Nespo

Procedural steps taken and scientific information after the authorisation
Changes made after 01/09/2003

For procedures finalised before 01/09/2003, please refer to module 8A

MAJOR CHANGES[1]

No	Scope	Opinion issued on	Commission Decision Issued/ amended on	Product Information affected[2]	Summary
II/0047	Update of Summary of Product Characteristics and Package Leaflet	25/09/2008	28/10/2008	SPC, PL	This variation primarily concerns an update of the SPC following the completion of a class safety review by the PhVWP and the CHMP. The safety review was initiated because recent data show a consistent unexplained excess mortality in cancer patients with anaemia treated with epoetins. As a result, CHMP requested to update section 4.4 of the SPC to include an additional ESA class warning in the epoetins with cancer indication. The Package Leaflet has been updated accordingly
II/0046	Update of DDPS (Pharmacovigilance) Update of Detail Description of the Pharmacovigilance System (Pharmacovigilance)	25/09/2008	28/10/2008	Annex II	The Marketing Authorisation Holder applied to update the Detailed Description of the Pharmacovigilance System (DDPS). There have been no significant changes made to the MAH's pharmacovigilance systems. Version 3.0 of the DDPS has been updated in line with the summary of pharmacovigilance systems submitted in May 2008. The changes are administrative and provide further clarity on the pharmacovigilance systems in place.
II/0045	Update of Summary of Product Characteristics and Package Leaflet Update of sections 4.4 and 4.8 of the SPC following an update of the Company Core Data Sheet. The package leaflet has also been amended accordingly. The MAH also introduced a Getting Started Guide (GSG) as additional information to the package leaflet.	24/07/2008	29/08/2008	SPC, PL	Update of sections 4.4 and 4.8 of the SPC following an update of the Company Core Data Sheet. The package leaflet has also been amended accordingly. The MAH also introduced a Getting Started Guide (GSG) as additional information to the package leaflet.

[1] Major changes e.g. Type II variations, Annex II applications, Renewals and Annual Reassessments
[2] SPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet)

No	Scope	Opinion issued on	Commission Decision Issued/ amended on	Product Information affected[2]	Summary
X/0043	01_vi_Qualitative change in declared active substance - Other	24/04/2008	03/07/2008	Annex II	
II/0044	Update of Summary of Product Characteristics and Package Leaflet	24/01/2008	26/02/2008	SPC, PL	This variation primarily concerns an update of the SPC following the completion of a class safety review by the PhVWP and the CHMP. The safety review was initiated because recent data show a consistent unexplained excess mortality in cancer patients with anaemia treated with epoetins, and that treatment of anaemia with epoetins in patients with chronic kidney disease to achieve relatively high target haemoglobin concentrations may be associated with an increase in the risk of mortality and cardiovascular morbidity. As a result, the main changes being implemented are: i) in section 4.1, to highlight that epoetins should be used only if associated with symptoms, ii) in Section 4.2 to establish a uniform target haemoglobin range for all epoetins, iii) in Section 4.4 to mention the observed negative benefit risk balance in patients treated with high target haemoglobin concentrations, and iv) in section 5.1 to include the relevant results of the trials triggering the safety review. The package leaflet has also been updated accordingly. Additional sections 2, 4.9 and 5.2 have also been amended to correct minor inconsistencies. In addition, the MAH has taken this opportunity to re-format the approved package leaflet and take into account the results of user testing.
II/0036	Extension of Indication The MAH has submitted an extension of indication to allow treatment to CRF paediatric subjects >/=11 years of age. As a result, sections 4.1, 4.2 and 5.2 of the SPC have been updated. New data from efficacy and safety based study 20000100 supports removing this restriction, and allow treatment of all ages of CRF paediatric subjects, in addition to adults. As a result of this, section 4.2 of the SPC has also been	19/07/2007	30/08/2007	SPC, PL	Please refer to the Scientific Discussion: Nespo-H-333-II-36-AR.

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	updated to provide clarity over dosing paediatric subjects. The data from pharmacokinetic (PK) study 20000126 investigated in paediatric subjects with nonmyeloid malignancies who were receiving chemotherapy supports an additional statement in section 5.2 of the SPC. The limited PK data in paediatric subjects receiving chemotherapy is only supportive of a statement in section 5.2 of the SPC, with regards to the study findings. The package leaflet was updated accordingly.				
II/0040	New presentation(s)	22/03/2007	02/05/2007	SPC, Labelling, PL	
II/0041	Change(s) to the manufacturing process for the finished product	22/03/2007	28/03/2007		
II/0039	Update of Summary of Product Characteristics and Package Leaflet	18/10/2006	28/11/2006	SPC, PL	To amend sections 4.2 and 5.1 of the SPC in response to CHMP request (FUM 056) requiring the MAH to remove the recommendation for dose increase in patients receiving darbepoetin alfa once weekly with an inadequate response. The Package Leaflet has been amended accordingly.
II/0038	Update of Summary of Product Characteristics	21/09/2006	30/10/2006	SPC	The MAH has applied to amend section 5.1 of the SPC to modify the language relating to influence of darbepoetin alfa on tumour progression and survival for lymphoproliferative subjects treated with darbepoetin alfa.
II/0035	Change(s) to the manufacturing process for the active substance	27/07/2006	03/08/2006		
R/0034	Renewal of the marketing authorisation	23/03/2006	19/05/2006	SPC, Labelling, PL	
II/0033	Update of or change(s) to the pharmaceutical documentation	23/02/2006	28/02/2006		
II/0032	Update of Summary of Product Characteristics and Package Leaflet	26/01/2006	28/02/2006	SPC, PL	The MAH has applied to amend sections 4.2 and 5.2 to modify the posology for patients with chronic renal failure switching from recombinant human erythropoietin to darbepoetin alfa during the maintenance phase of treatment. The Package Leaflet has also been amended accordingly.

No	Scope	Opinion issued on	Commission Decision Issued/ amended on	Product Information affected[2]	Summary
II/0031	Update of Summary of Product Characteristics and Package Leaflet	27/07/2005	08/09/2005	SPC, PL	The MAH has applied to update sections 4.4 and 4.8 of the SPC in relation to Pure Red Cell Aplasia. The Package Leaflet has also been updated accordingly.
II/0030	Change(s) to the manufacturing process for the active substance	27/07/2005	03/08/2005		
II/0029	Update of Summary of Product Characteristics and Package Leaflet	26/05/2005	08/07/2005	SPC, PL	Please refer to the Scientific Discussion: Nespo-H-333-II-29
II/0028	Quality changes The Marketing Authorisation Holder applied to change the product specifications.	16/03/2005	23/03/2005		
II/0027	New presentation(s) The Marketing Authorisation Holder applied to add a new pre-filled pen injection device to the product range.	20/01/2005	28/02/2005	SPC, Labelling, PL	
II/0025	Update of Summary of Product Characteristics and Package Leaflet	29/07/2004	09/09/2004	SPC, PL	The marketing authorisation holder applied to support the extension of the dosing intervals in the treatment of anaemia associated with chronic renal failure in adults and paediatric subjects 3 11 years of age (once monthly) and in adults with chemotherapy-induced anaemia (once every three week). The SPC and Package Leaflet have been updated accordingly.
II/0023	Update of Summary of Product Characteristics and Package Leaflet	26/02/2004	14/04/2004	SPC, PL	The marketing authorisation holder applied to introduce additional text to Section 4.4 "Special Warnings and Special Precautions for Use" and Section 4.8 "Undesirable Effects" of the SPC. The package leaflet has been updated accordingly.
II/0022	Update of Summary of Product Characteristics and Package Leaflet	21/01/2004	21/01/2004	SPC, PL	

MINOR CHANGES[3]

[3] Minor changes e.g. Type I variations and Notifications

No	Scope	Product Information affected[2]	Date[4]
N/0042	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	PL	31/07/2007
IB/0037	41_a_02_Change in pack size - change in no. of units outside range of appr. pack size IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	SPC, Labelling, PL	31/07/2006
IA/0026	28_Change in any part of primary packaging material not in contact with finished product 41_a_01_Change in pack size - change in no. of units within range of appr. pack size	SPC, Labelling, PL	26/05/2004

[4] Date of entry into force of the change