MEDICAL POLICY STATEMENT		
Effective Date	**Next Annual Review Date**	**Last Review / Revision Date**
06/15/2011	**06/15/2012**	**06/15/2011**
Author		
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CSMG Medical Policy Statements are derived from literature based and supported clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services are those health care services or supplies which are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative and are not provided mainly for the convenience of the member or provider.

A. SUBJECT

Infergen (Interferon Alfacon-1, recombinant)

B. BACKGROUND

Interferon alfacon-1(Infergen) is a recombinant hybrid protein based on the consensus amino acid sequence of naturally occurring human type-I interferon alphas. Interferons do not act directly on the virus, but bind to the interferon cell-surface receptor leading to the production of several interferon-stimulated gene products. Interferons induce pleiotropic biologic responses, which include antiviral, antiproliferative and immunomodulatory effects, regulation of cell surface major histocompatibility antigen (HLA class I and class II) expression and regulation of cytokine expression.

The patient selection criteria outlined was derived from the FDA-approved prescribing information for infergen (Interferon Alfacon-1, recombinant), the studies that were presented to the FDA in support of the pre-market approval application, and studies in the peer-reviewed published medical literature. The FDA label indications that are found in the manufacturer prescribing information and is described below are the treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease. Coverage decisions for conditions other than the above FDA approved indication will be reviewed on a case by case basis if proven effective through research documentation. The requesting provider will need to support his exception request with the appropriate literature.

C. Policy

CareSource will approve the use of interferon alfacon-1(Infergen) and consider its use as medically necessary as monotherapy, or in combination with ribavirin, when the following criteria have been met for:

- Chronic hepatitis C virus infection who have compensated liver disease and have not been previously treated with interferon alpha

- Compensated liver disease and histological evidence of cirrhosis (Child-Pugh score less than or equal to 6 - class A)
- Chronic hepatitis C/ HIV coinfection and CD4 count > 100 cells/mm3
- HBeAg positive and HBeAg negative chronic hepatitis B who have compensated liver disease and evidence of viral replication and liver inflammation.

Criteria Guidelines:

- Hepatitis C Virus RNA positive in serum
- 18 years of age or older
- Compensated liver disease:
    - Total serum bilirubin <1.5 g/dL
    - INR <1.5
    - Serum albumin >3.4
    - Platelet count >75,000 mm
    - No evidence of hepatic decompensation (hepatic encephalopathy or ascites)
- Acceptable hematological and biochemical indices
    - Hemoglobin 13 g/dL for men and 12 g/dL for women
    - Neutrophil count 1500/mm3
    - Serum creatinine 1.5 mg/dL
- Willing to be treated and to adhere to treatment requirements
- Age Guidelines:
    - Peginterferon alfa-2b (Pegintron) in combination with ribavirin: age 3 and older for the treatment of chronic hepatitis C and compensated liver disease.
    - Pegintron (peginterferon alfa-2b) monotherapy: Age 18 and older for use alone for the treatment of chronic hepatitis C with compensated liver disease previously untreated with interferon alpha.

NOTE: The NCCN (National Comprehensive Cancer Network) also approves the use of peginterferon alfa-2a (Pegasys) and peginterferon alfa-2b (PegIntron) for chronic myelogenous leukemia, non-hodgkins lymphoma and peginterferon alfa-2b (PegIntron) for melanoma.

All other uses of peginterferon alfa-2a (Pegasys) and peginterferon alfa-2b (PegIntron) are considered experimental/investigational, and therefore, not covered including:

- **Hepatitis C when there has been failure to respond to a previous treatment with a full course of peginterferon alfa therapy**
- **Treatment of chronic hepatitis B beyond 48 weeks**

Chronic Hepatitis C

Peginterferon alfa-2a (Pegasys) and peginterferon alfa-2b (PegIntron) is an antiviral indicated for the treatment of chronic Hepatitis C (CHC) when the following criteria are met:

In Combination With Ribavirin Prior Authorization Criteria:

- Documented diagnosis of Hepatitis C
- Detectable HCV RNA levels are higher than 50 IU/ml

AND

- Patient has not received previous treatment with peginterferon alfa-2a (Pegasys) or peginterferon alfa-2b (PegIntron)

AND

- Prescribed by a gastroenterologist or hepatologist or under the recommendation of a gastroenterologist or hepatologist

Monotherapy Prior Authorization Criteria:

- Documented diagnosis of Hepatitis C
- Ribavirin is contraindicated

AND

- Detectable HCV RNA levels are higher than 50 IU/ml

AND

- Patient has not received previous treatment with peginterferon alfa-2a (Pegasys) or peginterferon alfa-2b (PegIntron)

AND

- Prescribed by a gastroenterologist or hepatologist or under the recommendation of a gastroenterologist or hepatologist

Note: Documented diagnosis must be confirmed by portions of the individual's medical record, which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but not limited to, test reports, chart notes from provider's office or hospital admission notes.

For Special Needs Plan members, reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

For Medicare

LCD for Peginterferon alfa-2a (Pegasys) and alfa-2b (PegIntron)

Medicare does not have a National Coverage Determination (NCD) for peginterferon alfa-2a (Pegasys) and peginterferon alfa-2b (PegIntron). In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, section 50 Drugs and Biologicals at:

http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf.

Local Coverage Determinations (LCDs) for Peginterferon alfa-2a (Pegasys) and peginterferon alfa-2b (PegIntron) do not exist at this time. (Accessed March 29, 2011)

Safety

CareSource will only review requests for **peginterferon alfa-2a (Pegasys) and peginterferon alfa-2b (PegIntron)** if the patient has **none** of the following contraindications:

- Hypersensitivity to interferon alphas or to any component of the product or *E. coli*-derived products
- Clinically decompensated cirrhosis because of hepatitis C (Child-Pugh score >6 [class B and C])
- Autoimmune hepatitis
- Pregnant, planning to become pregnant, or are breast-feeding
- Severe psychiatric disorders

Precautions

- Use effective contraception in both males and females
- Cardiac disease

Black Box Warnings

Patients treated with peginterferon alfa-2a (Pegasys) and peginterferon alfa-2b (PegIntron) should be monitored closely with periodic clinical and laboratory evaluations, since it may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic and infectious disorders. Therapy should be withdrawn in patients with persistently severe or worsening signs or symptoms of these conditions.

Pregnancy Risk Factor = C

Peginterferon alfa-2a (Pegasys) or alfa-2b (PegIntron) Monotherapy

Peginterferon alfa-2a (Pegasys) has not been studied for its teratogenic effect. Peginterferon alfa-2a (Pegasys) should be assumed to have abortifacient potential. There are no adequate and well-controlled studies of Peginterferon alfa-2a (Pegasys) in pregnant women. Peginterferon alfa-2a (Pegasys) is to be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Peginterferon alfa-2a (Pegasys) is recommended for use in women of childbearing potential only when they are using effective contraception during therapy.

Pregnancy Category = X

Peginterferon alfa-2a (Pegasys) or alfa-2b (PegIntron) Combination Use with Ribavirin

Significant teratogenic and/or embryocidal effects have been demonstrated in all animal species exposed to ribavirin. Ribavirin therapy is contraindicated in women who are pregnant and in the male partners of women who are pregnant.

It is not known whether peginterferon or ribavirin or its components are excreted in human milk. The effect of orally ingested peginterferon or ribavirin from breast milk on the nursing infant has not been evaluated. Because of the potential for adverse reactions from the drugs in nursing infants, a decision must be made whether to discontinue nursing or discontinue Peginterferon alfa-2a (Pegasys) and Ribavirin treatment.

Conditions of Coverage

Quantity Limitations	**Monotherapy:** Recommended treatment is 9 mcg administered three times a week as a single subcutaneous injection for 24 weeks. Recommended dose for patients who tolerated previous interferon therapy and did not respond or relapsed following its discontinuation is 15 mcg administered three times a week as a single subcutaneous injection for up to 48 weeks. (Recommended dose for patients who do not tolerate initial standard interferon therapy should not be treated with 15 mcg three times a week.) **Combination Treatment with Ribavirin:** The recommended dose of Interferon alfacon-1 (Infergen) is 15 mcg daily administered as a single subcutaneous injection in combination with weight-based ribavirin at 1,000 mg - 1,200 mg (< 75 kg and ≥75 kg) orally in two divided doses for up to 48 weeks.
J-Code	J9212
NDC	**00187200601 55513056201 55513092706 64116003924** **00187200605 55513056206 64116003101 66435020115** **00187200702 55513092601 64116003106 66435020196** **00187200706 55513092606 64116003124 66435020209** **55513055401 66435020295 64116003901 00187200601** **55513055406 55513092701 64116003906 00187200605** **00187200702 55513055401** **00187200706 55513055406**
Applicable ICD-9 Codes	070.54 Chronic Hepatitis C
Place Of Service	Office, Outpatient, Home *****Preferred place of service is in the home/self administered**.** **Note:** CareSource supports administering injectable medications in various settings, as long as those services are furnished in the most appropriate and cost-effective setting that are supportive of the patient's medical condition and unique needs and condition. The decision on the most appropriate setting for administration is based on the member's current medical condition and any required monitoring or

	additional services that may coincide with the delivery of the specific medication.
Authorization Period	Approved initial authorizations are valid for 3 months. Continued treatment may be considered when the member has shown biological response to treatment. All authorizations are subject to continued eligibility.

D. REVIEW / REVISION HISTORY

6/15/2011

E. REFERENCES

Pegasys [Package Insert]. Nutley, NJ: Hoffman-La Roche Inc.; March 2010.

PegIntron [Package Insert], Kenilworth, NJ: Schering Corporation

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NIH guidelines on Chronic Hepatitis C. at http://consensus.nih.gov/2002/2002Hepatitisc2002116html.htm. (April 22, 2011)

Zeuzem S et al. "Peginterferon alfa-2a in patients with chronic hepatitis C." *NEJM* 2000;343:1666-72

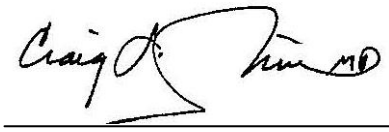
Manns MP et al. "Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial." *Lancet* 2001;358:958-65

Fried MW et al. "Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection." *NEJM* 2002;347:975-82

American Association for the Study of Liver Diseases. Strader DB, Wright T, Thomas, DL, Seeff LB. Practice Guideline: Diagnosis, management, and treatment of hepatitis C. Hepatology 2004;39:1147-1171.

http://www.aasld.org/practiceguidelines/Documents/Bookmarked%20Practice%20Guidelines/Diagnosis_of_HEP_C_Update.Aug%20_09pdf.pdf (April 26, 2011)

The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.



Chief Medical Officer June 1, 2011 **Date**

Senior Medical Director June 1, 2011 **Date**