Interferon-α-2a
A Review of its Use in Chronic Hepatitis C

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Data Selection
Sources: Medical literature published in any language since 1966 on interferon-α-2a, identified using AdisBase (a proprietary database of Adis International, Auckland, New Zealand), Medline and EMBASE. Additional references were identified from the reference lists of published articles. Bibliographical information, including contributory unpublished data, was also requested from the company developing the drug.

Search strategy: AdisBase search terms were interferon-α-2a, hepatitis-C and liver-cancer. Medline and EMBASE search terms were interferon-alfa-2a, hepatitis-C, carcinoma-hepatocellular and liver-neoplasms. Searches were last updated 28 May 1998.

Selection: Studies in patients with chronic hepatitis who received interferon-α-2a. Inclusion of studies was based mainly on the methods section of the trials. When available, large, well controlled trials with appropriate statistical methodology were preferred. Relevant pharmacodynamic and pharmacokinetic data are also included.

Index terms: Interferon-α-2a, chronic hepatitis C, pharmacokinetics, pharmacodynamics, therapeutic use.

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Interferon-α-2a, a single interferon-α subtype manufactured by use of recombinant DNA technology, has immunomodulatory, antiviral and antiproliferative properties. It is a beneficial treatment for about 30% of patients with well-compensated chronic hepatitis C.

Biochemical responses [defined as normalisation of serum alanine aminotransferase (ALT) levels] are achieved in 37 to 76% of patients at the end of treatment with interferon-α-2a at dosages of 3 to 6MU 3 times weekly (given intramuscularly or subcutaneously) for 6 to 12 months. In contrast, evidence of disease remission is seldom observed in untreated patients. Improvements in liver histology in patients receiving interferon-α-2a are associated with complete biochemical responses to the drug. Virological responses (defined as an absence of hepatitis C-RNA in the serum) occur in up to 86% of patients after treatment with interferon-α-2a 3 to 6MU 3 times weekly for 12 months.

After cessation of interferon-α-2a therapy, a considerable proportion of treatment responders experience disease reactivation. Rates of sustained biochemical response are generally higher after 12 months’ therapy (27 to 57%) than after 6-month courses of treatment (27 to 30%). The long term efficacy of interferon-α-2a in patients with chronic hepatitis C is improved by the concomitant administration of ribavirin.

Interferon-α-2a shows efficacy similar to that of interferon-α-2b or interferon-α-n1 in patients with chronic hepatitis C.

During the first few days of therapy with interferon-α-2a (or other forms of interferon-α), most patients experience a transient ‘influenza-like’ reaction, characterised by fatigue, fever, chills and headache. These symptoms are usually alleviated by paracetamol (acetaminophen). Lethargy, mild myelosuppression, alopecia and neuropsychiatric symptoms are dose-limiting adverse effects that may occur during longer term therapy. Severe adverse effects, experienced by <2% of interferon-α-2a recipients, include severe depression, seizures and generalised bacterial infections. Autoimmune thyroid dysfunction develops in 3 to 12% of patients during treatment with interferon-α-2a.

**Conclusion.** Interferon-α-2a produces sustained responses in about 30% of adults with chronic hepatitis C. Its efficacy appears to be similar to that of other interferon-α products. Thus, the drug remains a useful first-line treatment option for adults with well-compensated chronic hepatitis C. Further research into the optimal dosage of interferon-α-2a and its role in combination with other agents is likely to contribute towards future advances in the management of chronic hepatitis C.