



FDA MedWatch

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Hepatitis Updates

The FDA recently approved revisions to the MAVYRET™ (glecaprevir and pibrentasvir) tablets label to include safety and efficacy data from the HCV/HIV-1 coinfection study (M14-730) and from the liver and renal transplant study (M13-596). A summary of the major revisions includes the following:

Section 2: DOSAGE AND ADMINISTRATION was updated to include the following dosing recommendations.

2.3 Liver or Kidney Transplant Recipients

MAVYRET is recommended for 12 weeks in liver or kidney transplant recipients. A 16-week treatment duration is recommended in genotype 1-infected patients who are NS5A inhibitor-experienced without prior treatment with an NS3/4A protease inhibitor or in genotype 3-infected patients who are PRS treatment-experienced.

Section 6: ADVERSE REACTIONS was updated to include the following safety data.

Adverse Reactions in HCV/HIV-1 Co-infected Subjects

The safety of MAVYRET in subjects with HIV-1 co-infection with genotypes 1, 2, 3, 4 or 6 chronic HCV infection without cirrhosis or with compensated cirrhosis (Child-Pugh A) was assessed in 153 subjects (EXPEDITION-2) who received MAVYRET for 8 or 12 weeks. Thirty-three subjects with HIV-1 coinfection also received 8 or 12 weeks of therapy in ENDURANCE- 1.

The overall safety profile in HCV/HIV-1 co-infected subjects (ENDURANCE-1 and EXPEDITION-2) was similar to that observed in HCV mono-infected subjects. Adverse reactions observed in greater than or equal to 5% of subjects receiving MAVYRET in EXPEDITION-2 for 8 or 12 weeks were fatigue (10%), nausea (8%), and headache (5%).

Adverse Reactions in Subjects with Liver or Kidney Transplant

The safety of MAVYRET was assessed in 100 post-liver or -kidney transplant recipients with genotypes 1, 2, 3, 4, or 6 chronic HCV infection without cirrhosis (MAGELLAN-2). The overall safety profile in transplant recipients was similar to that observed in subjects in the Phase 2 and 3 studies, without a history of transplantation. Adverse reactions observed in greater than or equal to 5% of subjects receiving MAVYRET for 12 weeks were headache (17%), fatigue (16%), nausea (8%) and pruritus (7%). In subjects treated with MAVYRET who reported an adverse reaction, 81% had adverse reactions of mild severity. Two percent of subjects experienced a serious adverse reaction, and no subjects permanently discontinued treatment due to adverse reactions.

Section 14: CLINICAL STUDIES was updated to include the following efficacy outcomes data.

14.7 Treatment-Naïve or PRS Treatment-Experienced Adults with HCV/HIV-1 Coinfection without Cirrhosis or with Compensated Cirrhosis

EXPEDITION-2 was an open-label study in 153 HCV/HIV-1-coinfected subjects. Subjects without cirrhosis received MAVYRET for 8 weeks and subjects with compensated cirrhosis received MAVYRET for 12 weeks. The study included subjects who were HCV treatment-naïve or

treatment-experienced to combinations of (peg)interferon, ribavirin, and/or sofosbuvir, with the exception of GT3-infected subjects who were all treatment naïve.

Of the 153 subjects treated, the median age was 45 years (range: 23 to 74); 63% had HCV genotype 1, 7% had HCV genotype 2, 17% had HCV genotype 3, 11% had HCV genotype 4, 2% had HCV genotype 6; 11% had cirrhosis; 84% were male; and 16% were Black.

In EXPEDITION-2, the SVR12 rate in HCV/HIV-1 co-infected subjects was 98% (150/153). One subject experienced on-treatment virologic failure and no subjects relapsed.

14.8 Treatment-Naïve or PRS Treatment-Experienced Adults with Liver or Kidney Transplant without Cirrhosis

MAGELLAN-2 was a single-arm, open-label study in 100 post-liver or -kidney transplant HCV GT 1, 2, 3, 4, or 6 infected subjects without cirrhosis who received MAVYRET for 12 weeks. The study included subjects who were HCV treatment-naïve or treatment-experienced to combinations of (peg)interferon, ribavirin, and/or sofosbuvir, with the exception of GT3-infected subjects who were all treatment-naïve.

Of the 100 subjects treated, the median age was 60 years (range: 39 to 78); 57% had HCV genotype 1, 13% had HCV genotype 2, 24% had HCV genotype 3, 4% had HCV genotype 4, 2% had HCV genotype 6; 75% were male; 8% were Black; 80% of subjects were post-liver transplant and 20% were post-kidney transplant. Immunosuppressants allowed for co-administration were cyclosporine \leq 100 mg, tacrolimus, sirolimus, everolimus, azathioprine, mycophenolic acid, prednisone, and prednisolone.

The overall SVR12 rate in post-transplant subjects was 98% (98/100). There was one relapse and no on-treatment virologic failures.

The updated label will soon be available at drugs@fda or [DailyMed](#)

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