**Ledipasvir PK Fact Sheet**

**Details**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic Name</strong></td>
<td>Ledipasvir</td>
</tr>
<tr>
<td><strong>Trade Name</strong></td>
<td>Harvoni® (coformulated with sofosbuvir)</td>
</tr>
<tr>
<td><strong>Class</strong></td>
<td>HCV NS5A inhibitor</td>
</tr>
<tr>
<td><strong>Molecular Weight</strong></td>
<td>889.0</td>
</tr>
<tr>
<td><strong>Structure</strong></td>
<td>![Structure Image]</td>
</tr>
</tbody>
</table>

**Summary of Key Pharmacokinetic Parameters**

Ledipasvir is available in a fixed-dosed combination product with sofosbuvir.

- **Linearity/non-linearity**: Ledipasvir AUC is dose proportional over the dose range of 3-100 mg.
- **Steady state**: Not stated
- **Plasma half life**: 47 h
- **Cmax**: 323 ng/ml (mean, based on population PK analysis)
- **Cmin**: Not stated
- **AUC**: 7290 ng·h/ml (mean, based on population PK analysis)
- **Bioavailability**: Not determined
- **Absorption**: Relative to fasting conditions, the administration of a single dose of ledipasvir/sofosbuvir with a moderate fat or high fat meal had no effect on exposure of ledipasvir.
- **Protein Binding**: >99.8%
- **Volume of Distribution**: Not determined
- **CSF:Plasma ratio**: Not determined
- **Semen:Plasma ratio**: Not determined
- **Renal Clearance**: ~1%
- **Renal Impairment**: No dose adjustment of ledipasvir/sofosbuvir is required for patients with mild or moderate renal impairment. The pharmacokinetics of ledipasvir were studied with a single dose of 90 mg ledipasvir in HCV negative patients with severe renal impairment (eGFR <30 mL/min by Cockcroft-Gault, median [range] CrCl 22 [17-29] mL/min). No clinically relevant differences in ledipasvir pharmacokinetics were observed between healthy subjects and patients with severe renal impairment. The safety of ledipasvir/sofosbuvir has not been assessed in patients with severe renal impairment (eGFR <30 mL/min/1.73 m²) or end stage renal disease (ESRD) requiring haemodialysis. No dosage recommendation can be given for ledipasvir/sofosbuvir for patients with severe renal impairment or with ESRD due to higher exposures (up to 20-fold) of the predominant sofosbuvir metabolite.
- **Hepatic Impairment**: No dose adjustment of ledipasvir/sofosbuvir is required for patients with mild, moderate or severe hepatic impairment (Child-Pugh-Turcotte [CPT] class A, B or C). Ledipasvir plasma exposure was similar in patients with severe hepatic impairment and control patients with normal hepatic function. Population pharmacokinetics analysis in HCV-infected patients indicated that cirrhosis had no clinically relevant effect on the exposure to ledipasvir.

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Metabolism and Distribution

*Metabolised by*  
In vitro, no detectable metabolism of ledipasvir was observed by human CYP1A2, CYP2C8, CYP2C9, CYP2C19, CYP2D6 and CYP3A4. Evidence of slow oxidative metabolism via an unknown mechanism has been observed. Biliary excretion of unchanged ledipasvir is a major route of elimination.

*Inducer of*  
Weak inducer of CYP3A4, CYP2C and UGT1A1 in vitro.

*Inhibitor of*  
Intestinal CYP3A4 and UGT; P-gp, BCRP. Does not inhibit OATP1B1, OATP1B3, BSEP, OCT1, OCT2, OAT1, OAT3, MATE1, MRP2 or MRP4.

*Transported by*  
P-gp, BCRP. Ledipasvir is not a substrate for OCT1, OATP1B1 or OATP1B3.

References

*Unless otherwise stated (see below), information is from:*  
Harvoni® Summary of Product Characteristics, Gilead Sciences Ltd.  
Harvoni® US Prescribing Information, Gilead Sciences Inc.