

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

Policy # 00374

Original Effective Date: 11/01/2013

Current Effective Date: 02/01/2026

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. Trials and clinical studies are excluded from coverage under benefits.

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

When Services Are 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 no longer this regimen. Explanation will need to be provided for use of this 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 (1 st Re-auth)	HCV RNA levels from treatment week 12
	24 (2 nd 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:

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 1 st Re-auth Time (based on 12 week levels): Approve through treatment week 24 2 nd Re-auth Time (based on 24 week levels): Approve through treatment week 48

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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.

Pegylated interferons (Pegasys and PegIntron) were once used as one of the main components for the treatment of chronic hepatitis C virus but have since fallen out of favor due to newer, much more effective medications becoming available. These products are now effectively obsolete for the treatment of hepatitis C virus.

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, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

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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.

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.

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., Interleukin-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.
4. PegIntron [package insert]. Merck and Co, Inc. Whitehouse Station, NJ. 2001.
5. Pegasys [package insert]. Genentech USA, Inc. San Francisco, CA. 2013.

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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).

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

01/10/2019 Medical Policy Committee review. Recommend bringing back to active status.

01/23/2019 Medical Policy Implementation Committee approval. Brought back to active status.

01/03/2020 Medical Policy Committee review

01/08/2020 Medical Policy Implementation Committee approval. Removed reference to policy 00373 (retired). Updated background information and rationale/source to reflect most recent information.

01/07/2021 Medical Policy Committee review

01/13/2021 Medical Policy Implementation Committee approval. No change to coverage.

01/06/2022 Medical Policy Committee review

01/12/2022 Medical Policy Implementation Committee approval. No change to coverage.

01/05/2023 Medical Policy Committee review

01/11/2023 Medical Policy Implementation Committee approval. No change to coverage.

01/04/2024 Medical Policy Committee review

01/10/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

01/02/2025 Medical Policy Committee review

01/08/2025 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

01/05/2026 Medical Policy Committee review

01/07/2026 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 01/2027

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***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. Food and Drug Administration (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 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.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.