

7.0 Post-Marketing Commitments

Immunex proposes to establish a registry of patients with MS treated with mitoxantrone after it receives marketing approval from FDA for this indication. The objective of this registry is to collect long-term safety data, including information on hospitalizations, neutropenic fever, cardiac failures, and secondary leukemia.

8.0 Proposed Use of Mitoxantrone in Patients with MS

There is a substantial unmet medical need in the treatment of patients with secondary progressive MS or with rapidly deteriorating relapsing-remitting MS. In the U.S., no drug has been approved to treat progressive forms of MS. Study 901 showed that mitoxantrone administered to patients with progressive MS at a dose of 12 mg/m² every 3 months for 2 years resulted in significant slowing of progression of neurologic impairment, reduction in the rate of relapses, and decrease in new Gd-enhancing lesions on MRI scans. Study 902 provides further evidence of the efficacy of mitoxantrone in patients with highly active MS. The safety profile reported in Study 901 indicates that mitoxantrone adverse events are manageable. The results from Study 903, in which mitoxantrone was used at similar doses and schedules, suggested that long-term therapy was feasible in large number of patients without increased toxicity.

Mitoxantrone cumulative cardiac toxicity may limit the continuation of therapy above a certain total dose. Despite this limitation, however, many patients who are not responding to treatment with interferon beta or copolymer 1, and who are currently treated with various unproven salvage therapies, may benefit from mitoxantrone therapy for some years. The two randomized studies presented here suggest that the magnitude of benefit reported with mitoxantrone is superior to the effect that can be expected with interferon beta or with other cytotoxic therapies.

Mitoxantrone has been on the market for over 10 years for the treatment of patients with various types of cancer. It has been shown to be of significant therapeutic benefit to many cancer patients. In the Immunex filing, we have shown that mitoxantrone is also safe and effective in the treatment of patients with MS. We request FDA approval of

mitoxantrone as a new therapeutic option for patients who suffer from a serious disease with unsatisfactory treatment options.