Infergen Monotherapy

Description

Infergen (interferon alfacon-1)

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.

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 the protease inhibitors, telaprevir and boceprevir. In some cases, treatment with a single agent or two agents is most appropriate.

Regulatory Status
FDA-approved indication: Infergen (interferon alfacon-1) is indicated for treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease. This indication is
based on clinical trials conducted using Infergen alone at a time before combination treatment of chronic hepatitis C became the standard of care, and on a single trial evaluating Infergen in combination with ribavirin in patients who failed to respond to previous treatment with a pegylated interferon and ribavirin. Use of monotherapy with an interferon such as Infergen for the treatment of hepatitis C is not recommended unless a patient is unable to take ribavirin (1).

**Limitation of use:** The safety and efficacy of the combination of Infergen /ribavirin in treatment-naïve patients or in patients co-infected with HBV or HIV-1 have not been evaluated. Patients with the following characteristics are less likely to benefit from retreatment with Infergen /ribavirin combination therapy: response of <1 log10 drop HCV RNA on previous treatment, Genotype 1, high viral load (≥850,000 IU/mL), African American race, and/or presence of cirrhosis (1).

**Related policies**
Intron A, 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.*

Infergen monotherapy may be considered **medically necessary** for the treatment of chronic hepatitis C in patients 18 years of age and older who have a detectable viral load in serum, compensated liver disease, significant intolerance or contraindication to ribavirin, who are not pregnant and who have no history of unstable heart disease.

Infergen monotherapy may be considered **investigational** in patients less than 18 years of age or who do not meet the criteria for medical necessity.

**Prior-Approval Requirements**

**Age**
18 years of age and older

**Diagnosis**

Patient must have the following:
1. Chronic hepatitis C

AND ALL of the following:
1. Detectable viral load
2. Compensated liver disease
3. Significant intolerance or contraindication to ribavirin (examples include hemoglobin level below 8.5 g/dL, hemoglobinopathy such as thalassemia major or sickle-cell anemia)
4. NOT pregnant
5. 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 the protease inhibitors, telaprevir and boceprevir. In some cases, treatment with a single agent or two agents is most appropriate.
Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Infergen while maintaining optimal therapeutic outcomes.

References

Policy History
<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>June 2010</td>
<td><strong>Section 3 (Interferon Therapy)</strong>: Removed ICD-9s for follicular lymphoma, AIDS-related Kaposi’s sarcoma, chronic myelogenous leukemia in the first chronic phase with Philadelphia chromosome-positive CML, malignant melanoma, chronic granulomatous disease* (to reduce the frequency and severity of infections) and inflammatory pulmonary fibrosis.</td>
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<tr>
<td>July 2010</td>
<td><strong>Section 3 (Interferon Therapy)</strong>: Diagnosis of chronic hepatitis C moved from section 3 to section 2; done to allow expansion of the hepatitis C indication and to parallel current package insert guidelines. Actimmune verbiage and osteopetrosis indication removed as it does not apply to Infergen.</td>
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| July 2010  | New section created: **Section 2 (Chronic Hepatitis C Monotherapy)**. This section parallels existing monotherapy criteria already in place for Pegasys and Pegintron. Combination treatment of hepatitis C with pegylated interferon with ribavirin is currently the standard of care and has replaced monotherapy(3). The monotherapy criteria are in place to allow treatment for patients unable to take ribavirin. Per the current prescribing information the use of monotherapy with an interferon such as Infergen for
the treatment of hepatitis C is not recommended unless a patient is unable to take ribavirin (2).

July 2010

**Section 1 (Hepatitis C Combination Therapy):** FDA approved Infergen for daily use in combination with ribavirin for the retreatment of chronic hepatitis C patients who have failed initial therapy with pegylated interferon plus ribavirin. Per the package insert discontinuation of therapy should be considered at 24 weeks if the patient does not achieve an undetectable HCV-RNA as it is very unlikely they will achieve a sustained virological response (1,2.)

July 2010

All clinical rationale and revision notes moved to the end of the document. Each entry cross-referenced to its corresponding section and placed in chronological order.

August 2011

**Section 3 (Interferon Therapy) deleted from criteria.** The only current FDA labeled indication for Infergen is hepatitis C (1). The following indications removed from criteria due to either being an investigational use or no current clinical sources supporting its use: follicular lymphoma, hairy cell leukemia, AIDS-related Kaposi’s sarcoma, chronic myelogenous leukemia in the first chronic phase with Philadelphia chromosome-positive CML, malignant melanoma, condylomata acuminata, chronic hepatitis B, chronic granulomatous disease and inflammatory pulmonary fibrosis.

November 2011

The order of Section 1 and Section 2 switched listing monotherapy first. Section entitled *Hepatitis C Combination Therapy* changed to *Hepatitis C with RIBAVIRIN.*

Criteria reviewed and revised to follow the current Infergen package insert, as follows:

Infergen is indicated for treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease. This indication is based on clinical trials conducted using Infergen as monotherapy, prior to the time that combination treatment became the standard of care, and on a single trial evaluating Infergen in combination with ribavirin in patients who failed to respond to previous treatment with a pegylated interferon and
ribavirin (1).

**Monotherapy** is currently not recommended for treatment of chronic hepatitis C because combination therapy with ribavirin provides substantially better response rates than monotherapy. Monotherapy should be reserved for patients with contraindications or significant intolerance to ribavirin. Examples of contraindications to the use of ribavirin are a hemoglobin level below 8.5 g/dL, pregnancy, a female partner who is pregnant, a hemoglobinopathy such as thalassemia major or sickle-cell anemia, or a history of unstable heart disease (1-5). Duration of monotherapy can be up to 48 weeks. No safety and efficacy data are available for treatment of longer than one year, therefore criteria will not be renewable beyond one year (1).

**Combination** therapy of Infergen plus ribavirin provides substantially better response rates than Infergen alone (monotherapy). Furthermore, combination with pegylated interferon plus ribavirin has been shown to be even more superior to the combination of Infergen plus ribavirin (1-5). Combination therapy of Infergen plus ribavirin should, therefore, be reserved for members who have failed combination therapy with pegylated interferon plus ribavirin, as a last option. The manufacturer recommends the duration of combination therapy of Infergen with ribavirin to be up to 48 weeks. Discontinuation of therapy should be considered in patients whose viral load remains detectable after 24 weeks of therapy. If the viral load remains detectable at 24 weeks of therapy it is unlikely the patient will respond to additional treatment and therapy should be stopped (1-5). No safety and efficacy data are available for the use of Infergen in treatments longer than one year, therefore criteria will not be renewable beyond one year, for both monotherapy and combination therapy. Infergen in combination with ribavirin should not be used in patients with creatinine clearance <50mL/min (1).

The safety and efficacy of Infergen, alone or in combination with ribavirin, for the treatment of chronic hepatitis C infection in liver or other organ transplant recipients have not been evaluated (1). All mention of liver transplant removed from criteria.
Section: Prescription Drugs  Effective Date: April 1, 2014
Subsection: Anti-Infective Agents  Original Policy Date: June 1, 2010
Subject: Infergen Monotherapy  Page: 7 of 7

September 2012  Annual editorial and reference update.
March 2014  Annual editorial and reference update.

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 13, 2014 and is effective April 1, 2014.

Signature on File

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