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Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Anti-Infective Agents	**Original Policy Date:**	October 1, 2004
Subject:	Intron A Hepatitis C	**Page:**	1 of 5

Last Review Date: June 13, 2024

Intron A Hepatitis C

Description

Intron A (interferon alfa-2b)

Background
Hepatitis C is a viral disease caused by the hepatitis C virus (HCV) that leads to inflammation of the liver. Most people who were recently infected with hepatitis C do not have symptoms, but most people infected with hepatitis C develop a chronic infection. Untreated, chronic infection can lead to liver cirrhosis and/or liver cancer. Six genotypes of the hepatitis C virus exist and genotyping is essential to effective treatment. Hepatitis C infection may be detected in the blood by the HCV RNA assay. Disease status may be monitored by assays of biochemical liver tests or liver biopsy (1).

The goals of HCV treatment are to remove the virus from the blood and reduce the risk of cirrhosis and liver cancer that can result from long-term HCV infection. The most common treatment regimens are based on combinations of pegylated interferon alfa, ribavirin, and a protease inhibitor. In some cases, treatment with a single agent or two agents is most appropriate (1).

Regulatory Status (limited to hepatitis C)
FDA-approved indication: Intron A is an alpha interferon indicated for the treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease who have a history of blood or blood-product exposure and/or are HCV antibody positive. Studies in these patients demonstrated that Intron A therapy can produce clinically meaningful effects on this

disease, manifested by normalization of serum alanine aminotransferase (ALT) and reduction in liver necrosis and degeneration (2).

All alpha interferons, including Intron A, carry a boxed warning that they can cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Patients with persistently severe or worsening signs or symptoms of these conditions should be withdrawn from therapy. In many but not all cases these disorders resolve after stopping Intron A therapy (2).

A liver biopsy should be performed to establish the diagnosis of chronic hepatitis. Patients should be tested for the presence of antibody to HCV. Patients with other causes of chronic hepatitis, including autoimmune hepatitis, should be excluded. Prior to initiation of Intron A therapy, the physician should establish that the patient has compensated liver disease. The following patient entrance criteria for compensated liver disease were used in the clinical studies and should be considered before Intron A treatment of patients with chronic hepatitis C (2):

- No history of hepatic encephalopathy, variceal bleeding, ascites, or other clinical signs of decompensation
- Bilirubin Less than or equal to 2 mg/dL
- Albumin Stable and within normal limits
- Prothrombin Time Less than 3 seconds prolonged
- WBC Greater than or equal to 3000/mm^3
- Platelets Greater than or equal to 70,000/mm^3
- Serum creatinine should be normal or near normal (2).

Prior to initiation of Intron A therapy, CBC and platelet counts should be evaluated in order to establish baselines for monitoring potential toxicity. These tests should be repeated at Weeks 1 and 2 following initiation of Intron A therapy, and monthly thereafter. Serum ALT should be evaluated at approximately 3-month intervals to assess response to treatment (2).

Patients with preexisting thyroid abnormalities may be treated if thyroid stimulating hormone (TSH) levels can be maintained in the normal range by medication. TSH levels must be within normal limits upon initiation of Intron A treatment and TSH testing should be repeated at 3 and 6 months (2).

Non-pegylated interferons, such as Intron A are generally considered inferior to pegylated interferons, such as Pegasys and Pegintron (2).

Related policies
Actimmune, Alferon N, Pegasys, Pegintron

Policy

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

Intron A may be considered **medically necessary** if the conditions indicated below are met.

Intron A may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Chronic hepatitis C confirmed by liver biopsy, a history of blood or blood product exposure, or positive antibodies to hepatitis C

AND ALL of the following:

1. Compensated liver disease
2. **NOT** an immunosuppressed transplant recipient
3. Must **NOT** be an appropriate candidate for treatment with a pegylated interferon in combination with ribavirin and a protease inhibitor
4. Significant intolerance or contraindication to ribavirin (examples include hemoglobin level below 8.5 g/dL, a hemoglobinopathy such as thalassemia major or sickle-cell anemia)
5. **NOT** pregnant
6. **NO** history of unstable heart disease

Prior – Approval *Renewal* Requirements

None

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Rationale

Summary

Hepatitis C is a viral disease caused by the hepatitis C virus (HCV) that leads to inflammation of the liver. Untreated, chronic infection can lead to liver cirrhosis and/or liver cancer. The most common treatment regimens are based on combinations of pegylated interferon alfa, ribavirin, and a protease inhibitor. In some cases, treatment with a single agent or two agents is most appropriate (1-2).

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

References

1. Ghany MG, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: an update. Hepatology. 2009; 49(4):1335-1374.
2. Intron A [package insert]. Rahway, NJ: Merck Sharp & Dohme Corp.; March 2023.

Policy History

Date	Action
October 2004	Criteria updated to reflect current guidelines: NIH Consensus Statement on Management of Hepatitis C: 2002 NIH Consensus Statements and State-of-the-Science Statements Volume 19, Number 3, June 10-12, 2002 National Institutes of Health, Office of the Director Diagnosis, Management, and Treatment of Hepatitis C

	American Association for the Study of Liver Diseases Hepatology, April 2004
September 2011	Section 2 (Hepatitis C Monotherapy) reviewed and revised to follow the current Intron A package insert, as follows: Intron A is indicated for the treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease who have a history of blood or blood-product exposure and/or are hepatitis C viral antibody positive. A liver biopsy should be performed to establish the diagnosis of chronic hepatitis (2). Criteria will not be renewable after 6 months of therapy (2). Liver transplant removed from criteria and renewal will not be allowed (2).
September 2012	Annual editorial review and reference update
March 2014	Annual editorial review and reference update
March 2015	Annual editorial review and reference update
March 2016	Annual editorial review and reference update Policy number changed from 5.03.05 to 5.01.05
December 2017	Annual review and reference update
November 2018	Annual editorial review and reference update. Removal of examples of protease inhibitors
December 2019	Annual review and reference update
December 2020	Annual review
June 2021	Annual review
March 2022	Annual review
June 2023	Annual review and reference update. Changed policy number to 5.01.005
June 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.