STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

For procedures finalised after 01 March 2004 please refer to module 8B**.**

Subsequent post Marketing Authorisation applications agreed upon are summarised in the table below:

Scope	Application number	Type of modification[1]	Notification/ Opinion issued on[2]	Commission Decision Issued/amended on
Change in supplier of an intermediate compound used in manufacture of the active substance	I/0001	I	20.10.99	15.12.99
Update of Summary of Product Characteristics (SPC) and Package Leaflet (PL) sections "Therapeutic indications", "Special Warnings and special precautions for use"," Interaction with other medicinal products and other forms of interactions", "Undesirable effects", "Pharmacodynamic properties"), following the annual reassessment of the benefit/ risk profile, the evaluation of PSUR 6 and the availability of new safety data	II/0002	II	14.12.00	23.04.01
Annual reassessment All remaining specific obligations are fulfilled, there are no remaining grounds to keep the Marketing Authorisation under exceptional circumstances	S/0003	S	14.12.00	18.05.01
Update of the SPC, (sections "Special warnings and special precautions for use", "Pharmacodynamic properties") following the availability of new clinical data in paediatric patients with hepatitis B. Furthermore, the MAH proposed some minor changes in the SPC, Labelling and PL in order to bring the text in line with the latest QRD/ EMEA templates. The MAH also included changes to the name/ address of the local representatives.	II/0004	II	13.12.2001	02.04.02
Change in specification of starting material/intermediate used in manufacturing of the active substance	I/0005	I	08.05.02	17.05.02
Update of the SPC in order to provide prescribers with available information on the exacerbation of hepatitis, either upon treatment discontinuation or due to loss of efficacy with Zeffix. Also, to update information on the occurrence of YMDD variant HBV in patients receiving long-term therapy. Finally to include 5-year results from a clinical study. Changes relate to sections 4.4 ("Special warnings and special precautions for use") and 5.1 ("Pharmacodynamic properties") of the SPC.	II/0006	II	19.09.02	19.12.02
Change in or addition of manufacturing site(s) for part or all of the manufacturing process	I/0007	I	30.07.02	-
Change in or addition of manufacturing site(s) for part or all of the manufacturing process	I/0008	I	30.07.02	09.09.02
Change in the qualitative composition of immediate packaging material	I/0009	I	30.07.02	-
Minor changes in manufacture of the medicinal product	I/0010	I	30.07.02	-
Change in the batch size of finished product	I/0011	I	30.07.02	-
Changes to aspects of the PL to revise the list of the local representatives and to correct the name of the manufacturer and to the Labelling to add the name of active ingredient to the blister foil. Furthermore this notification amends the Danish, French, Italian and Swedish language versions of the PL to correctly reflect the English version. At this occasion the texts of the Labelling and PL have been amended in line with the EMEA/QRD templates.	N/0012	N	15.01.03	17.02.03
Change in test procedure of active substance	I/0014	I	05.08.2003	19.08.2003

[1] In accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended: **I** refers to a minor variation (Type I variation); **II** refers to a major variation (Type II variation); **I/II** refers to a minor variation following the procedure set out in Article 6, 7 and 8 of the Regulation; **X** refers to an Annex II application. **T** refers to a transfer of a Marketing Authorisation in accordance with Commission Regulation (EC) No 2141/96 of 7 November 1996.
N refers to a notification in accordance with Article 10(3) of Council Directive 92/27/EEC of 31 March 1992.

[2] For Notifications and Type I variations, the date of entry into force of the change is the EMEA Notification date. The Commission Decision will be amended accordingly.

Update of the SPC further to the CPMP assessment of the PSUR covering 1 June - 30 November 2002. This includes reformatting section 4.8 "Undesirable effects", presenting the adverse drug reactions by MedDRA system organ class and ranked by frequency and adding the adverse reactions thrombocytopenia and muscle disorders, including myalgia and cramps. Furthermore, the SPC has been updated in line with the latest EMEA/QRD templates. The PL has been updated accordingly. Furthermore, the name of manufacturer has been corrected in the Danish PL.	II/0015	II	22.10.2003	awaited
Change in BR/QC testing – repl./add. Of batch control/testing site	I/0016	I	29.10.2003	-
Minor change in the manufacturing process of the active substance	IB/0022	I	10.02.2004	-