## Lenacapavir PK Fact Sheet

### Details

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Lenacapavir (formerly GS-6207)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trade Name</td>
<td>Sunlenca®</td>
</tr>
<tr>
<td>Class</td>
<td>HIV-1 capsid inhibitor</td>
</tr>
<tr>
<td>Molecular Weight</td>
<td>968.3</td>
</tr>
<tr>
<td>Structure</td>
<td><img src="image" alt="Chemical Structure" /></td>
</tr>
</tbody>
</table>

### Summary of Key Pharmacokinetic Parameters

Initiation of treatment with lenacapavir requires tablets to be taken as oral loading prior to administration of a long-acting sub-cutaneous injection which is then administered every 6 months.

**Linearity/non-linearity**
- Single dose pharmacokinetics of lenacapavir after oral administration are non-linear and less than dose proportional over the dose range of 50 to 1800 mg.
- Single dose pharmacokinetics of lenacapavir after subcutaneous injection (309 mg/mL) are dose proportional over the dose range of 309 to 927 mg.

**Steady state**
- Not available

**Plasma half life**
- 10-12 days (oral)
- 8-12 weeks (subcutaneous)

**Cmax**
- 97.2 (70.3) ng/mL (mean (%CV) at steady state following subcutaneous administration)
- Cmax following subcutaneous administration occurs ~84 days post dose.

**Ctau**
- 36.2 (90.6) ng/mL (mean (%CV) at steady state following subcutaneous administration)

**AUC**
- 300,000 (68.5) h.ng/mL (mean (%CV) at steady state following subcutaneous administration)

**Bioavailability**
- Approximately 6-10% following oral administration

**Absorption**
- Oral tablets can be taken with or without food.

**Protein Binding**
- ~99.8%

**Volume of Distribution**
- 976 L

**CSF:Plasma ratio**
- Not available

**Semen:Plasma ratio**
- Not available

**Renal Clearance**
- <1%
# Dosing in Renal and Hepatic Impairment

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Renal Impairment</strong></td>
<td>No dose adjustment of lenacapavir is required in patients with mild, moderate, or severe renal impairment (CrCl ≥15 mL/min). The pharmacokinetics of oral lenacapavir (300 mg single dose) were evaluated in a dedicated study in subjects with severe renal impairment (estimated CrCl ≥15 and &lt;30 mL/minute). Lenacapavir AUC and Cmax increased by 84% and 162% in subjects with severe renal impairment compared with subjects with normal renal function; however, the increase was not considered clinically relevant. Lenacapavir has not been studied in patients with end stage renal disease (CrCl &lt;15 mL/min or on renal replacement therapy), therefore lenacapavir should be used with caution in these patients. As lenacapavir is approximately 99.8% protein bound, dialysis is not expected to alter exposures of lenacapavir.</td>
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<tr>
<td><strong>Hepatic Impairment</strong></td>
<td>No dose adjustment of lenacapavir is required in patients with mild or moderate hepatic impairment (Child-Pugh Class A or B). The pharmacokinetics of oral lenacapavir (300 mg single dose) were evaluated in a dedicated Phase 1 trial in subjects with moderate hepatic impairment (Child-Pugh Class B). Lenacapavir mean AUC and Cmax (total and unbound) were 1.47- to 2.84-fold and 2.61- to 5.03-fold higher in patients with moderate hepatic impairment compared to subjects with normal hepatic function. However, this increase is not considered clinically relevant based on lenacapavir exposure-response. Lenacapavir has not been studied in patients with severe hepatic impairment (Child-Pugh Class C), therefore lenacapavir should be used with caution in these patients.</td>
</tr>
</tbody>
</table>

## Metabolism and Distribution

<table>
<thead>
<tr>
<th>Metabolised by</th>
<th>CYP3A, UGT1A1</th>
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<tbody>
<tr>
<td>Inducer of</td>
<td>Does not induce CYP3A in vivo</td>
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<tr>
<td>Inhibitor of</td>
<td>CYP3A (moderate). If lenacapavir is discontinued, residual concentrations of lenacapavir may remain in the systemic circulation for prolonged periods. These concentrations may affect the exposures of other medicinal products (i.e. sensitive CYP3A substrates) that are initiated within 9 months after the last subcutaneous dose of lenacapavir. Not a clinically meaningful inhibitor of P-gp and BCRP.</td>
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<tr>
<td>Transported by</td>
<td>P-gp</td>
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## References

*Information is from:*

Sunlenca® Summary of Product Characteristics, Gilead Sciences Ltd.