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Section:	Prescription Drugs	**Effective Date:**	July 1, 2026
Subsection:	Anti-infective Agents	**Original Policy Date:**	January 1, 2019
Subject:	Pegasys Pegintron Ribavirin	**Page:**	1 of 10

Last Review Date: June 11, 2026

Pegasys Pegintron Ribavirin

Description

Pegasys (peginterferon alfa-2a), Pegintron (peginterferon alfa-2b), Ribavirin (Moderiba, Rebetol, RibaPak, Ribasphere, RibaTab, ribavirin tablets/capsules)

Background
Interferons are a group of proteins whose effects include antiviral activity, growth regulatory properties, inhibition of angiogenesis, regulation of cell differentiation, enhancement of major histocompatibility complex antigen expression, and a wide variety of immunomodulatory activities. Interferons were the first therapeutic agents that permitted successful antiviral therapy with acceptable sided effects in patients with chronic hepatitis B, C and D. However, in hepatitis C virus (HCV) infections, direct-acting antivirals have become the new paradigm of treatment and have largely replaced interferon therapy. Peginterferons are pegylated interferons. Pegylation is a process whereby a polyethylene glycol (PEG) polymer is attached to the molecule in order to improve drug solubility, stability, and retention time. Ribavirin is a synthetic antiviral used in the treatment of hepatitis C. It works well in combination with peginterferon but not as monotherapy (1-6).

Regulatory Status
FDA-approved indications:
Pegasys (peginterferon alfa-2a) is an inducer of the innate immune response indicated for the treatment of: (7)

1. Chronic Hepatitis C (CHC)
    a. Adult patients: In combination therapy with other hepatitis C virus drugs for adults

with compensated liver disease. Monotherapy is indicated only if patient has contraindication or significant intolerance to other HCV drugs.

b. Pediatric Patients: In combination with ribavirin for pediatric patients 5 years of age and older with compensated liver disease

2. Chronic Hepatitis B (CHB)
   a. Adult Patients: Treatment of adults with HBeAg-positive and HBeAg-negative chronic hepatitis B (CHB) infection who have compensated liver disease and evidence of viral replication and liver inflammation
   b. Pediatric Patients: Treatment of non-cirrhotic pediatric patients 3 years of age and older with HBeAg-positive CHB and evidence of viral replication and elevations in serum alanine aminotransferase (ALT)

Pegintron (peginterferon alfa-2b) is an antiviral indicated for: (8)

1. Chronic Hepatitis C (CHC) in patients with compensated liver disease
   a. In combination with ribavirin and an approved hepatitis C virus (HCV) NS3/4A protease inhibitor in adult patients with HCV genotype 1 infection
   b. In combination with ribavirin in patients with genotypes other than 1, pediatric patients (3-17 years of age), or in patients with genotype 1 infection where the use of HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications, or other clinical factors

Pegintron monotherapy should only be used in the treatment of chronic hepatitis C (CHC) in patients with compensated liver disease if there are contraindications to or significant intolerance to ribavirin and is indicated for use only in previously untreated adult patients. Combination therapy provides substantially better response rates than monotherapy (8).

Ribavirin a nucleoside analogue indicated in: (4-6)

1. Chronic Hepatitis C (CHC)
   a. In combination with interferon alfa-2b (pegylated and nonpegylated) for the treatment of chronic hepatitis C (CHC) in patients 3 years of age an older with compensated liver disease

Pegasys Limitations of Use: (7)

1. Pegasys alone or in combination with ribavirin without additional HCV antiviral drugs is not recommended for treatment of patients with CHC who previously failed therapy with an interferon-alfa
2. Pegasys is not recommended for treatment of patients with CHC who have had solid organ transplantation

Pegasys Off-Label Uses: (9)

1. Myeloproliferative neoplasms – Myelofibrosis
2. Myeloproliferative neoplasms – Polycythemia Vera
3. Myeloproliferative neoplasms – Essential Thrombocythemia

Interferon based therapy has been shown to be effective in the treatment of myeloproliferative neoplasms (MPNs) and the use of Pegasys is supported by the National Comprehensive Cancer Network (NCCN) Guidelines as a valid therapy for this disease state (9).

Pegasys and Pegintron carry a boxed warning regarding risk of serious disorders. The use of Pegasys or PegIntron may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Monitor closely and withdraw therapy with persistently severe or worsening signs or symptoms of the above disorders (7,8).

If Pegasys is administered with other antiviral agents, the contraindications to those agents also apply to the combination regimen (7).

Ribavirin carries boxed warnings regarding embryo-fetal toxicity, hemolytic anemia, and monotherapy. Ribavirin is contraindicated in pregnant women and men whose female partners are pregnant. Pregnancy should be avoided during therapy and for 6months after completion of treatment in both female patients and female partners of male patients who are taking ribavirin. Hemolytic anemia has been reported and may result in worsening of cardiac disease that has led to fatal and nonfatal myocardial infarctions. Patients with a history of significant or unstable cardiac disease should not be treated with ribavirin. Ribavirin monotherapy is not effective for the treatment of chronic hepatitis C infection (4-6).

The safety and efficacy of Pegasys in patients less than 5 years of age with chronic hepatitis C (CHC) or patients less than 3 years of age with chronic hepatitis B (CHB) have not been established (7)

The safety and efficacy of Pegintron in patients less than 3 years of age have not been established (8).

The safety and efficacy of ribavirin in patients less than 3 years of age have not been established (4-6).

Related policies

Intron A

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Pegasys and **Pegintron** may be considered **medically necessary** if the conditions indicated below are met.

Pegasys and **Pegintron** may be considered **investigational** for all other indications.

Prior-Approval Requirements

Pegasys or Pegintron alone for Hepatitis C

Age 18 years of age or older for

Diagnosis

Patient must have the following:

1. Chronic hepatitis C

AND ALL of the following:

a. Detectable viral load in the serum
b. Compensated liver disease
c. **NOT** previously treated with interferon alfa
d. Significant intolerance or contraindication to ribavirin or other antiviral agents
e. **Genotype 1 only**: HCV viral load will be drawn at treatment week 24

Pegasys with ribavirin or Pegintron with ribavirin for Hepatitis C

Age 5 years of age or older for Pegasys with ribavirin
3 years of age or older for Pegintron with ribavirin

Diagnosis

Patient must have the following:

1. Chronic hepatitis C

AND ALL of the following:

a. Detectable viral load in the serum
b. Compensated liver disease
c. Viral genotype must be provided and if genotype 1 must **NOT** be an appropriate candidate for treatment with a protease inhibitor
d. Females of reproductive potential **only**: patient is not pregnant and will be advised to use effective contraception during therapy and for 6 months after the final dose of ribavirin
e. Males with female partners of reproductive potential **only**: the patient's partner is not pregnant, and the patient will be advised to use effective contraception during therapy and for 6 months after the final dose of ribavirin
f. **Genotype 1 only**: HCV Viral load will be drawn at treatment week 24

Pegasys for Hepatitis B

Age 3 years of age or older

Diagnosis

Patient must have the following:

1. Chronic hepatitis B

AND ALL of the following:

a. Compensated liver disease
b. Evidence of viral replication

Pegasys for Myeloproliferative Neoplasms

Diagnoses

Patient must have **ONE** the following:

1. Myelofibrosis
   a. Symptomatic lower-risk myelofibrosis

2. Polycythemia Vera
    a. Symptomatic **OR** high-risk
    b. Inadequate response or loss of response to hydroxyurea or interferon therapy, if Pegasys not previously used

3. Essential Thrombocythemia
    a. Symptomatic **OR** high-risk
    b. Inadequate response or loss of response to hydroxyurea or interferon therapy, if Pegasys not previously used

Prior – Approval *Renewal* Requirements

Pegasys or Pegintron alone for Hepatitis C

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Hepatitis C

AND ALL of the following:
    a. Genotype 1
    b. **UNDETECTABLE** viral load after the initial 24 weeks of therapy

Pegasys with ribavirin or Pegintron with ribavirin for Hepatitis C

Age 5 years of age or older for Pegasys with ribavirin
3 years of age or older for Pegintron with ribavirin

Diagnosis

Patient must have the following:

1. Hepatitis C

AND ALL of the following:
   a. Genotype 1
   b. **UNDETECTABLE** viral load after initial 24 weeks of therapy

Pegintron with ribavirin only: OR ONE of the following:
1. History of null or partial response to previous (non-protease inhibitor) treatment

Pegasys for Myeloproliferative Neoplasms

Diagnoses

Patient must have **ONE** the following:

1. Myelofibrosis
2. Polycythemia Vera
3. Essential Thrombocythemia

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Hepatitis C: Genotype 1	
Medication	**Duration**
Pegasys with or without ribavirin	7 months
Pegintron with or without ribavirin	7 months
Hepatitis C: Genotypes 2 and 3	
Medication	**Duration**
Pegasys with or without ribavirin *No HIV Co-infection*	6 months
Pegasys with or without ribavirin *With HIV Co-infection*	12 months
Pegintron with or without ribavirin	6 months
Hepatitis C: Genotypes 4, 5 and 6	

Medication	Duration
Pegasys with or without ribavirin	12 months
Pegintron with or without ribavirin	12 months
Hepatitis B	
Medication	**Duration**
Pegasys	12 months
Myeloproliferative Neoplasms	
Medication and Diagnosis	**Duration**
Pegasys	12 months

Prior - Approval *Renewal* Limits

Hepatitis C: Genotype 1	
Medication	**Duration**
Pegasys with or without ribavirin	5 months
Pegintron with or without ribavirin	5 months
Hepatitis C: Genotypes 2, 3, 4, 5, 6	
Medication	**Duration**
Pegasys with or without ribavirin *Regardless of HIV co-infection*	No Renewal
Pegintron without ribavirin	No Renewal
Pegintron with ribavirin *History of null or partial response to previous (non-protease inhibitor) treatment*	12 months
Hepatitis B	
Medication	**Duration**
Pegasys	No Renewal
Myeloproliferative Neoplasms	
Medication and Diagnosis	**Duration**
Pegasys	12 months

Rationale

Summary

Interferons are a group of proteins whose effects include antiviral activity, growth regulatory properties, inhibition of angiogenesis, regulation of cell differentiation, enhancement of major histocompatibility complex antigen expression, and a wide variety of immunomodulatory activities. Interferons were the first therapeutic agents that permitted successful antiviral therapy

with acceptable sided effects in patients with chronic hepatitis B, C and D. However, in hepatitis C virus (HCV) infections, direct-acting antivirals have become the new paradigm of treatment and have largely replaced interferon therapy. Peginterferons are pegylated interferons. Pegylation is a process whereby a polyethylene glycol (PEG) polymer is attached to the molecule in order to improve drug solubility, stability, and retention time. Ribavirin is a synthetic antiviral used in the treatment of hepatitis C. It works well in combination with peginterferons but not as monotherapy. Ribavirin is contraindicated in pregnant women and men whose female partners are pregnant. The safety and efficacy of Pegasys in patients less than 5 years of age with chronic hepatitis C (CHC) or patients less than 3 years of age with chronic hepatitis B (CHB) have not been established. The safety and efficacy of ribavirin or Pegintron in patients less than 3 years of age have not been established (1-9).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Pegasys, Pegintron, and ribavirin while maintaining optimal therapeutic outcomes.

References

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8. PegIntron [package insert]. Whitehouse Station NJ: Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.; August 2019.
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Policy History

Date	Action

November 2018	Addition to PA Merge of policy numbers 5.01.02, 5.01.07, 5.01.08, 5.01.11, 5.01.12
February 2019	Reworded renewal requirement for Pegasys with ribavirin, co-infected with HIV: not already treated for 12 months for Hepatitis C
March 2019	Annual review
December 2020	Annual review and reference update
February 2021	Reference update. Revised Background, Regulatory and Summary sections. Changed age for Pegasys monotherapy from 5 years of age and older to 18 years and older to align with the PI. Removed the pediatric requirement of no diagnosis of renal failure from Pegasys/Pegintron with ribavirin to align with PI. Addition of off-label indications for Pegasys per NCCN Guidelines: myeloproliferative neoplasms- myelofibrosis, polycythemia vera and essential thrombocythemia.
June 2021	Annual review and reference update
March 2022	Annual review and reference update
June 2023	Annual review and reference update. Changed policy number to 5.01.047
June 2024	Annual review and reference update
June 2025	Annual review and reference update
June 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 11, 2026 and is effective on July 1, 2026.