

June 21, 2000

To: The Manitoba Drug Standards and Therapeutics Committee
Manitoba Health
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From: The Multiple Sclerosis Society of Canada, Manitoba Division
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INTRODUCTION

It has been a year since the federal Health Protection Branch approved the use of interferon beta-1b (Betaseron®) for treatment of secondary-progressive multiple sclerosis (MS). Since that time the drug has been approved for reimbursement in Quebec, New Brunswick and Nova Scotia. The Multiple Sclerosis Society of Canada, Manitoba Division urges the Manitoba Drug Standards and Therapeutics Committee to also approve this treatment for reimbursement so that people living in Manitoba with secondary-progressive MS, who meet the treatment criteria, can have the same access to treatment as those elsewhere in Canada.

CONSENSUS STATEMENT OF THE CANADIAN MS CLINICS NETWORK

Beta interferon has been proven to have an impact on the course of MS. Because of this, the MS Society has joined the Canadian Network of MS Clinics in issuing a consensus statement on the use of disease modifying drugs in the treatment of MS. The statement, which was published in *The Canadian Journal of Neurological Sciences* in November 1999, sets out prescribing criteria guidelines. A copy of the consensus statement is attached for your information.

The consensus statement was developed in response to increasing medical evidence that treatment of MS should begin as soon as possible after diagnosis in people with active disease. Recent scientific studies have found that irreparable damage to nerve fibres occurs early in MS, making timely treatment of people with active disease vitally important. Specifically, the statement recommends the use of an approved therapy for people who have definite MS, have had clinical attacks at some point in the disease course, have ongoing active disease and are able to walk with or without mobility aids. These criteria can apply to people who have either relapsing-remitting or secondary-progressive MS.

LACK OF CONVINCING EVIDENCE IN BRITISH MEDICAL JOURNAL ARTICLE

We recognize that the approval of Betaseron® for treatment of secondary-progressive MS has prompted some individuals to question the cost utility of expanding access to the therapy through provincial government drug reimbursement programs. As we are sure you are aware, this debate was fueled by a report in the December 1999 *British Medical Journal* (BMJ) suggesting that treating people with the secondary-progressive stage of

the disease is not cost effective. After carefully reviewing the findings reported in the BMJ, the MS Society of Canada rejects the claim that little benefit can be derived from funding access to treatment for secondary-progressive MS, and remains convinced about the importance of treatment.

Based on his review of the findings reported in the BMJ study, our national medical advisor, Dr. William J. McIlroy, has concluded that it fails to provide convincing evidence to support its claim that treating people with secondary-progressive MS with interferon beta 1-b is not cost effective, for the following reasons.

1. Limitations of the EQ-5D measurement scale

In calculating the cost effectiveness of interferon beta-1b, the researchers compared the cost of treatment against averted health care costs by using the EQ-5D health related quality of life scale to measure quality adjusted life years (QALY) gained. This scale is too simplistic for use in studying a complex and chronic illness such as MS because it does not consider key MS symptoms that are highly significant for a patient's quality of life, such as fatigue, cognition and sensory impairment.

In addition, the EQ-5D scale is not sufficiently sensitive to changes in a patient's condition over time to be useful in judging the efficacy of treatments for an illness such as MS with a natural history of 30-40 years.

Other researchers have recognized the limitations of the EQ-5D and other general quality of life scales, and believe a disease-specific instrument is needed to undertake an effective cost utility analysis.

2. No direct comparison of treatment with other forms of care

The study fails to include a direct comparison of the cost utility of beta interferon with other forms of MS care. It does not calculate, for example, the cost utility of specialist nursing or rehabilitation and compare this with treatment. In the absence of this type of analysis the authors cannot justifiably argue that funding for MS treatments should be redirected to other forms of MS care.

3. Costs limited to treated relapses

The study assumed that for every relapse treated there was one that was not, and that the untreated relapses had no health service costs. This assumption fails to consider the effect of any relapse, treated or not, on the quality of life of an individual with MS. This is a considerable limitation because the greatest impact of the treatment is on reducing the frequency and severity of relapses, and the resulting improvement in quality of life.

4. Impact of treatment on quality of life

The resource utilization analysis is misleading because it covers only hospitalizations and corticosteroid use, and fails to take into account loss of time from work and impact on quality of life.

This is a significant shortcoming since there is unequivocal medical evidence that treatment can significantly improve the quality of life of many people who have MS. A study published in the November 1999 *Canadian Journal of Neurological Sciences* (Treatment with Interferon Beta-1b Improves Quality of Life in MS, G.P. Rice, et al), found that there was overall improvement of quality of life such that treated patients approached quality of life levels reported for the general population. The study also found that patients with low disability receiving interferon beta-1b had better quality of life when compared to an untreated population at a similar disability level.

In addition, the researchers found that after an average treatment duration of five years, the EDSS (expanded disability status score) versus time since disease onset was shifted in the treated group, suggesting that treated patients benefit from a much slower disease progression over the treatment period.

NORTH AMERICAN CLINICAL TRIAL OF BETASERON®

As you are no doubt aware, the results of a large North American clinical trial of the use of Betaseron® in secondary-progressive MS were released on May 1, 2000 at the meeting of the American Academy of Neurology in San Diego. While the primary outcome of the slowing of progression of disability was negative, secondary outcomes of a reduction in the number of relapses and of MS brain lesions as measured by MRI were positive in those study participants who were still having relapses and developing new brain lesions.

In our opinion, the main reason for the difference in outcomes between the North American and the European trials of Betaseron® (that showed a positive primary outcome of the slowing of progression of disability) is the fact that the participants in the North American study were approximately six years older at the time of entry into the study and had had the disease for slightly longer than those in the European study. The participants in the North American study also had significantly less disease activity than those in the European study: 55% were relapse-free in the two years prior to study entry, compared to just 30% of the European participants.

It is our view that the North American study reinforces the advice of the Canadian MS Clinics Network and the MS Society of Canada, as outlined in the consensus statement, that people with active disease should be treated early and should continue to be treated while the disease is active. In addition, the results of European, North American and other studies point out that the disease remains active in many people even after they have technically reached the stage of the disease called secondary-progressive, and that they could benefit from treatment, especially if they are still able to walk.

CONCLUSION

We want to emphasize that we do not believe that everyone with MS can benefit from treatment with beta interferon. In supporting the consensus statement, we hope to clearly outline who can most benefit from current MS treatments. The purpose of the consensus statement is to provide an overall rationale of the importance of early treatment, given the increasing evidence that permanent damage to nerve fibres and brain atrophy occurs early in MS, as well as to ensure that consistent criteria are

implemented across the country. These criteria apply to both people with relapsing-remitting MS and those who have reached the secondary-progressive stage, have active disease and are able to walk with or without an aid.

We hope that this information is helpful. Once again, we urge the Manitoba Drug Standards and Therapeutics Committee to approve interferon beta-1b (Betaseron®) for reimbursement by the Manitoba Pharmacare program, for individuals with secondary-progressive MS who meet the treatment criteria. This will enable more Manitobans with MS to have timely and affordable access to the treatments that MS specialists are recommending for their care.