PRESCRIBING INFORMATION – UK AND IRELAND

REBIF® (Interferon beta-1a) (Please refer to the full Summary of Product Characteristics before prescribing)

PRESENTATION: Pre-filled glass syringes containing 8.8 µg/0.2 ml, 22 µg/0.5 ml, 44 µg/0.5 ml Rebif solution. Disposable pre-filled pen injector (RebiDose) containing 8.8 µg/0.2 ml, 22 µg/0.5 ml, 44 µg/0.5 ml Rebif solution. Pre-filled glass cartridges containing 22 µg/0.5 ml, 44 µg/0.5 ml, 8.8 µg/0.1 ml and 22 µg/0.25 ml Rebif cartridges.

INDICATIONS: For treatment of

- patients with a single demyelinating event with an active inflammatory process, if alternative diagnoses have been excluded, and if they are determined to be at high risk of developing clinically definite multiple sclerosis.

  N.B. Rebif 22 µg presentations are not indicated in the treatment of single clinical events suggestive of multiple sclerosis.

- patients with relapsing multiple sclerosis. In clinical trials, this was characterised by two or more acute exacerbations in the previous two years.

DOSAGE AND ADMINISTRATION: Initiate under supervision of a physician experienced in the treatment of multiple sclerosis. Administer by subcutaneous injection.

Dose: Weeks 1 and 2: 8.8 µg three times per week (TIW); weeks 3 and 4: 22 µg TIW: week 5 onwards: 44 µg TIW (22 µg TIW can be used if patients cannot tolerate higher dose, but only in treatment of relapsing multiple sclerosis). Do not use in patients under 2 years of age.

Prior to injection and for an additional 24 h after each injection, an antipyretic analgesic is advised. Evaluate patients at least every second year of the treatment period.

CONTRAINDICATIONS: Hypersensitivity to natural or recombinant interferon-beta, or to any of the excipients; treatment initiation in pregnancy; current severe depression and/or suicidal ideation.

PRECAUTIONS: Use with caution in patients: with previous or current depressive disorders and those with antecedents of suicidal ideation ; with a history of seizures or those receiving treatment with anti-epileptics, particularly if epilepsy is not controlled; with a history of significant liver disease, active liver disease, alcohol abuse or increased serum ALT; severe renal and hepatic failure or severe myelosuppression; receiving medicines with a narrow therapeutic index cleared by cytochrome P450.

Monitor: patients exhibiting depression and treat appropriately; patients with cardiac disease for worsening of their condition during initiation; serum ALT prior to start of therapy, at months 1, 3 and 6 and periodically thereafter - stop treatment if icterus or symptoms of liver dysfunction appear. Treatment has potential to cause severe liver injury including acute hepatic failure; patients with severe renal and hepatic failure or severe myelosuppression; haematological parameters at months 1, 3 and 6 and periodically thereafter; early signs and symptoms of nephrotic syndrome especially in patients at higher risk of renal disease. All monitoring should be more frequent when initiating Rebif 44.

Cases of thrombotic microangiopathy (TMA) have been reported. If clinical features are observed, testing of platelet levels, serum LDH, blood films and renal function is recommended. If TMA is diagnosed, treat promptly. Immediate discontinuation of Rebif is recommended. Cases of nephrotic syndrome have been reported during treatment with interferon-beta products. Prompt treatment of nephrotic syndrome is required and discontinuation of Rebif should be considered.

New or worsening thyroid abnormalities may occur. Thyroid function testing is recommended at baseline and if abnormal, every 6 – 12 months.

Serum neutralising antibodies may develop and are associated with reduced efficacy. If a patient responds poorly to therapy and has neutralising antibodies, reassess treatment.

Women of childbearing potential should use effective contraception. Limited data suggest possible increased risk of spontaneous abortion. During lactation, either discontinue Rebif or breast-feeding. If overdose occurs, hospitalise patient and give supportive treatment.

SIDE EFFECTS: In the case of severe or persistent undesirable effects, consider temporarily lowering or interrupting dose. **Very common:** flu-like symptoms, injection site inflammation/reaction, headache, asymptomatic transaminase increase, neutropenia, lymphopenia, leukopenia, thrombocytopenia, anaemia. **Common:** injection site pain, myalgia, arthralgia, fatigue, rigors, fever, pruritus, rash, erythematous/maculo-papular rash, alopecia, diarrhoea, vomiting, nausea, depression, insomnia, severe elevations of transaminases. **Other side effects include:** injection site necrosis/abscess/infections/cellulitis, urticaria, thyroid dysfunction, hepatic failure, hepatitis with or without icterus, autoimmune hepatitis, anaphylactic reactions, angio-edema, erythema multiforme, erythema multiforme-like skin reactions, drug-induced lupus erythematosus, nephrotic syndrome, glomerulosclerosis, seizures, transient neurological symptoms, thromboembolic events, TMA including thrombotic thrombocytopenic purpura/haemolytic uremic syndrome, pancytopenia, suicide attempt, Stevens-Johnson syndrome, dyspnoea, pulmonary arterial hypertension, retinal vascular disorders.

Prescribers should consult the Summary of Product Characteristics in relation to other side effects.

LEGAL CATEGORY: POM.

PRICE:

Rebif 8.8 µg and 22 µg: 6 (0.2 ml) + 6 (0.5 ml) syringes/pens – £552.19

Rebif 8.8 µg/0.1 ml and 22 µg/0.25 ml: 2x 1.5 ml cartridges – £406.61

Rebif 22 µg: 12x 0.5 ml syringes/12x0.5 ml pens/4x 1.5 ml cartridges – £613.52

Rebif 44 µg: 12 x0.5 ml syringes/12 x 0.5 ml pens/4 x1.5 ml cartridges – £813.21

For prices in Ireland, consult distributors Allphar Services Ltd.

Marketing Authorisation Holder and Numbers:

Merck Serono Europe Ltd, 56 Marsh Wall, London, E14 9TP; EU/1/98/063/007; 003 ; 006 ; 017; 013 ; 016 ; 010 ; 008 ; 009.

For further information contact:

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Republic of Ireland: Merck Serono, 4045 Kingswood Road, Citywest Business Campus, Dublin 24. Tel: 01 4687590.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. In the Republic of Ireland information can be found at www.hpra.ie. Adverse events should also be reported to Merck Serono Limited – Tel: +44(0)20 8818 7373 or email: medinfo.uk@merckgroup.com.