stop this medicine unless told to do so by your doctor.

If you have any further questions on the use of this medicine, ask your doctor or health care provider.

9.4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

In an ongoing Phase 3 study of 386 patients with mild to moderate COVID-19, treated with molnupiravir, the most common adverse reactions reported during treatment and during 14 days after the last dose were diarrhoea, nausea, dizziness and headache all of which were mild or moderate.

Common (may affect upto 1 in 10 people)

- dizziness
- headache
- diarrhoea
- nausea

Uncommon (may affect upto 1 in 100 people)

- vomiting
- rash
- hives

In an ongoing Phase 3 study being conducted in India (Phase 3 DRL-MOL-002) of 823 patients treated with Molnupiravir as add on to Standard supportive Care for treatment of Mild Patients with COVID-19 Disease, adverse reactions reported were

Uncommon (may affect upto 1 in 100 people)

- nausea

Rare (may affect upto 1 in 1000 people)

- eye irritation
- abdominal pain
- weakness
- sinusitis
- muscle pain
- headache

- cough
- fever

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: https://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this medicine.

9.5. How to store Molnupiravir

Keep this medicine out of the sight and reach of children.

Store below 30°C.

Do not use this medicine after the expiry date, which is stated on the carton and/or bottle after "EXP". The expiry date refers to the last day of that month.

Do not use this medicine if you notice that the packaging is damaged or shows signs of tampering. Store in the original package.

Do not throw away any medicines via wastewater or household waste. These measures will help protect the environment.

10. DETAILS OF MANUFACTURER

Torrent Pharmaceuticals Ltd.

Village: Bhud and Makhnu Majra,

Tehsil: Baddi, 173205,

Dist: Solan, H.P., India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Lic.No.MNB/05/183 (Date; Not Applicable)

12. DATE OF REVISION

28 Dec 2021

MARKETED BY

TORRENT PHARMACEUTICALS LTD.