Remdesivir  

\[
\text{C}_{27}\text{H}_{35}\text{N}_{6}\text{O}_{8}\text{P} \quad \text{Mol. Wt. 602.6}
\]

Remdesivir is \((2S)-2-\{\{2R,3S,4R,5R\}-5-\{\text{4}-\text{Aminopyrrolo}[2,1-f][1,2,4]\text{triazin-7-yl}\}-5\text{-cyano}-3,4\text{-dihydroxy}\text{-tetrahydro-furan-2-ylmethoxy}\text{phenoxy}-\text{(S)}\text{-phosphorylamino}\}\text{propionic acid 2-ethyl-butyl ester}.

Remdesivir contains not less than 98.0 per cent and not more than 102.0 per cent of \(\text{C}_{27}\text{H}_{35}\text{N}_{6}\text{O}_{8}\text{P}\), 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 remdesivir RS or with the reference spectrum of remdesivir.

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 (a).

**Tests**

**Appearance of solution.** A 1.0 per cent w/v solution in methanol is clear (2.4.1) and colourless (2.4.1).

**Specific optical rotation** (2.4.22). \(-17.0^\circ\) to \(-23.0^\circ\), determined in a 1.0 per cent w/v solution in methanol.

**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 \(\mu\)m) (Acquity UPLC BEH),
- column temperature: 50\(^\circ\)
- sample temperature: 20\(^\circ\)
- 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 \(\mu\)l.

<table>
<thead>
<tr>
<th>Time (in min)</th>
<th>Mobile phase A (per cent v/v)</th>
<th>Mobile phase B (per cent v/v)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>98</td>
<td>2</td>
</tr>
<tr>
<td>0.5</td>
<td>98</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>42</td>
<td>58</td>
</tr>
<tr>
<td>10</td>
<td>42</td>
<td>58</td>
</tr>
</tbody>
</table>
**Remdesivir**

**Primary components**

- Remdesivir impurity A
- Remdesivir impurity B
- Remdesivir impurity C
- Remdesivir impurity D
- Remdesivir impurity E
- Remdesivir

<table>
<thead>
<tr>
<th>Name</th>
<th>Relative retention time</th>
<th>Correction factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remdesivir impurity A</td>
<td>0.35</td>
<td>0.5</td>
</tr>
<tr>
<td>Remdesivir impurity B</td>
<td>0.41</td>
<td>0.8</td>
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<tr>
<td>Remdesivir impurity C</td>
<td>0.58</td>
<td>--</td>
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<tr>
<td>Remdesivir impurity D</td>
<td>0.76</td>
<td>--</td>
</tr>
<tr>
<td>Remdesivir impurity E</td>
<td>0.92</td>
<td>--</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>1.0</td>
<td>--</td>
</tr>
<tr>
<td>Remdesivir impurity F</td>
<td>1.37</td>
<td>1.2</td>
</tr>
</tbody>
</table>

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)methoxy(phenoxy)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 (1S)-(((2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl)methoxy(phenoxy)phosphoryl)-L-alanine (Butyl Impurity).
5. 2-ethylbutyl(R)-(((2R,3S,4R,5R)-5-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxytetrahydrofuran-2-yl)methoxy(phenoxy)phosphoryl)-L-alanine (Diastereomer Impurity).
6. 2-ethylbutyl(R)-(((3aR,4R,6R,6aR)-4-(4-aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-6-cyano-2,2-dimethyltetrahydrofuran[3,4-d][1,3]dioxol-4-yl)methoxy(phenoxy)phosphoryl)aminopropanoate (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 0.15 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.15 per cent) and the sum of the areas of all the secondary peaks is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent). Ignore any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

**Heavy metals** (2.3.13). 2.0 g complies with the limit test for heavy metals, Method B (10 ppm).

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

**Water** (2.3.43). Not more than 0.1 per cent, determined on 0.5 g.

**Bacterial endotoxins** (2.2.3). Not more than 0.5 Endotoxin Unit per mg of remdesivir.

**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$_2$H$_3$N$_3$O$_2$P**.

**Microbial contamination** (2.2.9). Total aerobic viable count is not more than 10$^2$ CFU per g and total fungal count is not more than 10$^2$ CFU per g, determined by plate count. 1 g is free from *Escherichia coli*, *Salmonella* and *Shigella*.

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

**2.4.26 Solubility.**

**Remdesivir.** Soluble in methanol; sparingly soluble in dimethylsulphoxide and insoluble in water.