Treatment of Hepatitis C with Dual Therapy (Ribavirin Plus Pegylated Interferon Alfa)

Archived Medical Policy

Archived medical policies are no longer subject to periodic review, are maintained for reference, and may be returned to active status if the need is identified.

Policy # 00374
Original Effective Date: 11/01/2013
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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Treatment of Hepatitis C with Triple Therapy (Ribavirin Plus Pegylated Interferon Alfa Plus Telaprevir [Incivek®] or Boceprevir [Victrelis®])‡ is addressed separately in medical policy 00373.

Note: Pegylated Interferons (Pegasys®, PegIntron®)‡ for Other (Non-Hepatitis C) Uses is addressed separately in medical policy 00375.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider dual therapy (combination of ribavirin plus pegylated interferon alfa [Pegasys or PegIntron]) for the treatment of individuals with Chronic Hepatitis C Virus (HCV) Genotypes 1 thru 6 to be **eligible for coverage.**

Patient Selection Criteria
Based on review of available data, the Company may consider the use of dual therapy (as defined above) when the following criteria are met:

- Patient has a diagnosis of chronic hepatitis C virus (HCV) genotypes 1 thru 6; (Note that the treatment of choice for chronic hepatitis C virus (HCV) genotype 1 is a triple therapy regimen (ribavirin plus pegylated interferon alfa plus HCV Protease Inhibitor). Explanation will need to be provided for use of a dual therapy regimen in patients with chronic HCV genotype 1); and
- Pegylated interferon alfa is used in combination with ribavirin (unless there is a contraindication to ribavirin therapy); and
- Patient has detectable hepatitis C virus (HCV) RNA levels; and
- Patient has compensated liver disease (including those with cirrhosis); and
    - Patient is 5 years of age and older if agent selected is pegylated interferon alfa-2a (Pegasys); or
    - Patient is 3 years of age and older if agent selected is pegylated interferon alfa-2b (PegIntron); and

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- One of the following has been met:
  - Patient has not received previous treatment with a pegylated interferon in combination with ribavirin; or
  - Patient is considered a relapser or non-responder to **one** of the following treatments:
    - Non-pegylated interferon monotherapy, or
    - Non-pegylated interferon with ribavirin, or
    - Pegylated interferon monotherapy

Note: An initial authorization will be granted based on the hepatitis C virus (HCV) genotype, re-authorization will be granted based on hepatitis C virus (HCV) RNA levels submitted (per the table below):

HCV Genotype:	At Treatment Week:	Submit:
1,4,5,6, or HIV Infected Patient	12 (1st Re-auth)	HCV RNA levels from treatment week 12
	24 (2nd Re-auth)	HCV RNA levels from treatment week 24
2,3, or Ribavirin Contraindication	N/A	N/A

Note: Due to time frames for hepatitis C virus (HCV) RNA level turnaround times, there is a window of extended approval time to allow for lab results to be obtained and submitted.

Note: Subsequent treatment lengths will be determined based on the table below:

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Genotype	**Week 12 HCV Results**	**Length of Therapy** (P = Pegylated interferon alpha, R=Ribavirin)	**Approvals**
1,4,5,6 OR HIV Infected Patient	Undetectable HCV RNA OR Early viral response (at least a 2 log decrease in viral load during first 12 weeks of treatment)	48 weeks (48 weeks of P/R)	Initial Auth Time: Approve through treatment week 12 1st Re-auth Time (based on 12 week levels): Approve through treatment week 24 2nd Re-auth Time (based on 24 week levels): Approve through treatment week 48
2-3	N/A	24 weeks (24 weeks of P/R)	Initial Auth Time: Approve through treatment week 24
Ribavirin Contraindication	N/A	48 weeks (48 weeks of P)	Initial Auth Time: Approve through treatment week 48

Note: If at any time treatment week 24 levels are detectable, all drugs should be discontinued.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of dual therapy (combination of ribavirin plus pegylated interferon alfa [Pegasys or PegIntron]) for the treatment of individuals with chronic hepatitis C virus (HCV) when patient selection criteria are not met to be **investigational.***

Background/Overview

Hepatitis C is the most common blood borne pathogen. In the US, there are approximately 3.2 million people chronically infected with hepatitis C. Hepatitis C, a single-stranded RNA virus, is genetically complex with several recognized genotypes. Genotypes 1, 2, and 3 are the most frequently encountered genotypes worldwide of HCV. Type 1a is most frequently found in Northern Europe and North America, while 1b is most common in Japan and Southern and Eastern Europe.

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Up until the last few years, Interferon alfa has been considered the only effective treatment of hepatitis C. A total of 40% of patients will show an initial response to interferon alfa, but most patients relapse soon after stopping treatment. Ribavirin (Rebetron®)‡†, a synthetic nucleoside analogue with antiviral activity, has also been investigated as a treatment of hepatitis C. In the past few years, pegylated interferon alfa (Pegasys and Pegintron) and ribavirin have become the standard treatment in patients with non-genotype 1 HCV infections. The addition of the pegylated moiety improved the pharmacokinetic profile of the drug as well as doubled sustained virologic response rates. The recent approval of hepatitis C protease inhibitors such as Victrelis and Incivek has improved the arsenal of treatment options for those patients with hepatitis C genotype 1. These new protease inhibitors are used in combination with pegylated inferferon alfa and ribavirin for a variety of timeframes depending on the patient's hepatitis C treatment status.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Pegasys (peginterferon alfa-2a) was approved by the FDA in 2002. It carries indications for both Hepatitis C and Hepatitis B Virus. Peg-Intron (peginterferon alfa-2b was approved by the FDA in 2001. It carries an indication for the treatment of hepatitis C.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Pegasys (Pegylated Interferon alfa-2a)
One study compared Pegasys + ribavirin vs. Pegasys + Placebo vs. Interferon alfa-2b + ribavirin. The study measured the sustained virological responses (SVRs) for the drug combinations. If all subjects are taken into account, the SVR associated with the groups previously mentioned were 53%, 29%, and 44% respectively, showing that the Pegasys + ribavirin group had the largest percentage of patients achieving a virologic response. If broken down into genotypes, the results are as follows: Genotype 1: SVRs were 44%, 20%, and 36% for Pegasys + ribavirin vs. Pegasys + Placebo vs. Interferon alfa-2b + ribavirin, respectively. For genotypes 2-6, the SVR rates were as follows: 70%, 46%, and 59% for Pegasys + ribavirin vs. Pegasys + placebo vs. Interferon alfa-2b + ribavirin, respectively. This study proved that Pegasys + ribavirin is a better treatment option than the standard interferon + ribavirin regimen.

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PegIntron (Pegylated Interferon alfa-2b)
One study compared PegIntron + ribavirin vs. Intron A (interferon) with ribavirin. Rates of response to treatment were tested at week 24. Overall, the patients treated with PegIntron plus ribavirin had a response rate of 52% vs. those being treated with Intron A + ribavirin (46%). If broken down into genotype, the results are as follows: for genotype 1: 41% of patients taking PegIntron + ribavirin had a response vs. 33% of those patients on Intron A + ribavirin. For genotypes 2-6, 75% of patients taking PegIntron + ribavirin had a higher response rate vs. 73% of patients taking Intron A + ribavirin.

Treatment
According to the AASLD (American Association for the Study of Liver Diseases), combination therapy with a pegylated interferon alfa and ribavirin is the standard of care for patients with genotypes 2-6. Current guidelines do not address which pegylated interferon is preferred. Since the publication of the above trials, new data has come out proving that a triple therapy regimen is the treatment of choice for patients with genotype 1.

References

1. Ge, D., Fellay, J., Thompson, A.J., Simon, J.S., Shianna, K.V., Urban, T.J., Heinzen, E.L., Qiu, P., Bertelsen, A.H., Muir, A.J., Sulkowski, M., McHutchison, J.G., Goldstein, D.B., Genetic variation in IL28B predicts hepatitis C treatment-induced viral clearance, Nature 2009;461(7262):399-401.
2. Thompson, A.J., Muir, A.J., Sulkowski, M.S., Ge, D., Fellay, J., Shianna, K.V., Urban, T., Afdhal, N.H., Jacobson, I.M., Esteban, R., Poordad, F., Lawitz, E.J., McCone, J., Shiffman, M.L., Galler, G.W., Lee, W.M., Reindollar, R., King, J.W., Kwo, P.Y., Ghalib, R.H., Freilich, B., Nyberg, L.M., Zeuzem, S., Poynard, T., Vock, D.M., Pieper, K.S., Patel, K., Tillmann, H.L., Noviello, S., Koury, K., Pedicone, L.D., Brass, C.A., Albrecht, J.K., Goldstein, D.B., McHutchison, J.G., Interlukin-28B polymorphism improves viral kinetics and is the strongest pretreatment predictor of sustained virologic response in genotype 1 hepatitis C virus, Gastroenterology 2010;139:120-129.
3. Ghany M, Strader D, Thomas D, Seeff L. AASLD: Diagnosis, Management, and Treatment of Hepatitis C: An Update. Hepatology; 2009: 1335-1374.
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5. PegIntron [package insert]. Merck and Co, Inc. Whitehouse Station, NJ. 2001.
6. Pegasys [package insert]. Genentech USA, Inc. San Francisco, CA. 2013.

Policy History

Original Effective Date: 11/01/2013
09/05/2013 Medical Policy Committee review
09/18/2013 Medical Policy Implementation Committee approval. New policy. One of three policies that replace medical policies 00171 Treatment of Hepatitis C and B with Pegylated Interferon and/or Ribavirin and 00310 Treatment of Hepatitis C with Pegylated Interferon, Ribavirin and/or Telaprevir (Incivek) and Boceprevir (Victrelis).

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09/04/2014	Medical Policy Committee review
09/17/2014	Medical Policy Implementation Committee approval. No change to coverage.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
09/03/2015	Medical Policy Committee review
09/23/2015	Medical Policy Implementation Committee approval. No change to coverage.
09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. No change to coverage.
09/07/2017	Medical Policy Committee review. Recommend archiving policy.
09/20/2017	Medical Policy Implementation Committee approval. Archived
Next Scheduled Review Date:	Archived medical policy.

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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