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SNAPSHOTS
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Hepatitis C Treatment Snapshots: Sofosbuvir

Sofosbuvir is a medication used to treat and cure infection caused by the hepatitis C virus (HCV). It is used in combination with other medications at a dose of one 400 mg pill per day. It 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]

Acronyms:

HCV: Hepatitis C virus
HIV: Human immunodeficiency virus
Peg-IFN: Pegylated interferon
RBV: Ribavirin

REGULATORY APPROVALS

Sofosbuvir was approved for use by the United States Food and Drug Administration (FDA) in December 2013, by the European Medicines Agency (EMA) in January 2014, and by the Drug Controller General of India (DCGI) in January 2015. These approvals include treatment for all genotypes of HCV and for co-infection with HIV; however, different drug combinations and durations of treatment are indicated for the various genotypes.

U.S. FDA-approved indications for use:

Genotypes	Regimen	Duration
1, 4	Sofosbuvir + Peg-IFN + RBV	12 weeks
2	Sofosbuvir + RBV	12 weeks
3	Sofosbuvir + RBV	24 weeks

EMA-approved indications for use:

Genotypes	Regimen	Duration
1, 4, 5, 6	Sofosbuvir + Peg-IFN + RBV	12 weeks
	Sofosbuvir + RBV	24 weeks
2	Sofosbuvir + RBV	12 weeks
3	Sofosbuvir + Peg-IFN + RBV	12 weeks
	Sofosbuvir + RBV	24 weeks

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SAFETY AND EFFICACY

The drug's safety and efficacy were initially evaluated in five phase 3 clinical trials with a total of 1,724 participants who were chronically mono-infected with HCV. A sixth trial was conducted in individuals co-infected with both HIV and HCV. In these studies, sofosbuvir was combined with the drugs pegylated interferon (Peg-IFN) and/or ribavirin (RBV).

Clinical trials involving sofosbuvir:

Clinical trial	Regimen	Population	Cure rates*
NEUTRINO[2]	12 weeks of sofosbuvir + Peg-IFN + RBV	Genotypes 1, 4, 5, 6; treatment-naïve	G1/12 wks/89% G4/12 wks/96%
FISSION[3]	12 weeks of sofosbuvir + RBV	Genotypes 2, 3; treatment-naïve	G2/12 wks/97% G3/12 wks/56%
POSITRON[4]	12 weeks of sofosbuvir + RBV	Genotypes 2, 3; unable to take Peg-IFN	G2/12 wks/93% G3/12 wks/61%
FUSION[5]	12 or 16 weeks of sofosbuvir + RBV	Genotypes 2, 3 treatment-experienced	G2/12 wks/86% G2/16 wks/94% G3/12 wks/30% G3/16 wks/62%
VALENCE[6]	12 or 24 weeks of sofosbuvir + RBV	Genotypes 2, 3; treatment-naïve or treatment-experienced	G2/12 wks/93% G3/24 wks/82%
PHOTON-1[7]	12 or 24 weeks of sofosbuvir + RBV	Genotypes 1, 2, 3; treatment-naïve or treatment-experienced; HIV co-infected	G1/24 wks/76% G2/12 wks/88% G2/24 wks/92% G3/12 wks/67% G3/24 wks/94%

**By genotype (G) and duration in weeks (wks). Cure rates for other patient groups are provided in the references.*

CURRENT AVAILABILITY OF GENERIC FORMULATIONS AND PRICING

After the regulatory approval of sofosbuvir in India in January 2015, marketing of generic sofosbuvir under a voluntary license started in March 2015. As of June 2015, eight Indian generic companies were distributing sofosbuvir in India and working towards regulatory approvals in other countries. The maximum retail price according to the product packaging is ~309 USD for a month's supply (one bottle). At this price, a 12-week course would cost 927 USD, and a 24-week course would cost 1,854 USD.

Cost comparison for combination therapy with Indian generic sofosbuvir:

Regimen	Treatment duration	Cost*
Peg-IFN + RBV	48 weeks	10,176 USD
Sofosbuvir + Peg-IFN + RBV	12 weeks	3,471 USD
Sofosbuvir + RBV	24 weeks	1,854 USD

**Peg-IFN price calculated at 13,600 INR (~212 USD) using the maximum retail price on Indian product packaging.*
**Sofosbuvir price calculated at 19,800 INR per bottle (~309 USD) using the maximum retail price on Indian product packaging.*
**Indian generic companies provide RBV at no additional cost with the purchase of PEG-IFN or sofosbuvir.*

CONCLUSION

Combination therapy regimens that include sofosbuvir are associated with higher cure rates (70–90%), improved side effect profiles, lower cost, and shorter treatment durations as compared to the regimens using Peg-IFN and RBV alone (which have response rates of 46–77%).[8] However, drug availability is still limited, and the current pricing of generic versions may be too high for national health programs in low- and middle-income settings. Advocacy work to support fast-tracking of drug registrations and price negotiations remain urgently needed to facilitate treatment access.

1. World Health Organization. WHO moves to improve access to lifesaving medicines for hepatitis C, drug-resistant TB and cancers. News release. May 2015. http://www.who.int/mediacentre/news/releases/2015/new-essential-medicines-list/en/.
2. Lawitz E, et al. Sofosbuvir for previously untreated chronic hepatitis C infection. *The New England Journal of Medicine.* May 2013, 368:1878-1887.
3. Ibid.
4. Jacobson IM, et al. Sofosbuvir for hepatitis C genotype 2 or 3 in patients without treatment options. *The New England Journal of Medicine.* May 2013, 368:1867-1877.
5. Ibid.
6. Zeuzem S, et al. Sofosbuvir and ribavirin in HCV genotypes 2 and 3. *The New England Journal of Medicine*. May 2014, 370:1993-2001.
7. Sulkowski MS, et al. Sofosbuvir and ribavirin for hepatitis C in patients with HIV coinfection. *The Journal of the American Medical Association*. July 2014, 312(4): 353-361
8. Fried MW, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *The New England Journal of Medicine*. September 2002, 347:975-982.

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