### Pegylated interferon alfa (2a)

**Indication**: Chronic hepatitis C

**INN**: Peginterferon alfa-2a

**Medicine type**: Biological agent

**List type**: Complementary

**Additional notes**: To be used in combination with ribavirin.

**Formulations**: Parenteral > General injections > SC: 180 µg in vial; 180 µg in prefilled syringe

**EML status history**: First added in 2013 (TRS 985)

**Sex**: All

**Age**: Adolescents and adults

**Therapeutic alternatives**: The recommendation is for this specific medicine

**Patent information**: Patents have expired in most jurisdictions

**Wikipedia**: Pegylated interferon alfa (2a)

**DrugBank**: Pegylated interferon alfa (2a) (Peginterferon alfa-2a)

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**Summary of evidence and Expert Committee recommendations**

An application for addition of pegylated interferon was submitted by Medecins Sans Frontieres – Access Campaign, Geneva, Switzerland. Comments were received from the Global Hepatitis Programme of WHO, AIDS treatment organizations, multiple civil society organizations and patients’ groups. Peginterferon is a covalent conjugate of recombinant interferon alfa-2 with polyethylene glycol (PEG). The 2a and 2b formulations differ in the size and nature of the covalently attached PEG, resulting in differences in pharmacokinetics and doses. Globally, approximately 150 million people are infected with hepatitis C and it is estimated that 350 000 people die each year from hepatitis C-related liver disease (1). The goal of therapy is to produce a sustainable virological response (SVR) which can potentially result in the reversal of liver injury and can prevent serious consequences such as cirrhosis, end-stage liver disease, hepatocellular carcinoma and death. When compared with standard interferon-alfa alone, interferon-alfa in combination with ribavirin increased the SVR from 10–20% to 40–60% (2, 3). The long-acting pegylated formulation in combination with ribavirin has further increased SVR rates to 50–60% for genotype 1 and to 80% for genotypes 2 and 3 (4, 5). A recent meta-analysis showed that treatment success rates in low- and middle-income countries were similar to those obtained in high-income countries (6). Head-to-head randomized controlled trials – including the large randomized IDEAL trial (n = 3070) – demonstrated similar SVR rates for peginterferon alfa-2a and alfa-2b (41% versus 39% in IDEAL) in combination with ribavirin (7). While peginterferon alfa-2a or alfa-2b in combination with ribavirin has been the standard of care for chronic hepatitis C, the new direct-acting oral antiviral agents (bocepravir and telaprevir) are more effective but more expensive (8, 9). The Expert Committee noted that there are several more direct-acting antivirals in development. Pegylated interferons + ribavirin are associated with a range of adverse events that often require dose reduction and discontinuation. Adverse events that resulted in treatment termination were reported in 39 studies and were present in 4% (95% CI: 3–5) (6). Peginterferon alfa-2a and alfa-2b appear to be similarly tolerated (3). Before treatment patients must be screened, RNA measurements and genotyping (which require high-level laboratory support) must take place, and facilities are required for liver biopsy and for detecting and...
managing complications. WHO is developing guidelines for the screening, care and treatment of hepatitis C. Other expert bodies such as NICE (10), the European Association for the Study of the Liver (11) and the American Association for the Study of Liver Diseases (12) recommend peginterferon alfa-2a or alfa-2b with ribavirin for treatment of hepatitis C. Ribavirin was already listed in the EML and EMLc for viral haemorrhagic fevers. The Expert Committee agreed on the public health need for this medicine and, because of the high level of expertise and facilities needed and the high cost, decided to list pegylated interferon alfa-2a and alfa-2b in the complementary list, to be used with ribavirin for treatment of hepatitis C when these products are available. The Expert Committee stressed the need to follow the development of direct oral hepatitis C protease inhibitors and to consider applications for triple therapy or all-oral options for the treatment of hepatitis C.

References: