CURING HEPATITIS C WITH PROVEN EFFICACY

#1 PRESCRIBED CHRONIC HCV PRODUCT
IQVIA, week ending 1/5/18–4/3/20.[2]

8 WEEKS: THE SHORTEST ROUTE TO CURE[1]

Only MAVYRET offers a pangenotypic 8-week duration for TN, NC and CC HCV patients

Liver or kidney transplant recipients are not eligible for an 8-week regimen.

Cure = Sustained virologic response (SVR12); HCV RNA <LLOQ at 12 weeks after the end of treatment.

CC = Compensated cirrhotic; HCV = Hepatitis C virus; LLOQ = Lower limit of quantification; NC = Non-cirrhotic; TN = Treatment-naïve.

INDICATION[1]

MAVYRET is indicated for the treatment of adult and pediatric patients 12 years and older or weighing at least 45 kg with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A).

SAFETY CONSIDERATIONS[1]

WARNING: RISK OF HEPATITIS B VIRUS REACTIVATION IN PATIENTS COINFECTED WITH HCV AND HBV: Test all patients for evidence of current or prior hepatitis B virus (HBV) infection before initiating treatment with MAVYRET. HBV reactivation has been reported in HCV/HBV coinfected patients who were undergoing or had completed treatment with HCV direct-acting antivirals and were not receiving HBV antiviral therapy. Some cases have resulted in fulminant hepatitis, hepatic failure, and death. Monitor HCV/HBV coinfected patients for hepatitis flare or HBV reactivation during HCV treatment and post-treatment follow-up. Initiate appropriate patient management for HBV infection as clinically indicated.

Please see Important Safety Information on page 4 and full Prescribing Information.

MAVYRET®
glecaprevir/pibrentasvir
100 mg/40 mg tablets

PROVEN 8-WEEK EFFICACY IN TREATMENT-NAÏVE PATIENTS WITHOUT CIRRHOSIS OR WITH COMPENSATED CIRRHOSIS[3]

98% CURE RATE (SVR12)

Based on an integrated pooled analysis of GT 1-6 TN, NC and CC patients across 8 clinical trials that included United States study locations (n=1218/1248, ITT). SVR12 range: 95-99% (ITT)

See study designs on page 5

0.1% on-treatment virologic failure (n=1/1248)

0.6% relapse (n=7/1226)

Cure = Sustained virologic response (SVR12); HCV RNA <LLOQ at 12 weeks after the end of treatment.[1]

Relapse = HCV RNA ≥LLOQ after end-of-treatment response among subjects who completed treatment.

ONLY RECOMMENDED 8-WEEK PANGENOTYPIC REGIMEN IN AASLD & IDSA GUIDELINES FOR TN, NC AND TN, CC PATIENTS[4] AS OF 11/06/19

SEE GUIDELINES FOR SPECIAL POPULATION RECOMMENDATIONS

AASLD and IDSA have not endorsed, and are not sponsors of, or otherwise affiliated with MAVYRET or AbbVie Inc.

AASLD is a registered trademark of the American Association for the Study of Liver Diseases and IDSA is a registered trademark of the Infectious Diseases Society of America.

AASLD = American Association for the Study of Liver Diseases; GT = Genotype; IDSA = Infectious Diseases Society of America; ITT = Intention to treat.

SAFETY CONSIDERATIONS[1]

WARNINGS AND PRECAUTIONS

Risk of Hepatic Decompensation/Failure in Patients with Evidence of Advanced Liver Disease

- Postmarketing cases of hepatic decompensation/failure, some fatal, have been reported in patients treated with HCV NS3/4A protease inhibitor-containing regimens, including MAVYRET. The median time to onset for MAVYRET was 27 days. The majority had moderate or severe hepatic impairment prior to initiating therapy, including some with compensated cirrhosis at baseline but with a prior decompensation event. Rare cases were reported in patients without cirrhosis or with compensated cirrhosis; many of these patients had evidence of portal hypertension. In patients with compensated cirrhosis or evidence of advanced liver disease, perform hepatic laboratory testing as clinically indicated; and monitor for signs and symptoms of hepatic decompensation such as the presence of jaundice, ascites, hepatic encephalopathy, and variceal hemorrhage. Discontinue MAVYRET in patients who develop evidence of hepatic decompensation/failure.

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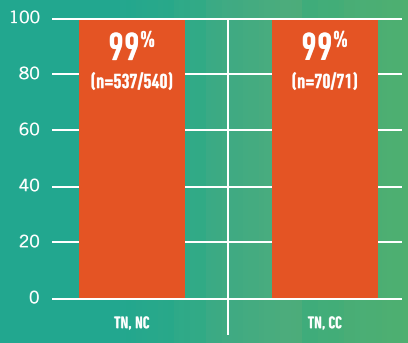
REAL-WORLD EVIDENCE SUPPORTS AN 8-WEEK DURATION OF MAVYRET[5,6]

RESULTS FROM 2 TRIO HEALTH NETWORK STUDIES



99% CURE RATE IN PER-PROTOCOL POPULATION

In GT 1-4 and 6, TN, NC and TN, CC patients treated for 8 weeks

ITT population: 96% cure rate (SVR12) across GT 1-4 and 6, TN, NC (n=537/560) and TN, CC (n=70/73) patients treated for 8 weeks

TN, NC STUDY:

- 2% lost to follow-up (n=13/560)
- 0.5% virologic failure (n=3/560)
- 1% discontinued (n=7/560)

TN, CC STUDY:

- 3% lost to follow-up (n=2/73)
- 1% virologic failure (n=1/73)
- 0% discontinued (n=0/73)

Reasons for discontinuation were medical care unrelated to treatment, patient choice, MD choice, insurance denial, positive drug or alcohol screening, and side effects. Data were insufficient to determine whether side effects are related or unrelated to treatment.

Real-world data are observational in nature, may be prospectively or retrospectively collected, and are not based on controlled clinical studies. Results from these cohorts may differ from those observed in clinical practice and are not presented in the MAVYRET Prescribing Information.

FIB-4 = Fibrosis-4; PP = Per protocol excluding patients with non-virologic failure.

METHODOLOGY[5,6]

The TRIO Health Network study electronically collected data on treatment-naïve, non-cirrhotic patients ≥18 years of age who were treated with MAVYRET for 8 weeks. Data were captured from 233 unique healthcare providers between August 2017 and April 2018. Of the 560 in the total population, the median age was 51 years; 54% were male, 30% were white race, 58% were other or unspecified race, and 20% had an HCV RNA level >6MM IU/mL.

The TRIO Health Network study electronically collected data on treatment-naïve, compensated cirrhotic patients >18 years of age who were treated with MAVYRET for 8 weeks. Data were captured between August 2017 and November 2018. Cirrhosis status was defined as a FIB-4 score >5.2 or was physician reported. Decompensated cirrhosis was defined as no current or past clinical evidence of Child-Pugh B or C classification or clinical history of liver decompensation including ascites, bleeding esophageal varices, or hepatic encephalopathy. Compensated cirrhosis was defined as cirrhosis with no prior history of liver decompensation. Of the 73 in the total population, the median age was 59 years; 60% were male, 27% were white race, 55% were other or unspecified race, and 15% had an HCV RNA level >6MM IU/mL.

Primary endpoint for both studies was the PP sustained virologic response at 12 weeks post treatment (SVR12).

SAFETY CONSIDERATIONS[1]

CONTRAINDICATIONS

- MAVYRET is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh B or C) or those with any history of prior hepatic decompensation.
- MAVYRET is contraindicated with atazanavir or rifampin.

Please see Important Safety Information, including BOXED WARNING on Hepatitis B Virus reactivation, on page 4, and full Prescribing Information.

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INDICATION AND IMPORTANT SAFETY INFORMATION

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MAVYRET is indicated for the treatment of adult and pediatric patients 12 years and older or weighing at least 45 kg with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis (Child-Pugh A).

IMPORTANT SAFETY INFORMATION[1]

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WARNINGS AND PRECAUTIONS

Risk of Hepatic Decompensation/Failure in Patients with Evidence of Advanced Liver Disease

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Risk of Reduced Therapeutic Effect Due to Concomitant Use of MAVYRET with Certain Drugs

- Carbamazepine, efavirenz, and St. John's Wort may significantly decrease plasma concentrations of glecaprevir and pibrentasvir, leading to reduced therapeutic effect of MAVYRET. The use of these agents with MAVYRET is not recommended.

ADVERSE REACTIONS

Most common adverse reactions observed with MAVYRET:

- >10% of subjects: headache and fatigue

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STUDY DESIGNS

ENDURANCE-1[1,7]

A randomized, open-label, phase 3 study in GT 1 TN or PRS-experienced NC subjects with or without HIV-1 co-infection (N=703). Subjects received MAVYRET for 8 to 12 weeks. Primary endpoints: SVR12 in the 12-week ITT-PS population (ITT population excluding subjects with HIV co-infection and subjects with SOF experience); SVR12 in 8-week vs 12-week arm in the ITT-PS and PP ITT-PS populations ("per-protocol" excludes subjects with premature discontinuation or virologic failure prior to week 8 and missing data in the SVR12 window).

ENDURANCE-3[1,7]

Partially randomized, open-label, active-controlled, phase 3 study in GT 3 TN, NC subjects (N=505). Subjects received MAVYRET for 8 or 12 weeks vs SOF + DCV for 12 weeks. Primary endpoints: Demonstrate noninferiority in the percentage of subjects achieving SVR12 with 12 weeks of MAVYRET to 12 weeks of SOF + DCV and demonstrate noninferiority of 8 weeks vs 12 weeks of MAVYRET.

ENDURANCE-5,6[1,8]

Single-arm, open-label 3b study in GT 5-6, TN or PRS-experienced, NC or CC subjects (N=84). Subjects received MAVYRET for 8 or 12 weeks. Primary endpoint: SVR12.

EXPEDITION-2[1,9]

Non-randomized, open-label, phase 3 study in subjects who were co-infected with GT 1-6/HIV-1, TN or PRS-experienced, NC or CC, and were antiretroviral therapy (ART)-naïve, or on a stable ART regimen (N=153). Subjects received MAVYRET for 8 and 12 weeks. Treatment-experienced GT 3–infected subjects were excluded. Primary endpoint: SVR12.

EXPEDITION-5[10]

Non-randomized, open-label, phase 3b study in GT 1-6 TN or PRS-experienced, NC or CC subjects with CKD stage 3b, 4 or 5 (N=101). Treatment-experienced GT 3–infected subjects were excluded. Subjects received MAVYRET for 8, 12, or 16 weeks. Primary endpoint: SVR12.

EXPEDITION-8[1,11]

Single-arm, open-label, phase 3b study in GT 1-6 TN, CC subjects (N=343) who received MAVYRET for 8 weeks. Primary endpoints: SVR12 vs the historical PP SVR12 rate of 100% and ITT SVR12 rate of 99% in GT 1, 2, 4-6 TN, CC subjects receiving 12-weeks of MAVYRET. Key secondary endpoints included the same PP and ITT SVR comparisons to GT 1-6 TN, CC subjects. PP excludes subjects from the ITT population with virologic breakthrough or discontinuation prior to week 8, and those missing data in the SVR12 window.

SURVEYOR-1, Part 2[12,13]

Open-label, two-part, phase 2 study in GT 1, 4-6 TN or PRS-experienced, NC or CC subjects (N=174). Part 2: Subjects received MAVYRET for 8 or 12 weeks. Primary endpoint: SVR12.

SURVEYOR-2, Parts 2 and 4[1,14-16]

Randomized, open-label, 4-part, phase 2 study in GT 2-6 TN or PRS-experienced NC or CC subjects (N=691). In Parts 2 and 4, subjects received MAVYRET for 8 or 12 weeks. Primary endpoints: SVR12 and noninferiority of SVR12 for GT 2 (Part 4) to historical control with 12 weeks of SOF + RBV.

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CKD = Chronic kidney disease; DCV = Daclatasvir; HIV = Human immunodeficiency virus; (peg)IFN = (Pegylated)interferon; PRS-experienced = Prior treatment experience with regimens containing (peg)IFN, RBV, and/or SOF, but no prior treatment experience with an HCV NS3/4A protease inhibitor or an NS5A inhibitor; PS = Primary subset; RBV = Ribavirin; SOF = Sofosbuvir.

References: 1. MAVYRET [package insert]. North Chicago, IL: AbbVie Inc.; 2020. **2.** Data on file. AbbVie Inc. IQVIA. National Prescription Audit (NPA), National Prescription Audit Market Dynamics (NPA MD) and Weekly Sales Perspective (WSP) week ending 1/5/2018 to week ending 4/3/2020, Longitudinal Prescription Claims (LRx) week ending 1/5/2018 to week ending 3/27/2020. May 2020. (IQVIA, all rights reserved). **3.** Data on file. ABVRRTI69094. AbbVie Inc.; 2019. **4.** The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America. HCV guidance: recommendations for testing, managing, and treating hepatitis C. www.hcvguidelines.org. Updated November 6, 2019. Accessed August 24, 2020. **5.** Curry MP, Kort J, Marx S, et al. Real-world effectiveness of 8-week glecaprevir/pibrentasvir (G/P) for treatment naïve, non-cirrhotic patients with HCV infection in the TRIO network. *GastroHep.* 2020; doi:10.1002/ygh2.388. **6.** Flamm SL, Kort J, Marx SE, et al. Effectiveness of 8-week glecaprevir/pibrentasvir for treatment-naïve, compensated cirrhotic patients with chronic hepatitis C infection. *Adv Ther.* 2020; doi:10.1007/s12325-020-01301-5. **7.** Zeuzem S, Foster GR, Wang S, et al. Glecaprevir–pibrentasvir for 8 or 12 weeks in HCV genotype 1 or 3 infection. *N Engl J Med.* 2018;378(4):354-369. **8.** Asselah T, Lee SS, Yao BB, et al. Efficacy and safety of glecaprevir/pibrentasvir in patients with chronic hepatitis C virus genotype 5 or 6 infection (ENDURANCE-5,6): an open-label, multicentre, phase 3b trial. *Lancet Gastroenterol Hepatol.* 2019;4:45-51. **9.** Rockstroh JK, Lacombe K, Viani RM, et al. Efficacy and safety of glecaprevir/pibrentasvir in patients coinfected with hepatitis C virus and human immunodeficiency virus type 1: the EXPEDITION-2 study. *Clin Infect Dis.* 2018;67:1010-1017. **10.** Lawitz E, Flisiak R, Abunimeh M, et al. Efficacy and safety of glecaprevir/pibrentasvir in renally impaired patients with chronic HCV infection. *Liver Int.* 2019. doi:10.1111/liv.14320. **11.** Brown RS Jr, Buti M, Rodrigues L, et al. Glecaprevir/pibrentasvir for 8 weeks in treatment-naïve patients with chronic HCV genotypes 1–6 and compensated cirrhosis: the EXPEDITION-8 trial. *J Hepatol.* 2020;72(3):441-449. **12.** Kwo PY, Poordad F, Asatryan A, et al. Glecaprevir and pibrentasvir yield high response rates in patients with HCV genotype 1–6 without cirrhosis. *J Hepatol.* 2017;67(2):263-271. **13.** Gane E, Poordad F, Wang S, et al. High efficacy of ABT-493 and ABT-530 treatment in patients with HCV genotype 1 or 3 infection and compensated cirrhosis. *Gastroenterology.* 2016;151(4):651-659. **14.** Data on file. ABVRRTI64729. AbbVie Inc.; 2017. **15.** Kwo PY, Wyles DL, Wang S, et al. 100% SVR12 with ABT-493 + ABT-530 with or without ribavirin in treatment-naïve HCV genotype 3-infected patients with cirrhosis. Oral presentation at: 51st Annual Meeting of the European Association for the Study of the Liver; April 16, 2016; Barcelona, Spain. **16.** Hassanein T, Wyles D, Wang S, et al. SURVEYOR-II, part 4: glecaprevir/pibrentasvir demonstrates high SVR rates in patients with HCV genotype 2, 4, 5, or 6 infection without cirrhosis following an 8-week treatment duration. Poster presented at: 52nd Annual Meeting of the European Association for the Study of the Liver; April 19-23, 2017; Amsterdam, the Netherlands.

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