



NEWS RELEASE

Merck Receives FDA Approval of ZEPATIER™ (elbasvir and grazoprevir) for the Treatment of Chronic Hepatitis C Virus Genotype 1 or 4 Infection in Adults Following Priority Review

1/28/2016

ZEPATIER Achieves High Cure Rates (SVR12) in Broad Range of Patients with Chronic Hepatitis C Infection, Including Those with Compensated Cirrhosis, Renal Impairment of Any Degree and HIV-1/HCV Co-infection

Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has approved ZEPATIER™ (elbasvir and grazoprevir) for the treatment of adult patients with chronic hepatitis C virus (HCV) genotype (GT) 1 or GT4 infection, with or without ribavirin (RBV), following priority review by the FDA. ZEPATIER (pronounced ZEP-ah-teer) is a once-daily, fixed-dose combination tablet containing the NS5A inhibitor elbasvir (50 mg) and the NS3/4A protease inhibitor grazoprevir (100 mg). The FDA previously granted two Breakthrough Therapy designations to ZEPATIER, for the treatment of chronic HCV GT1 infection in patients with end stage renal disease on hemodialysis, and for the treatment of patients with chronic HCV GT4 infection. Breakthrough Therapy designation is given to investigational medicines for serious or life-threatening conditions that may offer substantial improvement over existing therapies. Across multiple clinical studies, ZEPATIER achieved high rates of sustained virologic response ranging from 94 to 97 percent in GT1-infected patients, and 97 to 100 percent in GT4-infected patients. Sustained virologic response is defined as HCV RNA levels measuring less than the lower limit of quantification at 12 weeks after the cessation of treatment (SVR12), indicating that a patient's HCV infection has been cured.

ZEPATIER is not for use in patients with moderate or severe hepatic impairment (Child-Pugh B or C). ZEPATIER also



is not for use with organic anion transporting polypeptides 1B1/3 (OATP1B1/3) inhibitors (e.g., atazanavir, darunavir, lopinavir, saquinavir, tipranavir, cyclosporine), strong cytochrome P450 3A (CYP3A) inducers (e.g., carbamazepine, phenytoin, rifampin, St. John's Wort), and efavirenz. If ZEPATIER is administered with RBV, healthcare professionals should refer to the prescribing information for RBV as the contraindications, warnings and precautions, adverse reactions and dosing for RBV also apply to this combination regimen.

"Continued innovation is needed to help address the worldwide epidemic of chronic hepatitis C virus infection," said Dr. Roger M. Perlmutter, president, Merck Research Laboratories. "Our clinical program was designed to study a broad range of patients infected with the hepatitis C virus, including difficult-to-treat patients such as those with stage 4 or 5 chronic kidney disease. The approval of ZEPATIER is a testament to Merck's unwavering commitment to improving therapy for patients with hepatitis C virus infection, and we are eager to bring this innovation to patients and physicians in the United States."

ZEPATIER was approved with a treatment duration of 12 or 16 weeks, depending on HCV genotype, prior treatment history and, for patients with GT1a infection, the presence of certain baseline NS5A polymorphisms. A 12-week, once-daily regimen is recommended for the vast majority of patients for whom ZEPATIER is indicated.

Merck's broad clinical trial program supporting the efficacy of ZEPATIER included six studies in 1,373 patients with chronic HCV GT1 or GT4 infection. These studies assessed the rate of sustained virologic response 12 weeks after the completion of treatment with ZEPATIER (SVR12). The clinical development program for ZEPATIER enrolled diverse groups of HCV GT1- and GT4-infected patients, including treatment-naïve patients and those who had failed prior therapy with peginterferon alfa (PegIFN) and RBV, as well as patients suffering with meaningful co-morbidities and health complications, such as compensated cirrhosis and HIV-1 co-infection. GT1-infected patients with severe renal impairment on hemodialysis and those who previously failed therapy with PegIFN and RBV in combination with an HCV NS3/4A protease inhibitor (boceprevir, simeprevir or telaprevir) also were studied.

The following table provides a summary of clinical data that contributed to the efficacy assessment of ZEPATIER. The primary endpoint in each study was SVR12. Please see section entitled Summary of Study Designs below for additional study design information, including treatment arms and baseline characteristics.

Clinical Studies Supporting Efficacy of ZEPATIER (elbasvir and grazoprevir):

Clinical Trial(s)	Population	SVR12 (n/N)	Treatment Regimen and
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			Duration
GT1 C-EDGE TN (double blind, placebo controlled)	TN +/- cirrhosis	95% (273/288)	ZEPATIER 12 weeks
C-EDGE CO-INFXN (open-label, single arm)	TN +/- cirrhosis + HIV-1 co-infection	95% (179/189)	
C-SURFER (double blind, placebo controlled)	TN/TEa +/- cirrhosis + severe renal impairment	94% (115/122)	
C-EDGE TE ^d (open-label, comparative)	TEb +/- cirrhosis +/- HIV- 1 co-infection	94% (90/96)	ZEPATIER 12 weeks
		97% (93/96)	ZEPATIER + RBV 16 weeks
C-SALVAGE (open-label, single arm)	TEc +/- cirrhosis	96% (76/79)	ZEPATIER + RBV 12 weeks
GT4 C-SCAPE (open-label) C-EDGE TN	TN without cirrhosis TN +/- cirrhosis TN +/- cirrhosis + HIV-1 co-infection	97% (64/66)	ZEPATIER 12 weeks
C-EDGE CO-INFXN			
C-EDGE TE	TEb +/- cirrhosis	100% (8/8)	ZEPATIER + RBV 16 weeks

TE, treatment-experienced; TN, treatment-naïve.

a Failed prior IFN or PegIFN +/- RBV.

b Failed prior PegIFN + RBV.

c Failed prior PegIFN + RBV + HCV NS3/4A protease inhibitor (PI): boceprevir, simeprevir or telaprevir.

d C-EDGE TE treatment outcomes for ZEPATIER with RBV for 12 weeks (n=104) or without RBV for 16 weeks (n=101) not shown because these regimens are not recommended in PegIFN + RBV-experienced GT1 patients.

Selected Safety Information about ZEPATIER (elbasvir and grazoprevir)

Elevations of alanine transaminase (ALT) to greater than 5 times the upper limit of normal (ULN) occurred in 1% of subjects, generally at or after treatment week 8. These late ALT elevations were typically asymptomatic and most resolved with ongoing or completion of therapy. Healthcare professionals should perform hepatic lab testing on

patients prior to therapy, at treatment week 8, and as clinically indicated. For patients receiving 16 weeks of therapy, additional hepatic lab testing should be performed at treatment week 12.

Patients should be instructed to consult their healthcare professional without delay if they have onset of fatigue, weakness, lack of appetite, nausea and vomiting, jaundice or discolored feces. Healthcare providers should consider discontinuing ZEPATIER if ALT levels remain persistently greater than 10 times ULN. ZEPATIER should be discontinued if ALT elevation is accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalized ratio.

Recommended Dosage Regimens and Durations for ZEPATIER (elbasvir and grazoprevir)

The dosing regimens and durations for treatment with once-daily ZEPATIER for chronic HCV GT1 or GT4 infection in patients with or without cirrhosis, HIV-1 co-infection or renal impairment are as follows:

Patient Population	Treatment	Duration
GT1a: Treatment-naïve or PegIFN/RBV-experienced* without baseline NS5A polymorphisms†	ZEPATIER	12 weeks
GT1a: Treatment-naïve or PegIFN/RBV-experienced* with baseline NS5A polymorphisms†	ZEPATIER with RBV	16 weeks
GT1b: Treatment-naïve or PegIFN/RBV-experienced*	ZEPATIER	12 weeks
GT1a or GT1b: PegIFN/RBV/PI-experienced§	ZEPATIER with RBV	12 weeks
GT4: Treatment-naïve	ZEPATIER	12 weeks
GT4: PegIFN/RBV-experienced*	ZEPATIER with RBV	16 weeks

*Patients who have failed treatment with PegIFN + RBV.

†NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31 or 93.

§Patients who have failed treatment with PegIFN/RBV + HCV NS3/4A PI: boceprevir, simeprevir or telaprevir. For GT1a-infected PegIFN/RBV/PI-experienced patients with one or more baseline NS5A resistance-associated polymorphisms (positions 28, 30, 31 or 93), the optimal ZEPATIER-based treatment regimen and duration of therapy has not been established.

In patients with GT1a infection, some hepatitis C viruses may contain mutations that can confer resistance to treatment. These are called resistance-associated polymorphisms, also referred to as resistance-associated variants (RAVs). GT1a infection accounts for 46 percent of U.S. HCV cases. To help as many patients as possible to achieve SVR12, testing for NS5A resistance-associated polymorphisms (positions 28, 30, 31 or 93) is recommended for GT1a-infected patients prior to starting treatment with ZEPATIER to determine the optimal dosage regimen and duration. In clinical trials of ZEPATIER, 12 percent (37/309) of GT1a-infected U.S. study participants had these NS5A resistance-associated polymorphisms at baseline. A 16-week regimen of ZEPATIER with RBV is recommended for GT1a-infected patients with these baseline NS5A polymorphisms as described in the above table.

“This approval provides patients and physicians with an additional treatment option that has the potential to cure many patients with chronic hepatitis C in the United States,” said Dr. Ira Jacobson, site chair, department of medicine, Mount Sinai Beth Israel, New York. “ZEPATIER is a once-daily, single-tablet direct-acting antiviral that has demonstrated high cure rates in genotype 1 and in genotype 4, including treatment-naïve and treatment-experienced patients with or without compensated cirrhosis and those with chronic kidney disease.”

The company anticipates that ZEPATIER will be available for shipping to wholesalers within seven business days.

“Chronic hepatitis C is a potentially devastating illness that can cause serious long-term health consequences for patients, including reduced liver function, liver failure or liver cancer,” said Michael Ninburg, executive director, Hepatitis Education Project, Seattle. “Today, chronic hepatitis C is a curable condition for many patients, and we are fortunate to have multiple therapeutic tools that can mitigate its impact.”

Selected Safety Information about ZEPATIER (elbasvir and grazoprevir) (continued)

The concomitant use of ZEPATIER with certain drugs may lead to possible clinically significant adverse reactions from greater exposure to ZEPATIER or concomitant drugs. Coadministration of ZEPATIER is not recommended with certain strong CYP3A inhibitors (e.g., ketoconazole or the cobicistat-containing regimens of elvitegravir/cobicistat/emtricitabine/tenofovir [disoproxil fumarate or alafenamide]). Healthcare professionals should not exceed atorvastatin 20mg/daily or rosuvastatin 10mg/daily when given with ZEPATIER. If ZEPATIER is given with fluvastatin, lovastatin or simvastatin, healthcare professionals should give the lowest statin dose necessary and closely monitor for statin-associated adverse events. If ZEPATIER and tacrolimus are coadministered, frequent monitoring of tacrolimus whole blood concentrations, changes in renal function and tacrolimus-associated adverse events is recommended.

The concomitant use of ZEPATIER and certain drugs may cause significant decrease of elbasvir and grazoprevir plasma concentrations, which may lead to reduced therapeutic effect of ZEPATIER and possible development of resistance. Coadministration of ZEPATIER is not recommended with moderate CYP3A inducers (e.g., nafcillin, bosentan, etravirine, modafinil).

In subjects receiving ZEPATIER for 12 weeks, the most commonly reported adverse reactions of all intensity (greater than or equal to 5% in placebo-controlled trials) were fatigue, headache and nausea. In subjects receiving ZEPATIER with RBV for 16 weeks, the most commonly reported adverse reactions of moderate or severe intensity (greater than or equal to 5%) were anemia and headache.

Pricing Designed to Enable Broad Patient Access to ZEPATIER (elbasvir and grazoprevir)

The latest innovations in chronic HCV treatment that have become available over the past three years, now including ZEPATIER, provide the U.S. with an unprecedented opportunity to significantly reduce the burden of HCV. The scientific community believes that control of HCV infection may be possible and is actively working to achieve that goal by 2030. A significant medical need remains: it is estimated that less than one in five patients with chronic HCV infection are currently treated, with thousands of new cases each year.

ZEPATIER, which received two Breakthrough Therapy designations (for GT1 patients with end stage renal disease on hemodialysis and for GT4 patients) and was thereafter approved by the FDA following priority review, offers a highly effective option for a broad range of adult patients with chronic HCV GT1 or GT4 infection. Public reports indicate that net prices for the most commonly used direct-acting antiviral regimens are substantially lower than the list prices. However, the majority of patients with chronic HCV have not yet been treated, in some cases due to cost constraints. After considering these factors, Merck has established a list price of \$54,600 for a 12-week regimen, which the company believes to be in the range of net prices for other commonly used HCV direct-acting antiviral regimens at 12 weeks of therapy. Merck anticipates that this price, as well as our comprehensive access strategy to seek broad coverage across commercial and public segments, will help broaden and accelerate patient access to treatment and move us closer to our shared goal of reducing the burden of chronic HCV in the U.S.

“Merck’s decades-long commitment in chronic hepatitis C -- and infectious diseases overall -- has been to both scientific innovation and access,” said Robert McMahon, president, U.S. Market, Global Human Health, Merck. “We are embracing this opportunity to partner with payers and physicians to enable as many appropriate patients to be treated as possible, as quickly as possible.”

Financial Assistance Programs for Those Who Need Help With the Cost of Their Medicine

Merck also anticipates that the list price of ZEPATIER will result in lower out-of-pocket medication costs for some

patients. Lower out-of-pocket costs alone do not necessarily reflect a cost advantage in the outcome of the condition treated, because there are other variables that affect relative costs. The direct out-of-pocket costs to patients will vary, depending on an individual's insurance plan.

Privately insured patients who have difficulty affording the co-pay set by their insurance plan may be eligible for significant co-pay assistance and may pay as little as \$5 for each prescription. Maximum savings are limited and terms and conditions apply. Information is available at www.merckaccessprogram-ZEPATIER.com. Merck anticipates that the website for ZEPATIER will be accessible within 24 hours of FDA approval.

Merck also offers assistance to patients who cannot afford ZEPATIER through Merck's 50-year-old Patient Assistance Program. The Merck PAP provides certain Merck medicines free of charge to eligible patients. The Merck PAP for ZEPATIER is designed primarily for the uninsured who, without our assistance, could not afford their medication. Additionally, for those patients whose insurance plan covers ZEPATIER, but who still cannot afford their medication, a request for an exception may be made if they meet certain financial, medical, and/or insurance criteria. For more information about the Merck PAP, please visit www.merckhelps.com or call the Merck Patient Assistance Program at 1-800-405-5810.

Summary of Study Designs

Clinical Trials for GT1 HCV

C-EDGE TN was a randomized, double-blind, placebo-controlled trial in treatment-naïve patients with GT1 or GT4 infection with or without cirrhosis. Patients were randomized in a 3:1 ratio to: ZEPATIER for 12 weeks (immediate treatment group) (N=306) or placebo for 12 weeks followed by open-label treatment with ZEPATIER for 12 weeks (deferred treatment group) (N=102). Among patients with GT1 infection randomized to the immediate treatment group, the median age was 55 years (range: 20 to 78); 56% of the patients were male; 61% were white; 20% were black or African American; 8% were Hispanic or Latino; mean body mass index was 26 kg/m²; 72% had baseline HCV RNA levels greater than 800,000 IU per mL; 24% had cirrhosis; 67% had non-C/C IL28B alleles (CT or TT); and 55% had GT1a and 45% had GT1b chronic HCV infection.

C-EDGE COINFECTION (CO-INFXN) was an open-label, single-arm trial in treatment-naïve HIV-1/HCV co-infected patients with GT1 or GT4 infection with or without cirrhosis. Patients received ZEPATIER for 12 weeks (N=217). Among patients with GT1 infection, the median age was 50 years (range: 21 to 71); 85% of the patients were male; 75% were white; 19% were black or African American; 6% were Hispanic or Latino; mean body mass index was 25 kg per m²; 59% had baseline HCV RNA levels greater than 800,000 IU per mL; 16% had cirrhosis; 65% had non-C/C IL28B alleles (CT or TT); and 76% had GT1a, 23% had GT1b, and 1% had GT1-Other chronic HCV infection.

C-SURFER was a randomized, double-blind, placebo-controlled trial in patients with GT1 infection, with or without cirrhosis, with chronic kidney disease (CKD) Stage 4 (eGFR 15-29 mL/min/1.73 m²) or CKD Stage 5 (eGFR <15 mL/min/1.73 m²), including patients on hemodialysis, who were treatment-naïve or who had failed prior therapy with IFN or PegIFN ± RBV therapy. Patients were randomized in a 1:1 ratio to one of the following treatment groups: elbasvir 50 mg once daily + grazoprevir 100 mg once daily for 12 weeks (N=111) (immediate treatment group) or placebo for 12 weeks followed by open-label treatment with elbasvir + grazoprevir for 12 weeks (N=113) (deferred treatment group). In addition, 11 patients received open-label elbasvir + grazoprevir for 12 weeks (intensive pharmacokinetic [PK] group). Patients randomized to the immediate treatment group and intensive PK group had a median age of 58 years (range: 31 to 76); 75% of the patients were male; 50% were white; 45% were black or African American; 11% were Hispanic or Latino; 57% had baseline HCV RNA levels greater than 800,000 IU/mL; 6% had cirrhosis; and 72% had non-C/C IL28B alleles (CT or TT).

C-EDGE TE was a randomized, open-label comparative trial in patients with GT1 or GT4 infection, with or without cirrhosis, with or without HCV/HIV-1 co-infection, who had failed prior therapy with PegIFN + RBV therapy. Patients were randomized in a 1:1:1:1 ratio to one of the following treatment groups: ZEPATIER for 12 weeks (N=105), ZEPATIER + RBV for 12 weeks (N=104), ZEPATIER for 16 weeks (N=101), or ZEPATIER + RBV for 16 weeks (N=104). Among patients with GT1 infection, the median age was 57 years (range: 19 to 77); 64% of the patients were male; 67% were white; 18% were black or African American; 9% were Hispanic or Latino; mean body mass index was 28 kg/m²; 78% had baseline HCV RNA levels greater than 800,000 IU/mL; 34% had cirrhosis; 79% had non-C/C IL28B alleles (CT or TT); and 60% had GT1a, 39% had GT1b, and 1% had GT1-Other chronic HCV infection.

C-SALVAGE was an open-label single-arm trial in patients with GT1 infection, with or without cirrhosis, who had failed prior treatment with boceprevir, simeprevir, or telaprevir in combination with PegIFN + RBV. Patients received elbasvir 50 mg once daily + grazoprevir 100 mg once daily + RBV for 12 weeks (N=79). Patients had a median age of 55 years (range: 23 to 75); 58% of the patients were male; 97% were white; 3% were black or African American; 15% were Hispanic or Latino; mean body mass index was 28 kg/m²; 63% had baseline HCV RNA levels greater than 800,000 IU/mL; 43% had cirrhosis; and 97% had non-C/C IL28B alleles (CT or TT); 46% had baseline NS3 resistance-associated substitutions.

Clinical Trials for GT4 HCV

The efficacy of ZEPATIER in patients with GT4 chronic HCV infection was demonstrated in C-EDGE TN, C-EDGE CO-INFN, C-EDGE TE, and C-SCAPE. C-SCAPE was a randomized, open-label trial which included treatment-naïve patients with GT4 infection without cirrhosis. Patients were randomized in a 1:1 ratio to elbasvir 50 mg once daily + grazoprevir 100 mg once daily for 12 weeks (N=10) or elbasvir 50 mg once daily + grazoprevir 100 mg once daily + RBV for 12 weeks (N=10). In these combined studies in patients with GT4 infection, 64% were treatment-naïve; 66%

of the patients were male; 87% were white; 10% were black or African American; 22% had cirrhosis; and 30% had HIV-1/HCV co-infection.

About Merck

Today's Merck is a global health care leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to health care through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on **Twitter**, **Facebook**, **YouTube** and **LinkedIn**.

Forward-Looking Statement of Merck & Co. Inc., Kenilworth, NJ, USA

This news release of Merck & Co., Inc., Kenilworth, NJ, USA (the "company") includes "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include, but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2014 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

Please see Prescribing Information for ZEPATIER (elbasvir and grazoprevir) at http://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_pi.pdf and the Patient Information for ZEPATIER at http://www.merck.com/product/usa/pi_circulars/z/zepatier/zepatier_ppi.pdf

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