

Prior Authorization DRUG Guidelines

INFERGEN® (Interferon alfacon-1)

Effective Date: 7/28/05

Date Developed: 7/13/05 by C. Wilhelmy MD

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Infergen is an interferon. Alpha interferons are a family of proteins, produced by nucleated cells, that have antiviral, antiproliferative, and immune-regulating activity. There are at least 25 alpha interferons identified. Interferons interact with cells through high affinity cell surface receptors. Following activation, multiple effects can be detected. Interferons induce gene transcription, inhibit cellular growth, alter the state of cellular differentiation, interfere with oncogene expression, alter cell surface antigen expression, increase phagocytic activity of macrophages, and augment cytotoxicity of lymphocytes for target cells. Although all alpha interferons share similar properties, the actual biological effects vary between subtypes.

PreAuthorization Criteria:

Infergen is used for the treatment of chronic hepatitis C virus (HCV) infection in patients 18 years of age with compensated liver disease and anti-HCV serum antibodies or HCV RNA.

VCHCP requires that Infergen be prescribed by a gastroenterologist or Hepatitis C Clinic physician.

MONITORING PARAMETERS

Hemoglobin and hematocrit; white blood cell count; platelets; triglycerides; thyroid function. Laboratory tests should be taken prior to therapy, 2 weeks after therapy has begun, and periodically during treatment. HCV RNA, ALT to determine success/response to therapy.

The following guidelines were used during the clinical studies as acceptable baseline values:

Platelet count $75 \times 10^9/L$

Hemoglobin 100 g/L

ANC $1500 \times 10^6/L$

Scr $<180 \mu\text{mol/L}$ ($<2 \text{ mg/dL}$) or Clcr $>0.83 \text{ mL/second}$ ($>50 \text{ mL/minute}$)

Serum albumin 25 g/L

Bilirubin WNL

TSH and FT4 WNL

General Information:

- Pegylated interferon in combination with ribavirin is the current treatment of choice for adult patients with chronic hepatitis C. Combination therapy with ribavirin is required for coverage unless contraindicated.
- Patient's with the following characteristics are less likely to benefit from retreatment with Infergen/ribavirin combination therapy: response of < 1 log₁₀ drop in HCV RNA on previous treatment, Genotype 1, high viral load (≥ 850,000 IU/ml), African American race, and/or presence of cirrhosis.
- Alpha interferons, including Interferon alfacon-1, may 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 symptoms of these conditions should be withdrawn from therapy. In many, but not all cases, these disorders resolve after stopping interferon alfacon-1 therapy.

National consensus guidelines and hepatitis specialists recommend that patients with chronic HCV who have active disease as demonstrated by detectable HCV RNA, liver biopsy or elevated LFTs should be retreated with the combination of peginterferon and ribavirin if they relapsed during or following therapy or did not respond to therapies other than the combination of peginterferon and ribavirin

Adults: Recommended Dosing Regimen and Authorization Limit:

Drug	Dosing Regimen	Authorization Limit
Infergen (interferon alfacon-1) with ribavirin	<u>For Chronic HCV</u> 9 mcg SC TIW	<p style="text-align: center;"><u>Genotypes 1,4,6:</u></p> <p>Initial authorization for 12 weeks If viral load undetectable at 12 weeks, authorize for an additional 36 weeks.</p> <p>If viral load > 2 log reduction at 12 weeks, authorize for an additional 12 weeks, recheck viral load. If undetectable, authorize for an additional 24 weeks.</p> <p>If viral load is detectable, no additional authorization.</p> <p style="text-align: center;"><u>Genotypes 2, 3:</u></p>

		<p>24 weeks. No additional authorizations beyond 24 weeks</p> <p><u>Any genotype where ribavirin is contraindicated:</u> 48 weeks</p>
<p>Infergen (interferon alfacon-1) with ribavirin</p>	<p>Relapsers/non-responders: 9 or 15 mcg SC QD <u>Ribavirin: weight based</u> < 75 kg: 1000 mg/day ≥ 75 kg: 1200 mg/day</p>	<p>Initial authorization for 12 weeks If viral load undetectable at 12 weeks, authorize for an additional 36 weeks. If viral load > 2 log reduction at 12 weeks, authorize for an additional 12 weeks, recheck viral load.</p> <p>If undetectable, authorize for an additional 24 weeks. If viral load is detectable, no additional authorization</p> <p>If viral load is detectable at 12 weeks and there was not a 2 log reduction, no additional authorization.</p> <p>No more than one course of therapy as a non-responder or relapser.</p>

Patients who have previously tolerated interferon therapy but did not respond or relapsed: SubQ: 15 mcg 3 times/week for up to 48 weeks.

Dose reduction for toxicity: Dose should be held in patients who experience a severe adverse reaction, and treatment should be stopped or decreased if the reaction does not become tolerable. Doses were reduced from 9 mcg to 7.5 mcg in the pivotal study.

For patients receiving 15 mcg/dose, doses were reduced in 3 mcg increments. Efficacy is decreased with doses <7.5 mcg.

DOSING: PEDIATRIC — Not indicated for patients <18 years of age.

DOSING: ELDERLY — Refer to adult dosing.

DOSING: HEPATIC IMPAIRMENT —Use in decompensated hepatic disease is contraindicated.

DOSAGE FORMS — Injection, solution [preservative free]: 30 mcg/mL (0.3 mL, 0.5 mL)

ADMINISTRATION — Interferon alfacon-1 is administered by SubQ injection, 3 times/week, with at least 48 hours between doses

CONTRAINDICATIONS — Hypersensitivity to interferon alfacon-1 or any component of the formulation, other alpha interferons, or E. coli-derived products; decompensated liver disease; autoimmune hepatitis.

WARNINGS / PRECAUTIONS — Severe psychiatric adverse effects, including depression, suicidal ideation, and suicide attempt, may occur. Avoid use in severe psychiatric disorders. Use with caution in patients with a history of depression. Use with caution in patients with prior cardiac disease (ischemic or thromboembolic), arrhythmias, patients who are chronically immunosuppressed, and patients with endocrine disorders. Do not use in patients with hepatic decompensation. Ophthalmologic disorders (including retinal hemorrhages, cotton wool spots and retinal artery or vein obstruction) have occurred in patients using other alpha interferons. Prior to start of therapy, visual exams are recommended for patients with diabetes mellitus or hypertension. Treatment should be discontinued in patients with worsening or persistently severe signs/symptoms of autoimmune, infectious, ischemic (including radiographic changes or worsening hepatic function), or neuropsychiatric disorders (including depression and/or suicidal thoughts/behavior). Use caution in patients with autoimmune disorders; type-1 interferon therapy has been reported to exacerbate autoimmune diseases. Do not use interferon alfacon-1 in patients with autoimmune hepatitis. Use caution in patients with low peripheral blood counts or myelosuppression, including concurrent use of myelosuppressive therapy. Safety and efficacy have not been determined for patients <18 years of age.

DRUG INTERACTIONS

ACE inhibitors: Interferons may increase the adverse/toxic effects of ACE inhibitors, specifically the development of granulocytopenia. Risk: Monitor

Clozapine: A case report of agranulocytosis with concurrent use.

Erythropoietin: Case reports of decreased hematopoietic effect

Melphalan: Interferon alpha may decrease the serum concentrations of melphalan; this may or may not decrease the potential toxicity of melphalan. Risk: Monitor

Prednisone: Prednisone may decrease the therapeutic effects of Interferon alpha. Risk: Moderate

Theophylline: Interferon alpha may decrease the P450 isoenzyme metabolism of theophylline.

Risk: Moderate

Warfarin: Interferons may increase the anticoagulant effects of warfarin. Risk: Monitor

Zidovudine: Interferons may decrease the metabolism of zidovudine; the neutropenic effects of zidovudine may be synergistic. Risk: Monitor

Ribavirin: Concurrent therapy may increase the risk of hemolytic anemia.

PREGNANCY RISK FACTOR — C

PREGNANCY IMPLICATIONS — There have been no well-controlled studies in pregnant women. Animal studies have shown embryolethal or abortifacient effects. Males and females who are being treated with interferon alfacon-1 should use effective contraception.

LACTATION — Excretion in breast milk unknown/use caution (AAP rates "compatible")

BREAST-FEEDING CONSIDERATIONS — Women with hepatitis C should be instructed that there is a theoretical risk the virus may be transmitted in breast milk.

PATIENT EDUCATION — There are many different types of interferon products. Do not change brands or change your dose without consulting with your prescriber. Promptly report any adverse effects to your prescriber, including flu-like symptoms, signs of infection, signs of depression, suicidal thoughts, or visual complaints. Flu-like symptoms include fatigue, fever, rigors, headache, arthralgia, myalgia, and increased sweating. Your prescriber may instruct you to use this medication in the evening, or to take a non-narcotic analgesic to help prevent or decrease these symptoms. Because interferon alfacon-1 may have hazardous effects to a fetus, males and females using this medication should use effective contraception. You will need periodic laboratory tests while on this medication. If you have diabetes or hypertension you should also have an eye exam prior to starting therapy. If self-administering this medication at home, follow procedures for proper disposal of your syringes and needles.

REFERENCES

1.FDA Drug Info Web site. Available at:
http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Search_Drug_Name. Accessed June 28, 2010

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