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Dear Doctor

Important Safety Information for
Avonex®, Betaferon® and Rebif®.

Further to discussions with the Irish Medicines Board (IMB), the above companies are writing to you to advise you on the outcome of a class review of all beta interferons authorised for the treatment of multiple sclerosis (Avonex, Betaferon and Rebif) conducted at EU level by the Committee for Medicinal Products for Human Use (CHMP) in 2006. This review was based upon clinical trial, post-marketing data and literature submitted by the Marketing Authorisation Holders (Biogen Idec Ltd., Schering AG and Serono Ltd, respectively, who are also owners of the respective trademarks). The outcome of the review was to recommend revision of the contraindications, precautions and warnings and pregnancy sections of the Summary of Product Characteristics (SmPCs) for Avonex, Betaferon and Rebif, addressing the following:

- **Epilepsy**
  Removal of the absolute contraindication in patients with epilepsy not adequately controlled with treatment and a revision of the warning section to indicate that interferon beta should be used with caution in patients with epilepsy, particularly if their epilepsy is not adequately controlled.

- **Pregnancy**
  Revision of the contraindication in pregnancy to indicate that the initiation of treatment in pregnancy is contraindicated but leaving some room for clinical judgment as to whether a patient who becomes pregnant while taking interferon beta should continue or stop treatment.

- **Depressive disorders and suicidal information**
  Revision of the contraindication in patients with a history of severe depressive disorders and/or suicidal ideation, to indicate that treatment of patients with current severe depression and/or suicidal ideation is contraindicated.

The updated text of sections 4.3, 4.4 and 4.6 of the SmPCs for Avonex, Betaferon and Rebif are as follows:

Section 4.3 Contraindications
• Initiation of treatment in pregnancy (see Section 4.6 pregnancy and lactation).
• Patients with a history of hypersensitivity to natural or recombinant interferon-beta, human albumin or to any excipients.
• Patients with current severe depression and/or suicidal ideation (see sections 4.4 Special warnings and special precautions for use and 4.8 Undesirable effects).

Section 4.4 Special warnings and precautions for use
[Avonex / Betaferon / Rebif] should be administered with caution to patients with previous or current depressive disorders in particular to those with antecedents of suicidal ideation (see section 4.3). Depression and suicidal ideation are known to occur in increased frequency in the multiple sclerosis population and in association with interferon use. Patients treated with [Avonex / Betaferon / Rebif] should be advised to immediately report any symptoms of depression and/or suicidal ideation to their prescribing physician. Patients exhibiting depression should be monitored closely during therapy with [Avonex / Betaferon / Rebif] and treated appropriately. Cessation of therapy with [Avonex / Betaferon / Rebif] should be considered (see also section 4.3 and section 4.8). [Avonex / Betaferon /Rebif] should be administered with caution to patients with a history of seizures, to those receiving treatment with anti-epileptics, particularly if their epilepsy is not adequately controlled with anti-epileptics (see section 4.5 and section 4.8).

Section 4.6 Pregnancy and lactation
• Pregnancy
There is limited information on the use of [Avonex / Betaferon / Rebif] in pregnancy. Available data indicates that there may be an increased risk of spontaneous abortion. Initiation of treatment is contraindicated during pregnancy (see section 4.3).
• Women of child-bearing potential
Women of child-bearing potential should take appropriate contraceptive measures. If the patient becomes pregnant or plans to become pregnant while taking [Avonex / Betaferon / Rebif] she should be informed of the potential hazards and discontinuation of therapy should be considered (see section 5.3). In patients with a high relapse rate before treatments started, the risk of a severe relapse following discontinuation of [Avonex / Betaferon / Rebif] in the event of pregnancy should be weighed against a possible increased risk of spontaneous abortion.

Communication information
For further information concerning Avonex or Betaferon or Rebif, please contact Medical Information at the appropriate Marketing Authorisation Holder:
Avonex: Biogen Idec Ltd, telephone number ++ 44 1628 501000
e-mail: ukrecept@biogenidec.com
Betaferon: HE Clissmann, Irish Agent, Bayer Schering Pharma, Dublin,
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Rebif : Serono Ltd, telephone number ++ 44 208 818 7373,
e-mail: medinfo.uk@merckserono.net

Copies of the revised SmPCs for Avonex / Betaferon / Rebif may be found at www.medicines.ie

Call for reporting
Healthcare professionals are reminded to continue to report any suspected adverse reactions to the IMB and/or the relevant company.

Yours sincerely,

Conn Clissmann	Dr S. Hughes	Dr. G. L. Shepherd
HE Clissmann, Irish Agent	Medical Director	Medical Director
Bayer Schering Pharma	Biogen Ltd	Serono Ltd