Remdesivir for Injection

Remdesivir for Injection is a sterile material consisting of Remdesivir with or without buffering agents and other excipients. It is filled in a sealed container.

The injection is constituted by dissolving the contents of the sealed container in the requisite amount of sterile Water for Injections, immediately before use.

The constituted solution complies with the requirements for Clarity of solution and Particulate matter stated under Parenteral Preparations (Injections).

Remdesivir for Injection contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of remdesivir, $C_{27}H_{35}N_6O_8P$.

The contents of the sealed containers comply with the requirements stated under Parenteral Preparations (powder for Injections) and with the following requirements.

Usual strength. 100 mg per vial.

Description. A white to off white lyophilized solid or powder.

Identification

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

Tests

Appearance of solution. The reconstituted solution is clear (2.3.1) and colourless (2.3.1).

pH (2.4.24). 3.0 to 4.0, determined on constituted solution.

Light Absorption (2.4.7). Not more than 0.1, measured at 430 nm on 0.5 per cent w/v solution.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 60 volumes of mobile phase A and 50 volumes of *methanol.*

Test solution. Dissolve 20 mg of the substance under examination in 100.0 ml of the solvent mixture.

Reference solution (a). A 0.02 per cent w/v solution of *remdesivir RS* in the solvent mixture.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 100.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 10 cm x 2.1 mm, packed with octadecylsilane bonded to porous silica (1.7 µm) (Acquity UPLC BEH),
- column temperature: 50°
- sample temperature: 20°
- mobile phase: A. a buffer solution prepared by dissolving 1.54 g of *ammonium acetate* in 1000 ml of *water*, adjusted to pH 4.6 with *acetic acid*,
  B. *methanol*,
- a gradient programme using the conditions given below,
- flow rate: 0.4 ml per minute,
- spectrophotometer set at 245 nm,
- injection volume: 2 µl.

Time (in min)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0.01	98	2
0.5	98	2
6	42	58
10	42	58
12	32	68
15	22	78
17	5	95
18	5	95
18.5	98	2
22	98	2

Name	Relative retention time	Correction factor
Remdesivir impurity A[1]	0.35	0.5
Remdesivir impurity B[2]	0.41	0.8
Remdesivir impurity C[3]	0.58	--
Remdesivir impurity D[4]	0.76	--
Remdesivir impurity E[5]	0.92	--
Remdesivir	1.0	--
Remdesivir impurity F[6]	1.37	1.2

[1] (2R,3R,4S,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-3,4- dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-carbonitrile (TPH Impurity),
[2](2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4- dihydroxytetrahydrofuran-2-yl)methylphenylhydrogen(R)-phosphate (Phosphate Impurity),
[3](3aR,4R,6R,6aR)-4-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-6-(hydroxymethyl)-2,2-dimethyltetrahydrofuran[3,4-d][1,3]dioxole-4-carbonitrile (TPN Impurity),
[4]Butyl ((s)- (((2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano3,4- dihydroxytetrahydrofuran-2-yl)mthoxy)(phenoxy) phosphoryl)-L-alaninate (Butyl Impurity),
[5]2-ethylbutyl((R)-(((2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano3,4-dihydroxytetrahydrofuran-2-yl)methoxy)(phenoxy) phosphoryl)-L-alaninate (Diastereomer Impurity),
[6]2-ethylbutyl((R)-(((3aR,4R,6R,6aR)-6-(4-aminopyrrolo[2,1-f] [1,2,4]triazin-7-yl)-6-cyano-2,2-dimethyltetrahydrofuro[3,4-d][1,3]dioxol-4-yl)methoxy)(phenoxy)phosphoryl)amino)propanoate (PTP Impurity).

Inject reference solution (a).The test is not valid unless the column efficiency is not less than 30000 theoretical plates, the tailing factor is not less than 2.0.

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to remdesivir impurity A, B, C, D, E and F and any other secondary peak is not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent) and the sum of the areas of all the secondary peaks is not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.5 per cent). Ignore any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Water (2.3.43). Not more than 5.0 per cent, determined on 0.1 g.

Bacterial endotoxins (2.2.3). Not more than 1.5 Endotoxin Unit per mg of remdesivir.

Sterility (2.2.11). Complies with the test for sterility.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances with the following modifications.
Inject reference solution (a) and the test solution.

Calculate the content of $C_{27}H_{35}N_6O_8P$.

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