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State of Alaska Department of Health and Social Services, Division of Health Care Services

Submission Request Form for Pharmaceutical Manufacturers

Fax this request to: 1-888-656-6822 ATTN: John McCall, R.Ph.

Note: Processing May be Delayed if Information Submitted is Illegible or Incomplete

Members of the Pharmacy and Therapeutics (P&T) Committee have requested that all clinical information, questions, or comments about the Preferred Drug List (PDL) be sent directly to Magellan Medicaid Administration. Manufacturers and other interested parties have been requested not to contact the members directly. Written comments on the PDL from all interested parties should be submitted to Erin Narus, PharmD, R.Ph. at the State of Alaska.

Note: Manufacturers submitting comments are requested to do so through their Product Manager using this form. This form constitutes a request for *NEW* information pertaining to peer-reviewed literature including off-label peer-reviewed studies.

Contact Information

MANUFACTURER NAME: Gilead Sciences, Inc.

DATE: 10-28-2016

PRODUCT MANAGER'S NAME: Coleen Fong, PharmD

TITLE: Associate Director, Medical Sciences

ADDRESS: 333 Lakeside Dr.

CITY: Foster City

STATE: CA

ZIP CODE: 94404

PHONE NUMBER: 916-215-4048

FAX NUMBER:

PRODUCT: Sofosbuvir 400 mg and Velpatasvir 100 mg (Epclusa) tablet

Clinical Rationale Request for Consideration (If additional space is required, use Clinical Rationale Continuation Page).

Feld JJ, et al conducted a phase 3, double-blind, placebo-controlled study involving treatment naive and experienced patients with chronic HCV genotypes (GT) 1, 2, 4, 5 or 6 infection. The cohort also included those with compensated cirrhosis. Subjects were randomized in a 5:1 ratio to sofosbuvir 400 mg and velpatasvir 100 mg daily or matching placebo for 12 weeks. The primary end point was a sustained virologic response (SVR12) at 12 weeks after the end of therapy. Those who had previously received a nucleotide analogue HCV NS5B inhibitor or any NS5A inhibitor were excluded from the trial. 847 patients were initially screened; 741 were enrolled and 706 underwent randomization. There were 35 patients with GT 5 and all received the single tablet regimen (STR) of sofosbuvir and velapatasvir, per prespecified protocol due to the low numbers. One patient was lost to follow-up after undergoing randomization, and had been assigned to the sofosbuvir and velpatasvir group, prior to receiving drug treatment. A total of 624 patients received sofosbuvir and velpatasvir and 116 patients received placebo. In the sofosbuvir and velpatasvir group, there were 34% GT 1a, 19% GT 1b, 17% GT 2, 19% GT 4, 6% GT 5, and 7% GT 6. Most patients were white (79%) and male (60%); 19% had cirrhosis. Of the 201 sofosbuvir and velpatasvir patients with prior treatment experience, 28% had received peginterferon, ribavirin, and protease inhibitor; 61% had received peginterferon and ribavirin; 48% of these had persistently detectable HCV RNA while on therapy and 51% had a virologic relapse or breakthrough. Overall, the SVR12 for sofosbuvir and velpatasvir was 99% (618/624). Rates of SVR12 were similar regardless of HCV GT: 98% (206/210) GT 1a, 99% (117/118) GT 1b, 100% (104/104) GT 2, 100% (116/116) GT 4, 97% (34/35) GT 5, and 100% (41/41) GT 6. Of the 121 patients with compensated cirrhosis and any GT, SVR12 was 99% (120/121). Of the 624 patients who received one dose of sofosbuvir and velpatasvir, two (<1%) patients experienced a virologic failure. At baseline, NS5A resistant-associated variants (RAV) were detected in 257 of 616 (42%) of patients. 255 of 257 (99%) of patients had a SVR. Of the 624 patients receiving sofosbuvir and velpatasivr, one patient (<1%) discontined treatment prematurely due to an adverse event. There were no significant differences among the two groups in the rates of adverse events. The most common adverse events were headache, fatigue, nasopharyngitis, and nausea.

Reference: Feld JJ, Jacobson IM, Hezode C, et al. Sofosbuvir and velpatasvir for HCV Genotype 1, 2, 4, 5 and 6 Infection. N Engl J

Magellan HEALTH

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Published Citations (If additional space is required, use Published Citations Continuation Page).

Curry MP, et al, conducted a phase 3, open-label study with treatment naive and experienced patients with HCV GT 1 through 6 who had decompensated cirrhosis, as classified by Child-Pugh-Turcotte (CPT) class B. Patients were randomally assigned 1:1 to receive sofosbuvir and velpatasvir STR daily for 12 weeks, sofosbuvir-velpatasvir plus ribavirin for 12 weeks or sofosbuvir and velpatasivr for 24 weeks.. The primary end point was SVR12. Secondary efficacy end points included the change from baseline in the CPT and MELD scores at 12 weeks after the end of treatment. 438 patients were screened; 268 were randomized and 267 received treatment. 60% had GT 1a, 18% GT 1b, 4% GT 2, 15% GT 3, 3% GT 4, and less than 1% GT 6. A total of 6% of patients were black, and 55% had received prior HCV treatment. The median baseline CPT score was 8 (range, 5 to 10), the median baseline MELD score was 10 (range, 6 to 24), and the median creatinine clearance was 84.7 ml/min (range, 15 to 198). The majority (95%) had a baseline MELD score of 15 or less. All the patients had CPT class B cirrhosis at screening, however, 27 (10%) had CPT class A or CPT class C cirrhosis at treatment baseline. SVR12 was 83% for those receiving sofosbuvir and velpatasvir for 12 weeks versus 94% for those receiving sofosbuvir-velpatasvir plus ribavirin for 12 weeks versus 86% for those receiving sofosbuvir and velpatasvir for 24 weeks ($p<0.001$). Among those with GT 1, SVR was 88% for those who received sofosbuvir and velpatasvir for 12 week, 96% for those who received sofosbuvir-velpatasvir plus ribavirin for 12 weeks, and 92% for those who received sofosbuvir and velpatasvir for 24 weeks. Among those with GT 3, SVR was 85% for those who received sofosbuvir-velpatasvir plus ribavirin for 12 weeks compared to 50%, respsectively for those who receivied sofosbuvir and velpatasvir for 12 and 24 weeks. All the patients with GT 2, 4, or 6 had a SVR except for one patient with HCV GT 2 who was randomized to sofosbuvir and velpatasvir for 24 weeks. A total of 22 patients had virologic failure-11/90 (12%) received sofosbuvir and velpatasvir for 12 weeks, 3/87 (3%) received sofosbuvir-velpatasvir plus ribavirin for 12 weeks, and 8/90 (9%) received sofosbuvir and velpatasvir for 24 weeks. Of the 22 patients who had virologic failure, 20 had a relapse and two (both had GT 3) had virologic breakthrough. Of the 267 patients treated, 250 had CPT and MELD scores available at post-treatment week 12. 117/250 (47%) had an improvement in the CPT score over baseline, 106/250 (42%) had no change in the CPT score, and 27/250 (11%) had a worsening in the CPT score. Of the 223 patients with a baseline MELD score of less than fifteen, 114/223 (51%) had an improved MELD score, 49/223 (22%) had no change in the MELD score, and 60/223 (27%) had a worsening in the MELD score. Twenty-seven patients with a baseline MELD score of 15 or more. 22/27 (81%) had an improved MELD score, 3/27 (11%) had no change in the MELD score, and 2/27 (7%) had a worsening in the MELD score. 255 patients had pretreatment NS5A sequencing data available. 72/255 (28%) had pretreatment RAVs. 64/72 (89%) had a SVR, compared with 169/183 (92%) who did not. Among those with GT 1 receiving sofosbuvir-velpatasvir plus ribavirin, the SVR in those with NS5A RAVs was 100% compared to 98% in those without NS5A RAVs. Among those with GT 1 in the sofosbuvir and velpatasvir group, among those with NS5A RAVs, the SVR was 80% and 90% receiving 12 and 24 weeks of treatment, respectively. Among those that did not have NS5A RAVs, the SVR was 96% and 98%, respectively. A total of nine patients discontinued treatment prematurely due to an adverse event. Serious adverse events occurred in 19% of patients who received sofosbuvir and velpatasvir for 12 weeks, 16% of those who received sofosbuvir-velpatasvir plus ribavirin, and 18% of those who received sofosbuvir and velpatasvir for 24 weeks. The most common serious adverse events were hepatic encephalopathy and sepsis. The most common adverse events were fatigue, nausea, and headache. Reductions in hemoglobin, lymphocytes, and platelets were common in all three groups. In the group that received sofosbuvir-velpatasvir plus ribavirin, decreases in hemoglobin to less than 10 g per deciliter occurred in 23% of patients. In the groups that received sofosbuvir and velpatasvir, the rate of decrease in hemoglobin were 8% and 1%, respectively.

Reference: Curry MP, O'Leary JG, Bzowej N, et al. Sofosbuvir and Velpatasvir for HCV in Patients with Decompensated Cirrhosis. N Engl J Med 2015;373(27):2618-2628.

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Clinical Rationale Continuation Page (Use only if needed).

ASTRAL-5 is a phase 3, single, open-label, multicenter study evaluating sofosbuvir and velpatasvir STR once daily for 12 weeks in treatment naive or experienced HCV GT 1-4 patients co-infected with HIV. All subjects were suppressed (HIV RNA <50 copies/ml) and on a tenofovir disoproxil fumarate (TDF)-based or lamivudine (3TC)/abacavir (ABC) containing HIV regimens. The primary end point was SVR12. Baseline characteristics included median age of patients 54 years, 86% male, 45% Black, 18% cirrhotic, 29% treatment experienced, mean HCV RNA 6.3 log10IU/ml, mean CD4count 598 cells/ul, 62% GT 1a, 11% GT 1b, 10% GT 2, 11% GT 3, and 5% GT 4. Overall, SVR12 was achieved in 95% (101/106). Among those with GT 1a, SVR 95% (63/66); GT 1b 92% (11/12), GT 2 100% (11/11), GT 3 92% (11/12), and GT 4 100% (5/5). Two patients with GT 1a relapsed. SVR12 was similar based on treatment experience or cirrhosis status. Among those with cirrhosis, SVR12 100% (19/19) compared to 94% (82/87) without cirrhosis. Among those who were treatment experienced, SVR12 97% (30/31), compared to 93% (71/75) who were treatment naive. Of the 103 patients who had available data on virologic outcome, twelve had detectable NS5A RAVs at baseline. All twevle with a 15% deep sequencing cutoff achieved SVR12 100%. Among the 91 patients without baseline NS5A RAVs, 98% (89/91) achieved SVR12. Treatment was well tolerated and safe. The most common adverse events were fatigue, headache, arthralgia, upper respiratory tract infection, diarrhea, insomnia and nausea. The majority of adverse events were mild in severity (grade 1 or 2). Grade 3-4 adverse events or laboratory abnormalities were experienced by 8% and 18% of subjects, respectively.

Reference: Brau N, Wyles D, Kottili S, et al. Sofosbuvir/Velpatasvir for 12 Weeks in Patients Coinfeted with HCV and HIV-1: The ASTRAL-5 Study [Presentation]. Paper presented at: International AIDS Society (IAS); 18-22 July, 2016; Durban, South Africa.