
Notice of Independent Review Decision

IRO REVIEWER REPORT TEMPLATE – HC

[Date notice sent to all parties]:

06/15/2015

IRO CASE #:

DESCRIPTION OF THE SERVICE OR SERVICES IN DISPUTE: Harvoni for the treatment of naïve chronic hepatitis C genotype 1 without cirrhosis.

A DESCRIPTION OF THE QUALIFICATIONS FOR EACH PHYSICIAN OR OTHER HEALTH CARE PROVIDER WHO REVIEWED THE DECISION:

Board Certified in Internal Medicine and Board Certified in Infectious Disease

REVIEW OUTCOME:

Upon independent review, the reviewer finds that the previous adverse determination/adverse determinations should be:

- Upheld (Agree)
- Overturned (Disagree)
- Partially Overturned (Agree in part/Disagree in part)

Provide a description of the review outcome that clearly states whether medical necessity exists for each of the health care services in dispute.

PATIENT CLINICAL HISTORY [SUMMARY]:

The patient is a male who is being recommended for Harvoni for treatment of hepatitis C infection. This case was previously denied, as there was a lack of evidence the patient has stage 3 hepatic fibrosis, serious extrahepatic manifestation of HCV, or HIV co-infection. A clinical note dated 10/01/2014 indicated the patient was being seen for evaluation of hepatitis C infection. It was noted at that time the patient was seen approximately 3 years prior and decided on an expectant approach. The patient was noted to not have evidence of advanced liver disease and a baseline evaluation demonstrated stage 0 to 1 and the patient had genotype 1. A quantitative HCV report dated 10/07/2014 indicated that the patient had hepatitis C, quantitation

of 1,656,730. An HCV FibroSure report dated 10/07/2014 indicated the patient's fibrosis score was 0.29 with a fibrosis stage of F1. An ultrasound of the abdomen performed on 10/09/2014 was noted to reveal a mildly nodular liver without identification of hepatic mass. A follow-up visit on 01/09/2015 indicated that the physician was recommending that the patient undergo treatment with Harvoni 1 tablet once a day for 12 weeks for treatment of the patient's genotype 1 hepatitis C.

ANALYSIS AND EXPLANATION OF THE DECISION INCLUDE CLINICAL BASIS, FINDINGS, AND CONCLUSIONS USED TO SUPPORT THE DECISION:

According to the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America, treatment should be started in all HCV infected patients, except those with limited life expectancy (less than 12 months) due to non-liver related comorbid conditions; however, urgent initiation of treatment is recommended for patients who are at risk for developing complications of liver disease, such as those with advanced fibrosis and/or compensated liver cirrhosis or patients who have a history of IV drug use or female patients who are of child bearing age and wanting to have children. Additionally, according to the US Food and Drug Administration, Harvoni is indicated for treatment of hepatitis C virus in adults with genotype 1 infection for up to 12 weeks who are treatment naïve with or without liver cirrhosis. Furthermore, there is abundant scientific evidence for using Harvoni in the treatment of Hepatitis C positive patients with genotype 1 based on the very high rate of efficacy; Harvoni has been shown to provide 99 percent sustained virologic response after 12 weeks. After review of the referenced medical literature and clinical documentation submitted for review, the request for Harvoni is not supported. There is documentation that the patient has HCV genotype 1 infection. The provided documentation indicated that the patient was denied this medication previously for lack of evidence of stage 3 hepatic fibrosis, serious extrahepatic manifestations, and co-infection with HIV, however, the current medical literature to include the FDA does not indicate that these findings need to be present prior to patients being treated. In fact, the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America states that the only exception to treatment is patients with a limited life expectancy due to non-liver related comorbid conditions. Further, there is scientific evidence for using Harvoni in patients with HCV genotype 1a infection based on the very high rate of efficacy (99%). However, there is a need for clarification whether the patient is a genotype 1a versus 1b as Harvoni is currently only recommended for the treatment of genotype 1a patients. It was only documented that the patient was genotype 1. Without this clarification, the request for Harvoni is non-certified.

A DESCRIPTION AND THE SOURCE OF THE SCREENING CRITERIA OR OTHER CLINICAL BASIS USED TO MAKE THE DECISION:

- PEER REVIEWED NATIONALLY ACCEPTED MEDICAL LITERATURE** The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America (2014). Recommendations for Testing, Managing, and Treating Hepatitis C. AASLD Practice Guidelines.

Afdhal N, Zeuzem S, Kwo P, Chojkier M, Gitlin N, Puoti M, Romero-Gomez M, Zarski JP, Agarwal K, Buggisch P, Foster GR, Bräu N, Buti M, Jacobson IM, Subramanian GM, Ding X, Mo H, Yang JC, Pang PS, Symonds WT, McHutchison JG, Muir AJ, Mangia A, Marcellin P; ION-1 Investigators, (2014). Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. *N Engl J Med*; 370(20):1889-98.

Gentile I, Borgia G, (2014). Ledipasvir/Sofosbuvir administration achieves very high rate of viral clearance in patients with HCV genotype 1 infection without cirrhosis, regardless of ribavirin co-administration or length of treatment. *Evid Based Med*; 19(6):223-4.

Mangia, A., Marcellin, P., Kwo, P., Foster, G. R., Buti, M., Bräu, N., ... & Afdhal, N. (2014). All Oral Fixed-Dose Combination Sofosbuvir/Ledipasvir With or Without Ribavirin for 12 or 24 Weeks in Treatment-Naïve Genotype 1 HCV-Infected Patients: The Phase 3 Ion-1 Study. *Journal of Hepatology*, 60(1), S523-S524.

Kwo, P. Y., Reddy, K. R., Pockros, P. J., Di Bisceglie, A. M., Arora, S., Yang, J. C., ... & Afdhal, N. H. (2014). All oral fixed-dose combination Sofosbuvir/Ledipasvir with or without ribavirin for 12 or 24 weeks in treatment-experienced genotype 1 HCV-infected patients: The Phase 3 Ion-2 Study. *Gastroenterology*, 146(5), S-904.

Kowdley, K. V., Stuart, G. C., Reddy, R. K., Rossaro, L., Bernstein, D. E., An, D., ... & Fried, M. W. (2014). Sofosbuvir/Ledipasvir with and without Ribavirin for 8 weeks compared to Sofosbuvir/Ledipasvir for 12 weeks in treatment-naïve non-cirrhotic genotype-1 HCV-infected patients: The Phase 3 Ion-3 Study. *Journal of Hepatology*, 60(1), S23-S24.

OTHER EVIDENCE BASED, SCIENTIFICALLY VALID, OUTCOME FOCUSED GUIDELINES

U.S. Food and Drug Administration, (2014). Harvoni (ledipasvir and sofosbuvir). Medication Guide.
http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/205834s000lbl.pdf

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