**Grazoprevir PK Fact Sheet**

**Details**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Grazoprevir</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trade Name</td>
<td>Zepatier® (co-formulated with elbasvir)</td>
</tr>
<tr>
<td>Class</td>
<td>HCV NS3/4A protease inhibitor</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>766.90</td>
</tr>
</tbody>
</table>

**Summary of Key Pharmacokinetic Parameters**

Grazoprevir is available in a fixed-dose combination product with elbasvir.

**Linearity/non-linearity**

Grazoprevir pharmacokinetics increased in a greater than dose-proportional manner over the range of 10-800 mg once daily in HCV-infected subjects.

**Steady state**

Achieved after approximately 6 days of once daily dosing.

**Plasma half life**

~31 h

**Cmax**

165 (161, 176) ng/ml (mean, 90% CI, based on population PK modelling)

**C24**

18.0 (17.8, 19.9) ng/ml (mean, 90% CI, based on population PK modelling)

**AUC**

1420 (1400, 1530) ng.h/ml (mean, 90% CI, based on population PK modelling)

**Bioavailability**

Not determined

**Absorption**

Relative to fasting conditions, the administration of a single dose of elbasvir/grazoprevir with a high-fat (900 kcal, 500 kcal from fat) meal to healthy subjects increased grazoprevir AUC and Cmax by approximately 1.5-fold and 2.8-fold, respectively. These differences in exposure are not clinically relevant; therefore, elbasvir/grazoprevir may be taken without regard to food.

**Protein Binding**

>98.8%

**Volume of Distribution**

1250 L (based on population PK modelling)

**CSF:Plasma ratio**

Not determined

**Semen:Plasma ratio**

Not determined

**Renal Clearance**

<1%

**Renal Impairment**

No dosage adjustment of elbasvir/grazoprevir is recommended in patients with any degree of renal impairment including patients on haemodialysis. Grazoprevir is not removed by haemodialysis and is unlikely to be removed by peritoneal dialysis as it is highly protein bound.

**Hepatic Impairment**

No dosage adjustment of elbasvir/grazoprevir is recommended in patients with mild hepatic impairment (Child-Pugh A). Elbasvir/grazoprevir is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C) due to the expected significantly increased grazoprevir plasma concentration (a 12-fold increase in grazoprevir exposure was observed in non-HCV infected Child-Pugh C subjects) and the increased risk of alanine aminotransferase (ALT) elevations.
**Metabolism and Distribution**

<table>
<thead>
<tr>
<th>Metabolised by</th>
<th>CYP3A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inducer of</td>
<td>Unlikely to induce CYP1A2, CYP2B6, CYP3A.</td>
</tr>
<tr>
<td>Inhibitor of</td>
<td>Inhibits BCRP. Weak inhibitor of CYP3A. Does not inhibit P-gp. No clinically significant inhibition of CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, and CYP2D6, UGT1A1, and esterases (CES1, CES2, and CatA) expected.</td>
</tr>
<tr>
<td>Transported by</td>
<td>OATP1B1/3, P-gp</td>
</tr>
</tbody>
</table>

**References**

Unless otherwise stated (see below), information is from:

Zepatier® Summary of Product Characteristics, Merck Sharp & Dohme Ltd.
Zepatier® US Prescribing Information, Merck & Co Inc.