

**PEGASYS, PEGINTRON, AND RIBAVIRIN**

**Pegasys (peginterferon alfa-2a), PegINTRON (peginterferon alfa-2b), Ribavirin (Moderiba, Rebetol, RibaPak, Ribasphere, RibaTab, ribavirin tablets/capsules)**

**RATIONALE FOR INCLUSION IN PA PROGRAM****Background**

Interferons are a group of proteins whose effects include antiviral activity, growth regulatory properties, inhibition of angiogenesis, regulation of cell differentiation, enhancement of major histocompatibility complex antigen expression, and a wide variety of immunomodulatory activities. Interferons were the first therapeutic agents that permitted successful antiviral therapy with acceptable side effects in patients with chronic hepatitis B, C and D. However, in hepatitis C virus (HCV) infections, direct-acting antivirals have become the new paradigm of treatment and have largely replaced interferon therapy. Peginterferons are pegylated interferons. Pegylation is a process whereby a polyethylene glycol (PEG) polymer is attached to the molecule in order to improve drug solubility, stability, and retention time. Ribavirin is a synthetic antiviral used in the treatment of hepatitis C. It works well in combination with peginterferon but not as monotherapy (1-6).

**Regulatory Status**

FDA-approved indications:

**Pegasys** (peginterferon alfa-2a) is an inducer of the innate immune response indicated for the treatment of: (7)

1. Chronic Hepatitis C (CHC)

- a. Adult patients: In combination therapy with other hepatitis C virus drugs for adults with compensated liver disease. Monotherapy is indicated only if patient has contraindication or significant intolerance to other HCV drugs.
- b. Pediatric Patients: In combination with ribavirin for pediatric patients 5 years of age and older with compensated liver disease

2. Chronic Hepatitis B (CHB)

- a. Adult Patients: Treatment of adults with HBeAg-positive and HBeAg-negative chronic hepatitis B (CHB) infection who have compensated liver disease and evidence of viral replication and liver inflammation
- b. Pediatric Patients: Treatment of non-cirrhotic pediatric patients 3 years of age and older with HBeAg-positive CHB and evidence of viral replication and elevations in



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serum alanine aminotransferase (ALT)

**Pegintron** (peginterferon alfa-2b) is an antiviral indicated for: (8)

1. Chronic Hepatitis C (CHC) in patients with compensated liver disease

- a. In combination with ribavirin and an approved hepatitis C virus (HCV) NS3/4A protease inhibitor in adult patients with HCV genotype 1 infection
- b. In combination with ribavirin in patients with genotypes other than 1, pediatric patients (3-17 years of age), or in patients with genotype 1 infection where the use of HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications, or other clinical factors

**Pegintron** monotherapy should only be used in the treatment of chronic hepatitis C (CHC) in patients with compensated liver disease if there are contraindications to or significant intolerance to ribavirin and is indicated for use only in previously untreated adult patients. Combination therapy provides substantially better response rates than monotherapy (8).

**Ribavirin** a nucleoside analogue indicated in: (4-6)

1. Chronic Hepatitis C (CHC)

- a. In combination with interferon alfa-2b (pegylated and nonpegylated) for the treatment of chronic hepatitis C (CHC) in patients 3 years of age and older with compensated liver disease

**Pegasys** Limitations of Use: (7)

1. Pegasys alone or in combination with ribavirin without additional HCV antiviral drugs is not recommended for treatment of patients with CHC who previously failed therapy with an interferon-alfa
2. Pegasys is not recommended for treatment of patients with CHC who have had solid organ transplantation

**Pegasys** Off-Label Uses: (9)

1. Myeloproliferative neoplasms – Myelofibrosis
2. Myeloproliferative neoplasms – Polycythemia Vera



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##### **3. Myeloproliferative neoplasms – Essential Thrombocythemia**

Interferon based therapy has been shown to be effective in the treatment of myeloproliferative neoplasms (MPNs) and the use of Pegasys is supported by the National Comprehensive Cancer Network (NCCN) Guidelines as a valid therapy for this disease state (9).

Pegasys and PegINTRON carry a boxed warning regarding risk of serious disorders. The use of Pegasys or PegINTRON may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Monitor closely and withdraw therapy with persistently severe or worsening signs or symptoms of the above disorders (7,8).

If Pegasys is administered with other antiviral agents, the contraindications to those agents also apply to the combination regimen (7).

Ribavirin carries boxed warnings regarding embryo-fetal toxicity, hemolytic anemia, and monotherapy. Ribavirin is contraindicated in pregnant women and men whose female partners are pregnant. Pregnancy should be avoided during therapy and for 6 months after completion of treatment in both female patients and female partners of male patients who are taking ribavirin. Hemolytic anemia has been reported and may result in worsening of cardiac disease that has led to fatal and nonfatal myocardial infarctions. Patients with a history of significant or unstable cardiac disease should not be treated with ribavirin. Ribavirin monotherapy is not effective for the treatment of chronic hepatitis C infection (4-6).

The safety and efficacy of Pegasys in patients less than 5 years of age with chronic hepatitis C (CHC) or patients less than 3 years of age with chronic hepatitis B (CHB) have not been established (7)

The safety and efficacy of PegINTRON in patients less than 3 years of age have not been established (8).

The safety and efficacy of ribavirin in patients less than 3 years of age have not been established



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(4-6).

### **Summary**

Interferons are a group of proteins whose effects include antiviral activity, growth regulatory properties, inhibition of angiogenesis, regulation of cell differentiation, enhancement of major histocompatibility complex antigen expression, and a wide variety of immunomodulatory activities. Interferons were the first therapeutic agents that permitted successful antiviral therapy with acceptable side effects in patients with chronic hepatitis B, C and D. However, in hepatitis C virus (HCV) infections, direct-acting antivirals have become the new paradigm of treatment and have largely replaced interferon therapy. Peginterferons are pegylated interferons. Pegylation is a process whereby a polyethylene glycol (PEG) polymer is attached to the molecule in order to improve drug solubility, stability, and retention time. Ribavirin is a synthetic antiviral used in the treatment of hepatitis C. It works well in combination with peginterferons but not as monotherapy. Ribavirin is contraindicated in pregnant women and men whose female partners are pregnant. The safety and efficacy of Pegasys in patients less than 5 years of age with chronic hepatitis C (CHC) or patients less than 3 years of age with chronic hepatitis B (CHB) have not been established. The safety and efficacy of ribavirin or Pegintron in patients less than 3 years of age have not been established (1-9).

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

### **References**

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