Molnupiravir

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

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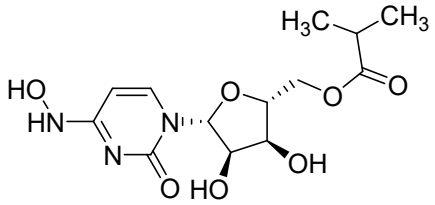
Further follow-up action as required.	

Molnupiravir



$C_{13}H_{19}N_3O_7$ Mol. Wt. 329.3

Molnupiravir is ((2R,3S,4R,5R)-3,4-dihydroxy-5-(4-(hydroxyamino)-2-oxopyrimidin-1(2H)-yl)tetrahydrofuran-2-yl)methyl Isobutyrate.

Molnupiravir contains not less than 97.0 per cent and not more than 102.0 per cent of $C_{13}H_{19}N_3O_7$, calculated on the anhydrous basis.

Category. Antiviral.

Description. A white to off-white powder.

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *molnupiravir IPRS* or with the reference spectrum of molnupiravir.

B. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

Tests

Specific optical rotation (2.4.22). –12.0°, to –6.0° determined in a 1.0 per cent w/v solution in *methanol*.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 90 volumes of *water* and 10 volumes of *methanol*.

Test solution. Dissolve 50 mg of the substance under examination in the solvent mixture and dilute to 100.0 ml with the solvent mixture.

Reference solution. Dissolve 10 mg of *molnupiravir IPRS* in 10 ml of *methanol*, with the aid of ultrasound, and dilute to 100.0 ml with *water*. Dilute 5.0 ml of the solution to 100.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (2.7µm) (Such as Ascentis Express C18),
- sample temperature: 5º,
- mobile phase: A. 0.1 per cent v/v solution of *trifluoroacetic acid* in *water*,
  B. *methanol*,
- a gradient programme using the conditions given below,
- flow rate: 0.8 ml per minute,
- spectrophotometer set at 275 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	97	3
2	97	3
15	70	30
20	65	35
30	30	70
40	30	70
40.1	97	3
50	97	3

Name	Relative retention time	Correction factor
Molnupiravir impurity A[1]	0.2	0.78
Molnupiravir	1.0	--
MOL-Hydroxylamine[2]	1.65	1.34

[1]1-((2R,3R,4S,5R)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-4-(hydroxyamino)pyrimidin-2(1H)-one,
[2]((3aR,4R,6R,6aR)-6-(4-(hydroxyamino)-2-oxopyrimidin-1(2H)-yl)-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methyl isobutyrate.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 50000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to molnupiravir Impurity A is not more than the area of the principal peak in the chromatogram obtained with the reference solution (1.0 per cent), the area of any peak corresponding to MOL-Hydroxylamine impurity is not more than 0.2 times the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent), the area of any other secondary peak is not more than 0.1 times the area of the principal peak in the chromatogram obtained with the reference solution (0.1 per cent) and the sum of the areas of all the secondary peaks is not more than twice the area of the principal peak in the chromatogram with the reference solution (2.0 per cent). Ignore any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with the reference solution (0.05 per cent).

Heavy metals (2.3.13). 1.0 g complies with the limit test for heavy metals, Method B (20 ppm).

Sulphated ash (2.3.18). Not more than 0.2 per cent.

Water (2.3.43). Not more than 1.0 per cent, determined on 0.3 g.

Assay. Determine by liquid chromatography (2.4.14).

Solvent mixture. 90 volumes of *water* and 10 volumes of *methanol*.

Test solution. Dissolve 50 mg of the substance under examination in the solvent mixture and dilute to 100.0 ml with the solvent mixture. Dilute 5.0 ml of the solution to 50.0 ml with the solvent mixture.

Reference solution. A 0.005 per cent w/v solution of *molnupiravir IPRS* in the solvent mixture.

Use chromatographic system as described under Related substances with the following modification.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	97	3
10	25	75
14	25	75
14.1	97	3
20	97	3

Inject the reference solution. The test is not valid unless the column efficiency is not less than 50000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{13}H_{19}N_3O_7$.

Storage. Store protected from moisture, at a temperature not exceeding 30°.

2.4.26. Solubility

Molnupiravir. Soluble in *methanol.*