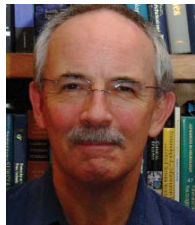


# ABN Guidelines for Treatment of Multiple Sclerosis with $\beta$ -Interferon and Glatiramer Acetate

As the new chairman of the ABN Multiple Sclerosis panel I am responding, on behalf of the Council, to the criticism of the ABN's latest guidelines for the use of disease modifying treatments in MS by Neil Scolding and his colleagues in Bristol. The first point to make is that all ABN guidelines are expressions of consensus and are formulated, as were these, after extensive consultation with ABN members. The MS panel is made up of a combination of ABN members expert in the disease and 'ordinary' clinical neurologists (expert only in talking to patients about these difficult issues); the present chairman is in the latter group. Guidelines are for guidance; they are not operating instructions, and the Appendix to the ABN guidelines makes clear that the informed patient should be involved in decisions so that, after a Clinically Isolated Syndrome (CIS), further MRI imaging may be performed even in the absence of a second event to discover if that person meets revised criteria for the diagnosis of MS, i.e. 'has MS'. Such a patient, in the opinion of the majority of MS experts in the UK, would in principle benefit from an effective disease modifying treatment. As Alasdair Coles has pointed out in these columns, this majority feels vindicated by the BENEFIT study's recently published latest report.

I suspect that what has provoked this 'controversy' is the knowledge that better disease modifying treatments are around the corner and likely, in the view of many, to supplant the two agents which are currently accepted as having some effect. However, for the moment,  $\beta$ -interferon and Glatiramer Acetate are the only ones that are available (outside trials) for 'ordinary', as opposed to 'aggressive', MS (Natalizumab has just been accepted by NICE as a cost effective treatment of the latter). The MS panel feel they have identified from the available evidence, by applying the modified McDonald criteria, those patients with CIS who may benefit from the early use of disease modifying treatments and the latest from the BENEFIT study tends to support this assessment. Of course we and Professor Scolding hope and expect that therapies of less ambiguous efficacy will soon be available for this group of patients. Clinical Guidelines are based upon evidence, but in dealing with patients it is also wise to interpret that evidence in the patients' favour. So far, it looks as if the MS panel has been right in its advice.

The facts that more information from future trials will inform this debate and better disease modifying treatments are needed are acknowledged. However clinicians in the field need to manage their patients now and must often extend decisions beyond the hard, academically uncontroversial, evidence in their interests. In view of the relative speed with which advances are being made in the treatment of MS it is very likely that the ABN will be issuing new guidelines before too long but I would be surprised if these do not advocate early treatment in patients with identified active disease (even after only one clinical event), but whilst nevertheless offering more effective (and we can hope cheaper) treatments.



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Interferon beta-1a

#### Initiation Pack

**Presentation** Each pre-filled glass syringe contains 8.8 or 22 micrograms of Interferon beta-1a in respectively 0.2 or 0.5 ml. **Indication** For the treatment of relapsing multiple sclerosis. Efficacy has not been demonstrated in patients with secondary progressive multiple sclerosis without ongoing relapse activity. **Dosage and administration** Treatment should be initiated under supervision of a physician experienced in the treatment of multiple sclerosis. For patients initiating treatment with Rebif®, the dosage recommended for the first month of treatment is 8.8 micrograms three times a week by subcutaneous injection for the first two weeks and 22 micrograms three times a week by subcutaneous injection for the following two weeks. From the fifth week Rebif 44 micrograms should be administered. Limited published data suggest that the safety profile in adolescents from 12 to 16 years of age receiving Rebif 22 micrograms by subcutaneous injection three times per week is similar to that seen in adults. Not to be used in patients under 12 years of age. Evaluate patients at least every second year of treatment period. **Contraindications** History of hypersensitivity to natural or recombinant interferon beta, human albumin, or to any of the excipients; initiation of treatment in pregnancy; current severe depression and/or suicidal ideation. **Precautions** Inform patients of the most common adverse reactions. Symptoms tend to be most prominent at the initiation of therapy and decrease in frequency and severity with continued treatment. Use with caution in patients with previous or current depressive disorders and those with antecedents of suicidal ideation. Patients should be advised to report immediately any symptoms of depression and/or suicidal ideation. Patients exhibiting depression should be monitored closely during therapy and treated appropriately. Cessation of therapy should be considered. Administer with caution to patients with a history of seizures and to those receiving treatment with anti-epileptics, particularly if their epilepsy is not adequately controlled. Patients should use an aseptic injection technique and rotate injection sites to minimise risk of injection site necrosis. Patients with cardiac disease should be closely monitored for worsening of their clinical condition during initiation of therapy. Use with caution in patients with history of significant liver disease, active liver disease, alcohol abuse or increased serum ALT. Serum ALT levels should be monitored prior to the start of therapy, at months 1, 3 and 6 on therapy and periodically thereafter. Stop treatment if icterus or other clinical symptoms of liver dysfunction appear. Treatment has a potential to cause severe liver injury including acute hepatic failure. Laboratory abnormalities are associated with the use of interferons. Liver enzyme and full haematological monitoring are recommended at regular intervals (months 1, 3 and 6 on therapy) and periodically thereafter. New or worsening thyroid abnormalities may occur. Thyroid function testing is recommended at baseline and if abnormal every 6 – 12 months. Administer with caution to and monitor closely patients with severe renal and hepatic failure or patients with severe myelosuppression. Serum neutralising antibodies against Interferon beta-1a may develop. The clinical significance of these antibodies has not been fully elucidated but is associated with reduced efficacy. If a patient responds poorly and has neutralising antibodies, reassess treatment. Women of childbearing potential should use effective contraception during treatment. **Side effects** The majority of adverse reactions observed with Interferon beta-1a are usually mild and reversible, and respond well to dose reductions. In case of severe or persistent undesirable effects, the dose of Rebif® may be temporarily lowered or interrupted, at the discretion of the physician. Very common adverse drug reactions (ADRs) are injection site inflammation/reaction, influenza like symptoms, headache, asymptomatic transaminase increase, neutropenia, lymphopenia, leucopenia, thrombocytopenia, anaemia. Common ADRs are injection site pain, myalgia, arthralgia, fatigue, rigors, fever, pruritus, rash, erythematous or maculo-papular rash, diarrhoea, vomiting, nausea, depression and insomnia. Serious AEs are injection site necrosis, hepatitis with or without icterus, severe liver damage, anaphylactic reactions, angioedema, erythema multiforme, erythema multiforme-like skin reactions, seizures, thromboembolic events, suicide attempt. Consult the Summary of Product Characteristics for more information relating to side effects. Additional information is available on request. **Pharmaceutical precautions** Store in a refrigerator at 2°C to 8°C in the original package. Do not freeze. **Legal category** POM **Basic NHS price** Rebif® Initiation Pack containing: Rebif® 8.8 micrograms - solution for injections: 6 pre-filled syringes (0.2 ml) Rebif® 22 micrograms – solution for injections: 6 pre-filled syringes (0.5 ml) £586.19 Prices in Ireland may differ, consult distributors Allphar Services Ltd **Marketing Authorisation Numbers:** EU/1/98/063/007 **Name and Address of Marketing Authorisation Holder** Sero Europe Ltd, 56 Marsh Wall, LONDON E14 9TP **Name and Address of Distributor in UK** Sero Ltd, Bedford Cross, Stanwell Road, Feltham, Middlesex TW14 8NX **Name and Address of Distributor in Ireland** Allphar Services Ltd, Pharmaceutical Agents and Distributors Belgard Road, Tallaght, Dublin 24, Ireland

**Date of Preparation:** May 2007

**Job Bag:** REB07-0074

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