
Interferon
Ribavirin
Complex regimen
Creating options

Sofosbuvir 400 mg + Ledipasvir 90 mg

Drug of choice for genotype-1

≤1% Discontinuations due to AEs[4]

Recommended treatment durations[4]

1 TABLET ONCE A DAY WITHOUT RIBAVIRIN

GT 1	8 weeks	Can be considered in TN patients without cirrhosis who have pre-treatment HCV RNA <6 million IU/mL
	12 weeks	*TN patients with or without cirrhosis *TE patients without cirrhosis
	24 weeks	TE patients with cirrhosis
GT 4 - 6	12 weeks	TN patients and TE patients with or without cirrhosis

*TN=Treatment-naïve, TE=Treatment-experienced

Soforal-LP

Sofosbuvir 400 mg +
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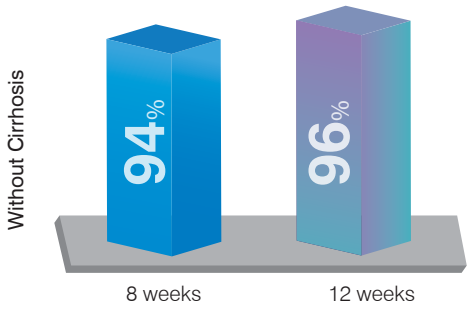
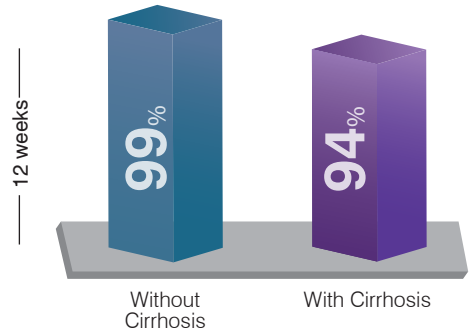
Drug of choice for genotype-1

Soforal-LP delivers high cure rates in genotype-1

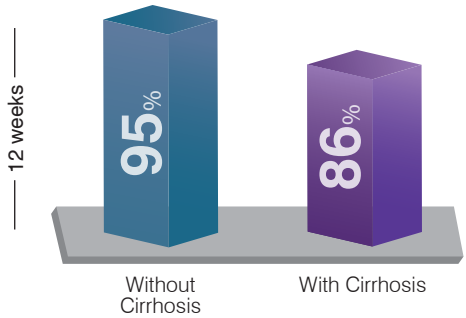
Treatment-naïve



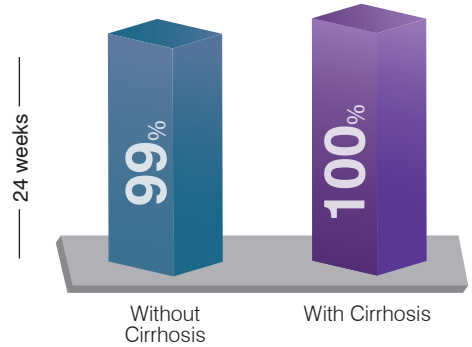
Treatment-naïve



Treatment-experienced



Treatment-experienced



Soforal-LP

Sofosbuvir 400 mg +
Ledipasvir 90 mg

Drug of choice for genotype-1

- Shortest treatment duration[4]
- Superior SVR12 against HCV genotype-1
- Outstanding safety profile
- Superior patient compliance
- Highly recommended by AASLD and EASL[5,6]

Prescribing Information

COMPOSITION: Soforal-LP Tablet: Each film coated tablet contains Sofosbuvir INN 400 mg and Ledipasvir INN 90 mg. **PHARMACOLOGICAL INFORMATION:** Therapeutic class: Antiviral Agent. **PHARMACOLOGICAL ACTION: Mechanism of Action:** Soforal-LP is a fixed-dose combination of Ledipasvir and Sofosbuvir which are direct acting antiviral agents against the hepatitis C virus. Ledipasvir is an HCV NS5A inhibitor and Sofosbuvir is a nucleotide analog inhibitor of HCV NS5B polymerase. **Pharmacodynamics:** *Cardiac Electrophysiology:* Thorough QT studies have been conducted for Ledipasvir and Sofosbuvir.The effect of Ledipasvir 120 mg twice daily (2.67 times the maximum recommended dosage) for 10 days on QT_C interval was evaluated in a randomized, multiple-dose, placebo- and active- controlled (moxifloxacin 400 mg) three period crossover thorough QT trial in 59 healthy subjects. At the dose of 120 mg twice daily (2.67 times the maximum recommended dosage), Ledipasvir does not prolong QTc interval to any clinically relevant extent. **Pharmacokinetics:** *Absorption:* The pharmacokinetic properties of Ledipasvir, Sofosbuvir and the predominant circulating metabolite GS-331007 have been evaluated in healthy adult subjects and in subjects with chronic hepatitis C. Following oral administration of Soforal-LP, Ledipasvir median peak concentrations were observed 4 to 4.5 hours post-dose. Sofosbuvir was absorbed quickly and the peak median plasma concentration was observed ~0.8 to1 hour post-dose. Median peak plasma concentration of GS-331007 was observed between 3.5 to 4 hours post-dose. *Metabolism:* 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. Unchanged Ledipasvir is the major species present in feces. Sofosbuvir is extensively metabolized in the liver to form the pharmacologically active nucleoside analog triphosphate GS-461203. The metabolic activation pathway involves sequential hydrolysis of the carboxyl ester moiety catalyzed by human cathepsin A (CatA) or carboxylesterase 1 (CES1) and phosphoramidate cleavage by histidine triad nucleotide-binding protein 1 (HINT1) followed by phosphorylation by the pyrimidine nucleotide biosynthesis pathway. *Elimination:* Following a single 90 mg oral dose of [$_{14}$C]-Ledipasvir, mean total recovery of the[$_{14}$C]-radioactivity in feces and urine was approximately 87%, with most of the radioactive dose recovered from feces (approximately 86%). Unchanged Ledipasvir excreted in feces accounted for a mean of 70% of the administered dose and the oxidative metabolite M19 accounted for 2.2% of the dose. **THERAPEUTIC INDICATIONS:** Soforal-LP is a fixed-dose combination tablet containing Ledipasvir and Sofosbuvir for oral administration. Soforal-LP is indicated with or without ribavirin for the treatment of patients with chronic hepatitis C virus (HCV) genotype 1, 4, 5, or 6 infection. **Side Effects:** The most common adverse reactions (incidence greater than or equal to 10%, all grades) observed with Soforal-LP for 8, 12 or 24 weeks are fatigue, headache, nausea, diarrhea and insomnia. **Contraindications:** Soforal-LP is administered with ribavirin, the contraindications to ribavirin also apply to this combination regimen. Refer to the ribavirin prescribing information for a list of contraindications for ribavirin. **Drug interactions:** As Soforal-LP contains Ledipasvir and Sofosbuvir, any interactions that have been identified with these agents individually may occur with Soforal-LP.After oral administration of Soforal-LP, Sofosbuvir is rapidly absorbed and subject to extensive first-pass hepatic extraction. In clinical pharmacology studies, both Sofosbuvir and the inactive metabolite GS-331007 were monitored for purposes of pharmacokinetic analyses. Ledipasvir is an inhibitor of the drug transporters P-gp and Breast Cancer Resistance Protein (BCRP) and may increase intestinal absorption of Co-administered substrates for these transporters. **Precautions :** Cases of symptomatic bradycardia, as well as fatal cardiac arrest and cases requiring pacemaker intervention, have been reported when amiodarone is co-administered with Soforal-LP. Bradycardia has generally occurred within hours to days, but cases have been observed up to 2 weeks after initiating HCV treatment. Patients also taking beta blockers, or those with underlying cardiac comorbidities and/or advanced liver disease, may be at increased risk for symptomatic bradycardia with co-administration of amiodarone. Bradycardia generally resolved after discontinuation of HCV treatment. The mechanism for this effect is unknown. **Pregnancy:** If Soforal-LP is administered with ribavirin, the combination regimen is contraindicated in pregnant women and in men whose female partners are pregnant. Refer to the ribavirin prescribing information for more information on use in pregnancy. No adequate human data are available to establish whether or not Soforal-LP poses a risk to pregnancy outcomes. In animal reproduction studies, no evidence of adverse developmental outcomes was observed with the components of Soforal-LP (Ledipasvir or Sofosbuvir) at exposures greater than those in humans at the recommended human dose. **Nursing Mothers:** No information regarding the presence of Soforal-LP in human milk, the effects on the breastfed infant, or the effects on milk production is available. Soforal-LP is present in the milk of lactating rats. **Pediatric Use:** Safety and effectiveness of Soforal-LP in children less than 18 years of age have not been established. **Geriatric Use:** Clinical trials of Soforal-LP included 225 subjects aged 65 and over (9% of total number of subjects in the clinical studies). No overall differences in safety or effectiveness were observed between these subjects and younger subjects and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. No dosage adjustment of Soforal-LP is warranted in geriatric patients. **Patients with Impaired Renal Function:** No dosage adjustment of Soforal-LP is required for patients with mild or moderate renal impairment. The safety and efficacy of Soforal-LP have not been established in patients with severe renal impairment (eGFR less than 30 mL/min/1.73m2) or ESRD requiring hemodialysis. **Hepatic Impairment :** No dosage adjustment of Soforal-LP is required for patients with mild, moderate or severe hepatic impairment (Child-Pugh Class A, B or C) **Overdosage:** No specific antidote is available for overdose with Soforal-LP. If overdose occurs, the patient must be monitored for evidence of toxicity. **PHARMACEUTICAL INFORMATION: Storage Conditions:** Store in a cool & dry place, away from light. Keep out of the reach of children.

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Light for life

REF: [1] Mymensingh Med J. 2015 Jan;24(1):143-51., [2] BSMMU J 2009; 2(1): 14-17, [3] www.worldometers.info, [4] HARVONI US full Prescribing Information, [5] AASLD treatment guideline on HCV 2015, [6] EASL treatment guideline on HCV 2016.