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TREATASIA
SNAPSHOTS
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Hepatitis C Treatment Snapshots: Velpatasvir + Sofosbuvir

Velpatasvir is a medication used to treat and cure infection caused by the hepatitis C virus (HCV). It is given in combination with sofosbuvir as a single, fixed-dose tablet of 100 mg of velpatasvir and 400 mg of sofosbuvir. The tablet is taken once a day, has few side effects, and can be used to treat HCV in people who are co-infected with HIV. The World Health Organization (WHO) has included it in its Model List of Essential Medicines.[1]

REGULATORY APPROVALS

The velpatasvir and sofosbuvir fixed-dose combination tablet was initially approved for use by the United States Food and Drug Administration (US FDA) in June 2016. The European Commission (EC) provided marketing authorization in July 2016, and the Drug Controller General of India (DCGI) approved it in May 2017. These approvals include treatment for all genotypes of HCV and for co-infection with HIV.

US FDA-approved indications for use

Patient population*	Regimen	Duration
Patients without cirrhosis and patients with compensated cirrhosis (Child Pugh[2] A)	Velpatasvir + sofosbuvir	12 weeks
Patients with decompensated cirrhosis (Child Pugh B and C)	Velpatasvir + sofosbuvir + ribavirin	12 weeks

**Includes patients co-infected with HIV and with all genotypes of HCV.*

European Medicines Agency-approved indications for use

Patient population*	Regimen	Duration
Patients without cirrhosis and patients with compensated cirrhosis	Velpatasvir + sofosbuvir**	12 weeks
Patients with decompensated cirrhosis	Velpatasvir + sofosbuvir + ribavirin	12 weeks

**Includes patients co-infected with HIV and with all genotypes of HCV.*
***Addition of ribavirin may be considered in patients with genotype 3 with compensated cirrhosis.*

SAFETY AND EFFICACY

The drug was initially evaluated across all genotypes in four phase 3 clinical trials with a total of 1,825 participants who were chronically mono-infected with HCV.

Clinical trials involving velpatasvir + sofosbuvir

Clinical trial	Regimen	Population	Cure rate*	
ASTRAL 1[3]	Velpatasvir + sofosbuvir	Genotypes 1, 2, 4, 5, 6; treatment-naïve and treatment-experienced	G1/12 wks/99% G2/12 wks/100% G4/12 wks/100% G5/12 wks/97% G6/12 wks/100%	
ASTRAL 2 & 3[4]	Velpatasvir + sofosbuvir	Genotypes 2, 3; treatment-naïve, treatment-experienced with or without compensated cirrhosis (Child Pugh Score A)	G2/12 wks/99% G3/12 wks/95%	
ASTRAL 4[5]**	Velpatasvir + sofosbuvir ± ribavirin	Genotypes 1, 2, 3, 4, 6; treatment-naïve, treatment experienced with decompensated cirrhosis (Child Pugh Score B)	12 wks G1a/88% G1b/89% G2/100% G3/50% G4/100%	24 wks G1a/93% G1b/88% G2/75% G3/50% G4/100% G6/100%

**By genotype (G) and duration in weeks. Cure rates for other patient groups are provided in the referenced articles.*
***Cure rates shown are without ribavirin. Please refer to the referenced article for cure rates with ribavirin.*

[1] World Health Organization, News release, WHO updates Essential Medicines List with new advice on use of antibiotics, and adds medicines for hepatitis C, HIV, tuberculosis and cancer http://www.who.int/mediacentre/news/releases/2017/essential-medicines-list/en/.
[2] https://www.qxmd.com/calculate/calculator_43/child-pugh-score
[3] J.J. Feld, et al. Sofosbuvir and Velpatasvir for HCV Genotype 1, 2, 4, 5, and 6 Infection. *The New England Journal of Medicine*, December 2015.
[4] G.R. Foster, et al, Sofosbuvir and Velpatasvir for HCV Genotype 2 and 3 Infection. *The New England Journal of Medicine*, December 2015.
[5] M.P. Curry, et al, Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis. *The New England Journal of Medicine*, December 2015.

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INTERACTIONS WITH HIV AND TUBERCULOSIS MEDICINES

Velpatasvir + sofosbuvir can interact with some medicines for HIV and tuberculosis. Please see below for dose adjustments, cautions, and drugs that should not be co-administered. If velpatasvir + sofosbuvir is co-administered with methadone for opiate substitution, no dose adjustments for velpatasvir, sofosbuvir, or methadone are required.

HIV medicine	Interaction	Recommendation[6]
Atazanavir boosted with ritonavir	No clinically relevant changes	No dose adjustment of velpatasvir + sofosbuvir or atazanavir is required.
Darunavir boosted with ritonavir	No clinically relevant changes	No dose adjustment of velpatasvir + sofosbuvir or darunavir is required.
Dolutegravir	No clinically relevant changes	No dose adjustment of velpatasvir + sofosbuvir or dolutegravir is required.
Efavirenz	Concentration of velpatasvir likely to decrease	Do not co-administer efavirenz with velpatasvir + sofosbuvir.
Elvitegravir	No clinically relevant changes	No dose adjustment of velpatasvir + sofosbuvir or elvitegravir is required.
Emtricitabine/ rilpivirine/ tenofovir disoproxil fumarate	No clinically relevant changes	No dose adjustment of velpatasvir + sofosbuvir or emtricitabine/rilpivirine/ tenofovir disoproxil fumarate is required.
Lopinavir boosted with ritonavir	No clinically relevant changes	No dose adjustment of velpatasvir + sofosbuvir or lopinavir is required.
Raltegravir	No clinically relevant changes	No dose adjustment of velpatasvir + sofosbuvir or raltegravir is required.
Tenofovir disoproxil fumarate	Increases concentration of tenofovir	Use with caution with frequent renal monitoring.
Tuberculosis medicine		
Rifabutin	Decreases concentrations of velpatasvir and sofosbuvir	Do not co-administer with velpatasvir + sofosbuvir.
Rifampicin	Decreases concentration of sofosbuvir	Do not co-administer with velpatasvir + sofosbuvir.
Rifapentine	Decreases concentrations of velpatasvir and sofosbuvir	Do not co-administer with velpatasvir + sofosbuvir.

CURRENT AVAILABILITY OF INDIAN GENERIC FORMULATIONS AND PRICING

As of August 2017, at least five Indian generic companies were distributing the co-formulated velpatasvir and sofosbuvir in India. The maximum retail price, according to the product packaging, is 18,500 Indian Rupees (INR), which is ~289 US Dollars (USD)[7] for a one-month supply (one bottle). At this price, a 12-week course would cost ~867 USD.

Cost comparison for combination HCV therapy in India using generic medicines

Regimen	Treatment duration	Cost*
Sofosbuvir + ribavirin	24 weeks	1,740 USD
Ledipasvir + sofosbuvir	12 weeks	1,173 USD
Daclatasvir + sofosbuvir	12 weeks	1,152 USD
Velpatasvir + sofosbuvir	12 weeks	867 USD

**Sofosbuvir price calculated at 18,566 INR (~290 USD) per bottle using the maximum retail price on Indian product packaging.*

Ledipasvir + sofosbuvir price calculated at 25,000 INR (~391 USD) per bottle using the maximum retail price on Indian product packaging.

Daclatasvir price calculated at 6,000 INR (~94 USD) per bottle using the maximum retail price on Indian product packaging.

Indian generic companies provide ribavirin at no additional cost with the purchase of the direct-acting antivirals.

CONCLUSION

Combination therapy using velpatasvir and sofosbuvir can be used across all HCV genotypes and is associated with high cure rates (95–100%) after 12 weeks of treatment, even when a patient has compensated liver cirrhosis. Pan-genotypic regimens provide the opportunity to simplify the diagnostic process and mitigate costs, as pre-treatment genotyping and expensive procedures such as transient elastography to assess liver fibrosis are not required.

As of August 2017, licensed Indian generic companies were marketing the velpatasvir + sofosbuvir combination in India, but it is registered in only two other countries in the region. Generic companies should expand regional distribution and access by proactively pursuing drug registration in more countries. To facilitate this process, fast-track registration needs to be allowed by national regulators.

However, the current pricing of generic versions may still be too high for public health programs in low- and middle-income settings. Advocacy work to support rapid drug registrations and additional price reductions remains an urgent priority.

For more information on drug pricing and registration of generic DAAs, please refer to http://hepcasia.com

[6] http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/004210/human_med_001997.jsp&mid=WC0b01ac058001d124

[7] 1 USD=63.94 Indian Rupees https://www.rbi.org.in/ accessed August 11, 2017.

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