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Glecaprevir-Pibrentasvir *(Mavyret)*

Table of Contents

Drug Summary

Glecaprevir-pibrentasvir (*Mavyret*) is the first pangenotypic NS3/4A protease inhibitor-NS5A inhibitor combination to be approved that offers a potent ribavirin-free option for the vast majority of patients with chronic hepatitis C, including a potential 8-week option for non-cirrhotic patients with renal disease or HIV coinfection. This drug is not an option for patients with decompensated cirrhosis (Child B/C) given the presence of the protease inhibitor. In the main registration trials, sustained virologic response rates for 8 or 12 weeks of glecaprevir-pibrentasvir for genotypes 1, 2, 5 or 6 were in the range of 98-100% with very few if any on-treatment virologic breakthroughs or post-treatment relapses. Despite earning an 8-week FDA indication for all genotypes (treatment-naïve) without cirrhosis, the efficacy of 8 weeks of glecaprevir-pibrentasvir was numerically lower for genotype 3 and 4 at 95% and 93% respectively. Glecaprevir-pibrentasvir is by far the least expensive of all DAAs, priced at $26,400 for an 8-week course (less than half the wholesale acquisition cost of 8 weeks of ledipasvir-sofosbuvir), and it is anticipated to expand and transform the treatment landscape worldwide.

Class and Mechanism

Glecaprevir (GLE, formerly ABT-493) is an NS3/4A protease inhibitor that prevents the cleavage of the HCV polyprotein. It has potent in vitro activity (on the order of less than or equal to 5 nanomolar), across the HCV genotypes including common HCV genotype 1 variants that have substitutions (at Q80, R155 and D168) conferring resistance to older-generation HCV protease inhibitors. Pibrentasvir (PIB, formerly ABT-530) is a next-generation NS5A inhibitor with pangenotypic activity in vitro; it maintains potent antiviral activity against common HCV NS5A single-position variants that confer resistance to first-generation NS5A inhibitors, including daclatasvir, ledipasvir, and ombitasvir.

Manufacturer for United States

The fixed dose medication glecaprevir-pibrentasvir (*Mavyret*) (Figure 1) is manufactured by AbbVie Inc. Each fixed-dose tablet contains 100 mg of glecaprevir and 40 mg of pibrentasvir (Figure 2).

Cost and Medication Access

The wholesale acquisition cost (WAC) for a 8-week course of glecaprevir-pibrentasvir is $26,400. The 8-week course of glecaprevir-pibrentasvir is indicated for treatment-naïve noncirrhotic patients with genotypes 1-6 HCV; this 8-week treatment course makes glecaprevir-pibrentasvir by far the least expensive option among all of the recommended treatment options for non-cirrhotic treatment-naïve patients. The 12-week treatment course has a cost of $39,600 and this duration is indicated for treatment-naive patients with compensated cirrhosis (Child-Pugh A) and some treatment experienced patients. The 16-week treatment course is $52,800 and is indicated for some subsets of treatment-experienced patients.

Adverse Effects

The most common adverse effects, observed in at least 10% of phase 3 trial participants, were headache and fatigue.

Key Drug Interactions

For complete information on glecaprevir-pibrentasvir-related drug interactions, see the Drug Interactions section in the Glecaprevir-Pibrentasvir (*Mavyret*) Prescribing Information.

Figures

Figure 1 Glecaprevir-Pibrentasvir (*Mavyret*) Packaging

Note each daily packet contains 3 glecaprevir-pibrenatasvir fixed-dose tablets and each tablet consists of 100 mg of glecaprevir and 40 mg of pibrentasvir.

This photograph is courtesy of AbbVie

Figure 2 Fixed-Dose Tablet of Glecaprevir-Pibrentasvir (*Mavyret*)

Each fixed dose tablet contains contains 100 mg of glecaprevir and 40 mg of pibrentasvir. The recommended daily dose is 3 tablets once daily.

Photo: Andrew Karpenko, University of Washington