



## MEDICAL POLICY

Date Reviewed: 04/24/09, 07/27/10, 04/15/11

**Subject:** Interferons (Infergen, Intron A, PegaSys, PegIntron, Roferon-A) for the Treatment of Hepatitis

**Description:** Interferons are naturally occurring proteins which, through the body's immune system, attack invaders such as viruses and bacteria and interfere with reproduction.

**Indications of Coverage:**

**Note:** see table at the end of this guideline for modified Child-Turcotte-Pugh score information.

**Interferon alfa** (Intron A) is considered medically necessary for the treatment of **chronic hepatitis B** in individuals over the age of one when all of the following are met:

The medical record documents compensated liver disease (Class A modified Child-Turcotte-Pugh score), identification of HBeAg (hepatitis B "e" antigen) positive or negative disease, HBV-DNA (hepatitis B virus DNA) levels greater than 20000 IU/mL, and a serum alanine aminotransferase (ALT) greater than 100 U/L (or double the upper limit of normal for the reference range that is used).

There is documentation of a contraindication to pegylated interferon (PegaSys or PegIntron). (Pegylated interferon is the preferred treatment.)

**Dosage and administration:** The recommended dose for adults is five million U daily or ten million U three times a week. The recommended dose for children is six million U per square meter three times a week to a maximum of ten million U. Interferon alfa-2b therapy is administered via subcutaneous injection and may be approved for sixteen weeks for HBeAg positive disease or one year for HBeAg negative disease.

**Interferon alfa** (Intron A) is considered medically necessary for the treatment of **chronic hepatitis C** in individuals over the age of three when all of the following are met:

The medical record documents compensated liver disease (Class A modified Child-Turcotte-Pugh score)

A baseline HCV-RNA (hepatitis C virus RNA) level and viral genotype is documented prior to treatment

There is documentation of a contraindication to pegylated interferon (PegaSys or PegIntron). (Pegylated interferon alfa and ribavirin is the recommended treatment.)

**Dosage and administration:** The recommended dose is three million U three times a week. Interferon alfa is administered via subcutaneous or intramuscular injection and may be approved for sixteen weeks. Subsequent treatment may be approved for an additional 56 weeks (total of 72 weeks) in individuals who are tolerating therapy and have normalized ALT levels (levels are within the reference range). Individuals whose ALTs have not normalized or have persistently high levels of HCV-RNA after sixteen weeks of therapy rarely achieve a sustained response with extension of treatment.

**Peginterferon alfa-2a** (PegaSys) is considered medically necessary for the treatment of **chronic hepatitis C** in individuals over the age of three when all of the following are met:

The medical record documents compensated liver disease (Class A modified Child-Turcotte-Pugh score)

A baseline HCV-RNA (hepatitis C virus RNA) level and viral genotype is documented prior to treatment

No previous interferon treatment OR no response or relapse following previous standard (non-pegylated) interferon therapy

Peginterferon alfa-2b will be used as combination therapy in conjunction with ribavirin (unless the use of ribavirin is contraindicated)

Dosage and administration: The recommended dose is 180 micrograms subcutaneously once a week for 48 weeks.

**Peginterferon alfa-2a** (PegaSys) is considered medically necessary for the treatment of **chronic hepatitis B** in individuals over the age of 18 when all of the following are met:

HBeAg positive or HBeAg negative disease has been established

The medical record documents compensated liver disease (Class A modified Child-Turcotte-Pugh score), identification of HBeAg (hepatitis B "e" antigen) positive or negative disease, HBV-DNA (hepatitis B virus DNA) levels greater than 20000 IU/mL, and a serum alanine aminotransferase (ALT) greater than 100 U/L (or double the upper limit of normal for the reference range that is used).

No previous interferon treatment OR no response or relapse following previous non-pegylated interferon therapy

Dosage and administration: The recommended dose is 180 micrograms subcutaneously once a week for 48 weeks.

**Peginterferon alfa-2b** (PegIntron) is considered medically necessary for the treatment of **chronic hepatitis C** in individuals over three years of age when all of the following are met:

The medical record documents compensated liver disease (Class A modified Child-Turcotte-Pugh score)

A baseline HCV-RNA (hepatitis C virus RNA) level and viral genotype is documented prior to treatment

No previous interferon treatment OR no response or relapse following previous standard (non-pegylated) interferon therapy

Peginterferon alfa-2b will be used as combination therapy in conjunction with ribavirin (unless the use of ribavirin is contraindicated)

Dosage and administration: (**Note:** duration of treatment will vary based on genotype.) The recommended dose is 1.5 mcg/kg/week subcutaneously in combination with 800 to 1400 mg of Rebetol orally based on patient body weight.

For adults who have not previously received interferon alfa, 48 weeks may be approved for individuals with genotype 1. Discontinuation of therapy should be considered in individuals with an undetectable level (less than or equal to 50 IU/mL) of HCV-RNA at twelve weeks or if the HCV-RNA remains detectable (greater than 50 IU/mL) after 24 weeks of therapy. For individuals with genotype 2 and 3, 24 weeks of treatment may be approved.

For adults receiving retreatment following prior treatment failures, 48 weeks may be approved regardless of genotype. Discontinuation of therapy should be considered in individuals with an undetectable level (less than or equal to 50 IU/mL) of HCV-RNA at twelve weeks or if the HCV-RNA remains detectable (greater than 50 IU/mL) after 24 weeks of therapy. Re-treated patients who fail to achieve undetectable HCV-RNA levels at twelve weeks of therapy, or whose HCV-RNA remains detectable after 24 weeks of therapy, are highly unlikely to achieve sustained virologic response (SVR) and discontinuation of therapy should be considered.

For pediatric individuals, dosing is determined by body surface area for peginterferon alfa-2b and by body weight for Rebetol. The recommended dose of PegIntron is 60mcg/m<sup>2</sup>/week subcutaneously in combination with 15 mg/kg/day of Rebetol orally in divided doses. For pediatric individuals with genotype 1, 48 weeks of treatment may be approved. For pediatric individuals with genotype 2 and 3, 24 weeks of treatment may be approved.

**Interferon alfacon-1** (Infergen) is considered medically necessary for the treatment of **chronic hepatitis C** in individuals over the age of 18 when all of the following are met:

The medical record documents compensated liver disease (Class A modified Child-Turcotte-Pugh score)

A baseline HCV-RNA (hepatitis C virus RNA) level is documented prior to treatment

Documentation of the failure of or a contraindication to pegylated interferon (PegaSys or PegIntron)

Dosage and administration: (**Note:** duration of treatment will vary based therapy type.) For individuals receiving interferon alfacon-1 **monotherapy** (interferon alfacon-1 alone) as the initial treatment, the recommended dose is 9 mcg per week administered via three weekly subcutaneous injections for a total of 24 weeks. For individuals receiving interferon alfacon-1 monotherapy (interferon alfacon-1 alone) following previous interferon therapy who did not respond or have relapsed, the recommended dose is 15 mcg per week administered via three weekly subcutaneous injections for a total of 48 weeks. Individuals who do not tolerate standard interferon therapy should not be treated with interferon alfacon-1 three times a week as the initial treatment. For individuals receiving interferon alfacon-1 as **combination** therapy (interferon alfacon-1/ ribavirin), the recommended dose of interferon alfacon-1 is 15 mcg daily administered via subcutaneous injection in combination with weight-based ribavirin at 1000 mg - 1200 mg orally in divided doses for up to 48 weeks.

#### Limitations of Coverage:

Review contract and endorsements for exclusions and prior authorization or benefit requirements.

If used for a condition/diagnosis other than is listed in the Indications of Coverage, deny as experimental or investigative.

If used for a condition/diagnosis that is listed in the Indications of Coverage, but the criteria are not met, deny as not medically necessary.

The use of standard interferon therapy is considered investigational following the failure of pegylated interferon therapy as there is insufficient peer-reviewed scientific literature supporting the superior efficacy of standard interferon therapy when compared to pegylated interferon therapy.

Standard interferon therapy and pegylated interferon therapy are considered investigational for an individual who is pregnant or for the management of autoimmune hepatitis.

Maintenance therapy with peginterferon alfa-2b is considered investigational for individuals who have failed previous treatment with pegylated interferons as there is insufficient peer-reviewed scientific literature supporting the effectiveness of maintenance therapy in this situation.

Interferon alfacon-1 is considered not medically necessary when any of the following are documented:

The individual is under the age of 18

When the individual did not respond to standard interferon therapy

The individual has been diagnosed with a hepatitis B or HIV infection

**Documentation Required:**

Office notes

Laboratory results

**Rationale:** Treatment with interferons has been demonstrated to reduce the amount of hepatitis virus for many patients, preventing further liver injury and scarring. Interferons may be used by themselves or with other medications for the treatment of either hepatitis B or hepatitis C in individuals with compensated liver disease. Compensated liver disease means that the disease is present, but there are either few symptoms or the symptoms are stable. Several methods of classifying the extent of the disease have been utilized, the most recent being the Child-Turcotte-Pugh Score.

Not all types of hepatitis infections can be treated with interferon therapy, so testing is frequently performed in the early stages of treatment to see if the disease is responding to the interferons. Studies have shown that the likelihood of future response is low if there is inadequate response after twenty four weeks for individuals with certain genotypes. If the disease is not responding to the interferon therapy, further therapy is generally not necessary.

These criteria are generally based on the Practice Guidelines from the American Association for the Study of Liver Diseases, a professional organization of scientists and healthcare professionals researching how to prevent and cure liver disease.

**References:** American Gastroenterological Association Medical Position Statement on the Management of Hepatitis C. *Gastroenterology* 2006; 130:225–230.

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*These guidelines are designed for reference purposes only, do not guarantee coverage, and should not be construed as medical advice. See full Medical Policy Disclaimer.*

*Approved by the Medical Director*

#### Modified Child-Turcotte-Pugh Score for Grading Severity of Liver Disease

Variable	1	2	3
Serum bilirubin, mg/dL	Less than 2.0	2.0 – 3.0	Greater than 3.0
Serum albumin, g/dL	Greater than 3.5	2.8 – 3.5	Less than 2.8
Prothrombin time INR	Less than 1.7	1.7 – 2.3	Greater than 2.3
Ascites	None	Easily controlled	Poorly controlled
Encephalopathy	None	Minimal	Advanced coma

The score is calculated as the sum of the scores for albumin, bilirubin, prothrombin time, acites and encephalopathy (range 5-15). Class A is defined as 5-6, class B as 7-9, and class C as 10-15.

From Ghany MG, Strader DB, Thomas DL, Seeff LB; American Association for the Study of Liver Diseases. Diagnosis, management, and treatment of hepatitis C: An update. *Hepatology*. 2009; 49(4):1335-1374.