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 ≤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

Kimberly Struble
Division of Antiviral Products
Food and Drug Administration

Elizabeth Thompson
Division of Antiviral Products
Food and Drug Administration

Michael Stanfield Jr.
Division of Antiviral Products
Food and Drug Administration