

# Emerging Drug List

## INTERFERON GAMMA-1B



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**Generic (Trade Name):** Interferon gamma-1b (Actimmune®)

**Manufacturer:** InterMune Pharmaceuticals, Inc.

**Indication:** According to the American product prescribing information, interferon gamma-1b is indicated for two purposes: for reducing the frequency and severity of serious infections associated with chronic granulomatous disease and for delaying the time to disease progression in patients with severe, malignant osteopetrosis.<sup>1</sup> It is also being explored in an off-label capacity, particularly for the treatment of idiopathic pulmonary fibrosis (IPF), which will be the focus of this review.

**Current Regulatory Status:** Actimmune is currently marketed in the US for the aforementioned indications however, there are ongoing clinical trials exploring the efficacy and safety of this product in other roles. The FDA granted InterMune's Actimmune product Fast Track Designation for the treatment of IPF in January 2002.<sup>2</sup> In Canada, Actimmune is available by request from Health Canada's Special Access Programme. In January 2001, InterMune filed a New Drug Submission with the Therapeutics Products Programme of Health Canada for both chronic granulomatous disease and severe malignant osteopetrosis.<sup>3</sup>

**Description:** Interferon gamma-1b is a biologic response modifier produced via a non-pathogenic strain of genetically engineered *E. coli*. It has been explored in the treatment of IPF as it possesses antifibrotic activity, possibly owing to reducing the activity of pro-fibrotic mediators, such as transforming growth factor beta-1.<sup>1,4</sup> In the US, Actimmune is available as a 100 µg (2 MIU)/0.5 mL vial.<sup>1</sup>

**Current Treatment:** Treatment options for IPF are rather limited and have met with questionable efficacy in practice. The more frequent intervention is the use of corticosteroids (prednisone or equivalent), while immunosuppressants [e.g. azathioprine (Imuran - GSK), cyclophosphamide (Cytoxan - BMS)] have also been utilized. None of these options are curative and most patients will succumb to this disease within three to five years from diagnosis. There have been many agents that have been investigated or are being investigated for use in this condition including interferon gamma-1b, anti-tumor necrosis factor alfa and pirfenidone.<sup>5,6</sup>

**Cost:** At this time, interferon gamma-1b is not commercialized in Canada therefore the Canadian price has not been included. In examining several online pharmacies based in the US, one vial of Actimmune (3 MIU/0.5 mL or 2 MIU/0.5 mL) has been quoted to cost from \$199.45 to \$203.48.<sup>7,8</sup> If you assume a cost of US\$200 per vial, used at dose of 200 µg sc three times weekly, this translates to a total yearly requirement of 312 vials and a cost of approximately US\$62,400.

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### Evidence:

Ziesche et al. published a preliminary study examining the use of interferon gamma-1b, in combination with low-dose prednisolone for the treatment of IPF. Adults (n=18) received either interferon gamma-1b, 200 µg sc three times a week, plus 7.5 mg oral prednisolone daily or 7.5 mg oral prednisolone (increased to 25 - 50 mg, as needed) alone for 12 months. Lung function at 12 months, measured as mean total lung capacity, declined in the prednisolone alone group ( $68 \pm 8\%$  of the predicted value at baseline to  $62 \pm 6\%$ ) while it improved in the patients treated with interferon gamma-1b ( $70 \pm 6\%$  of the predicted value at baseline to  $79 \pm 12\%$ ), yielding a statistically significant increase in total lung capacity in the interferon group ( $P < 0.001$ ).<sup>9</sup>

In May 2002, long-term follow-up data of this trial was presented at the 98th Annual Conference of the American Thoracic Society. Sixteen of the original 18 patients received one or more doses of Actimmune at the end of the 12 month study period. The estimate of survival at five years (Kaplan-Meier) was 77.8% and 16.7% in the interferon and control groups, respectively (log-rank test  $p = 0.009$ ).<sup>10</sup>

The company is currently conducting a phase III study to further elucidate the efficacy and safety of interferon gamma-1b in IPF. The trial is of a multicentre, double-blind design and enrolled steroid-unresponsive patients (n=260) randomized to receive either placebo or interferon gamma-1b, 200 µg sc three times weekly for 48 weeks. Enrollment was initiated in September of 2000 and the results of this trial expect to be reported at the end of 2002.<sup>11,12</sup>

### Adverse Effects:

In the Ziesche et al. study, those patients who received interferon gamma-1b with prednisolone reported fever and chills of variable severity (n=9), along with bone and muscle pain (n=3), during the first two to three weeks of therapy. Other noted adverse effects included brief migraine-like headaches and mild lymphopenia. Side effects reported in the control group included hyperglycemia, weight gain, skin changes and one report of aseptic necrosis of the femur.<sup>9</sup>

### Commentary:

Based on preliminary findings, Interferon gamma-1b has shown some promise in the treatment of IPF. This is welcome news; as to date other pharmacological interventions have had minimal impact on morbidity and mortality associated with this condition. If approved for IPF, it will be the first entity with this formal indication. The results of the phase III trial are highly anticipated and will be able to confirm or refute the favourable findings of the phase II trial. The true impact on morbidity will only be defined with long-term usage.

# Emerging Drug List

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This series highlights medical technologies that are not yet in widespread use in Canada and that may have a significant impact on health care. The contents are based on information from early experience with the technology; however, further evidence may become available in the future. These summaries are not intended to replace professional medical advice. They are compiled as an information service for those involved in planning and providing health care in Canada.

These summaries have not been externally peer reviewed.

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