Pegylated Interferons (Pegasys®, PegIntron®) for Other (Non-Hepatitis C) Uses

Policy # 00375
Original Effective Date: 11/01/2013
Current Effective Date: 11/11/2024

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.

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.*

Chronic Hepatitis B

Based on review of available data, the Company may consider the use of pegylated interferon alfa-2a (Pegasys®)‡ or pegylated interferon alfa-2b (PegIntron®)‡ for the treatment of chronic hepatitis B to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the treatment of chronic hepatitis B with pegylated interferon alfa-2a (Pegasys) or pegylated interferon alfa-2b (PegIntron) for 48 weeks will be considered when ALL of the following criteria are met:

- Patient is ≥ 18 years of age; AND
- Patient has a confirmed diagnosis of compensated chronic hepatitis B; AND
- Patient has not received previous treatment with pegylated interferon therapy.

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Other Indications
Based on review of available data, the Company may consider the use of pegylated interferon alfa-2a (Pegasys) or pegylated interferon alfa-2b (PegIntron) for certain other off-label indications to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for the treatment of certain other off-label indications with pegylated interferon alfa-2a (Pegasys) or pegylated interferon alfa-2b (PegIntron) will be considered when ONE of the following criteria is met:

- Patient has a diagnosis of chronic myeloid leukemia (CML); OR
- Patient has a diagnosis of essential thrombocythemia.

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 pegylated interferon alfa-2a (Pegasys) or pegylated interferon alfa-2b (PegIntron) when patient selection criteria are not met or for indications not listed in the patient selection criteria to be **investigational.***

Background/Overview

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. There are however, other uses for the pegylated interferons. Pegasys (pegylated interferon alfa-2a) is indicated for use in chronic hepatitis C as well as for use as monotherapy in patients with chronic hepatitis B virus. PegIntron (pegylated interferon alfa-2b) is currently only indicated for the treatment of chronic hepatitis C virus.

Hepatitis B
There are an estimated 1.25 million hepatitis B carriers in the United States. Carriers of Hepatitis B are at an increased risk of developing cirrhosis, hepatic decompensation, and hepatocellular carcinoma. It is estimated that 15-40% of carriers of hepatitis B will develop some sort of serious sequelae during their lifetime. Hepatitis B is often transmitted parenterally (by either contaminated blood or blood products) but can also be spread through sex partners and in closed institutions.

Other Uses
There is literature on the usage of pegylated interferons for the treatment of patients with CML. There is also literature on its usage in patients with essential thrombocythemia.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Pegasys (pegylated interferon alfa-2a) was approved by the FDA in 2002. It carries indications for both Hepatitis C and Hepatitis B Virus. PegIntron (pegylated interferon 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. Food and Drug Administration 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.

Pegylated interferon alfa-2a (Pegasys) 180 mcg weekly was studied in a Phase III trial as monotherapy vs. pegylated interferon alfa-2a 180 mcg weekly plus lamivudine 100mg daily vs. lamivudine 100 mg daily as monotherapy for 48 weeks. HBeAg seroversion was similar in the three groups at the end of treatment: 27%, 24%, and 20%, respectively, but the HBeAg seroconversion was significantly higher in the two groups that received pegylated interferon alfa-2a therapy when assessed 24 weeks after therapy was stopped (32%, 27%, and 19%, respectively). The data indicated that the pegylated interferon alfa-2a monotherapy was superior to lamivudine monotherapy and

comparable to pegylated interferon alfa-2a plus lamivudine combination therapy in sustaining HBeAg seroconversion. There have also been studies looking at the efficacy of pegylated interferon alfa-2b for the treatment of patients with hepatitis B that have somewhat similar results as pegylated interferon alfa-2a.

There is also evidence of using pegylated interferon alfa in patients with CML. In CML, the interferon class has typically shown evidence of cytogenetic response and improved survival. This has been tested in pegylated interferon alfa as well. A number of studies also exist for the use of pegylated interferon alfa in the treatment of essential thrombocythemia. Data shows that pegylated interferon alfa decreased the platelet count in patients with essential thrombocythemia and maintained the lower platelet count throughout treatment. Length of therapy depends on the patient's tolerance to the pegylated interferon alfa since it can typically cause unpleasant adverse events.

References

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3. Lok A, McMahon B. American Association for the Study of Liver Diseases (AASLD) Practice Guideline Update Chronic Hepatitis B: Update 2009. Hepatology. 2009.
4. Jabbour E, Kantarjian H, Cortes J, et al. PEG-IFN alfa 2b Therapy in BCR-ABL- Negative Myeloproliferative Disorders. Cancer. 2007;110: 2012-2018.
5. Samuelsson J, Hasselbalch H, Bruserud O, et al. A Phase II Trial of Pegylated Interferon alfa 2b Therapy for Polycythemia Vera and Essential Thrombocythemia. Cancer. 2006;106: 2397-2405.
6. Langer C, Lengfelder E, Thiele J, et al. Pegylated interferon for the treatment of high-risk essential thrombocythemia: results of a phase II study. Haematologica. 2005;90 (10): 1333-1338.
7. Pegylated Interferon Alfa-2a Yields High Rates of Hematologic and Molecular Response in Patients With Advanced Essential Thrombocythemia and Polycythemia Vera. Journal of Clinical Oncology. 2009;27(22): 5418-5424.
8. Michallet M, Maloisel F, Delain M, et al. Pegylated recombinant interferon alfa 2 b vs recombinant interferon alfa 2b for the initial treatment of chronic myelogenous leukemia: a phase III study.

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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. Coverage eligibility unchanged.
01/06/2015	Policy reposted with corrections to clerical error.
09/03/2015	Medical Policy Committee review
09/23/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/07/2017	Medical Policy Committee review. Recommend archiving policy.
09/20/2017	Medical Policy Implementation Committee approval. Archived.
10/04/2018	Medical Policy Committee review.
10/17/2018	Medical Policy Implementation Committee approval. Returned to active status with coverage eligibility unchanged.
10/03/2019	Medical Policy Committee review
10/09/2019	Medical Policy Implementation Committee approval. Removed the notes referencing hepatitis C policies as these drugs are obsolete for those conditions. Updated background information regarding hepatitis C.
10/01/2020	Medical Policy Committee review
10/07/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/07/2021	Medical Policy Committee review

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10/13/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/06/2022	Medical Policy Committee review
10/11/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/05/2023	Medical Policy Committee review
10/11/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/03/2024	Medical Policy Committee review
10/08/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 10/2025

*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.

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**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.

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.