CONCEPT LIFE SCIENCES
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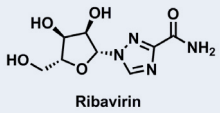
Selected Hepatitis C Therapy Highlights

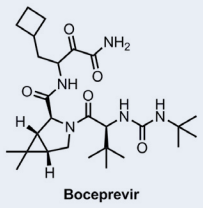
Hepatitis C is a virus (HCV) that can infect the liver and cause liver disease. It can be spread through exposure to blood that contains the virus and can cause both acute and chronic infections. An estimated 350,000 to 500,000 people die from HCV-related complications each year and 71 million people are living with chronic HCV worldwide. Although antiviral medicines have a cure rate of >95%, access to diagnosis and treatment is low (WHO, www.who.int). The infographic below highlights some important advances in HCV treatment and prevention over the last 20 years.

1997/1998


Ribavirin

The first alpha interferon, Schering-Plough's Intron A (interferon alpha-2b), was approved for treatment of hepatitis C in the UK and is taken IM or IV. The addition of ribavirin to interferon-based regimens markedly improves virological responses in adults. However, DD interactions with zidovudine and didanosine causes increased risk of anaemia and mitochondrial toxicity respectively. Please visit our website to find out about Concept's Toxicological Services.

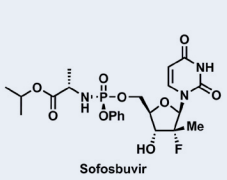
2011

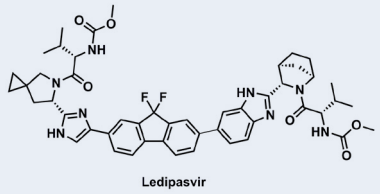

Boceprevir

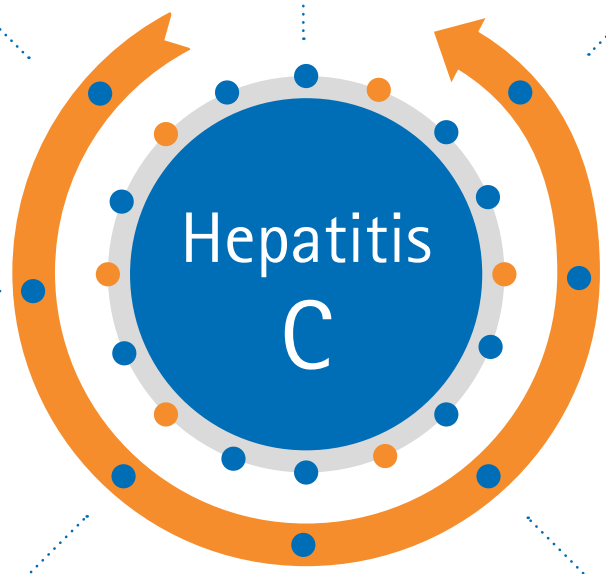
Protease inhibitors (such as Boceprevir) in combination with Pegylated Interferon alfa-2b and ribavirin was used to treat people with HCV genotype 1. However, Boceprivir was withdrawn in 2015 due to competitor superiority. Five step synthesis from known chiral building blocks. To find out how Concept can accelerate your medicinal chemistry programmes click here.

2014

Harvoni (ledipasvir/sofosbuvir) is used to treat genotype 1. Ledipasvir/sofosbuvir are substrates for P-Glycoprotein (P-gp). Intestinal absorption of these drug transporter substrates may be decreased by inducers such as rifampin and St. John's wort. Concept offer a range of ADMET assays and industry-leading turnaround times.


Sofosbuvir


Ledipasvir



2019

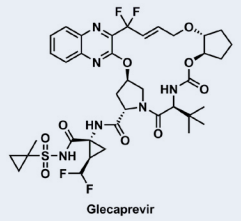
Although traditional therapies have had a significant impact on HCV infections, patients can still be at risk of re-infection and treatment alone will not completely eradicate the virus. Results from a two stage, phase I/II, double-blinded, randomized, placebo-controlled study of an HCV vaccine has recently concluded (June 2019, NCT01436357) and is pending quality control review. The results of which could have huge implications on HCV control and prevention.

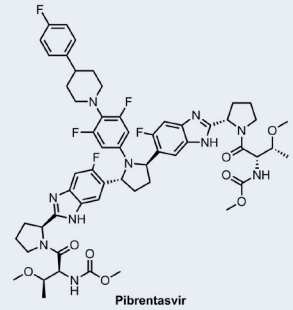
2017

Epclusa (sofosbuvir/velpatasvir) was the first Hep C therapy proven to effectively treat all six main Hep C genotypes with one-pill, taken once daily. Sofosbuvir inhibits NS5B, an RNA-dependent RNA polymerase and velpatasvir inhibits NS5A, a protein necessary for hep C virus replication and assembly.

2017

Mavyret (glecaprevir/pibrentasvir) is a pan-genotypic drug combination that acts as a protease inhibitor and an NS5A inhibitor. Mavyret gained FDA approval in 2017 with once a day dosing and 98% cure rate in clinical trials. This was the first HCV treatment regimen with a potential duration of 8 weeks. Glecaprevir is a complex macrocycle. Concept have a track-record of completing complex syntheses on small and large scale.

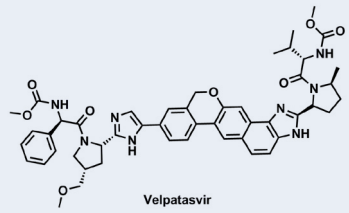

Glecaprevir


Pibrentasvir

2017

Vosevi, (sofosbuvir/velpatasvir/voxilaprevir) - a NS5B RNA polymerase inhibitor, NS5A inhibitor and NS3/4A protease inhibitor combination was approved by the FDA in July 2017.

Velpatasvir has a Human plasma protein binding of >99% which is slowly metabolised by CYP2B6, CYP2C8 and CYP3A4. It also has a half-life of 15 hours.


Velpatasvir

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