Visudyne

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
IAIN/0103	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	02/09/2020		Annex II and PL	
IAIN/0102	B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing	20/11/2019		Annex II and PL	

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

PSUSA/3110/ 201812	Periodic Safety Update EU Single assessment - verteporfin	05/09/2019	n/a		PRAC Recommendation - maintenance
T/0100	Transfer of Marketing Authorisation	07/06/2019	25/07/2019	SmPC, Labelling and PL	
II/0098/G	This was an application for a group of variations. B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	29/05/2019	n/a		

	B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
II/0097	Update of section 4.4. of the SmPC to amend the existing warning on hypersensitivity reactions and of section 4.8 to include "Anaphylactic Reaction" with frequency 'not known'. The Package Leaflet has been updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/07/2018	25/07/2019	SmPC and PL	Cases of anaphylactic reactions have been observed in patients receiving Visudyne. If an anaphylactic or other serious allergic reaction occurs during or following infusion, administration of Visudyne should be discontinued immediately and appropriate therapy initiated.

T/0096	Transfer of Marketing Authorisation	18/04/2018	06/07/2018	SmPC, Labelling and PL	
II/0095	Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning with information on localised skin necrosis upon extravasation and to add injection site necrosis as a new adverse drug reaction with frequency unknown. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/10/2017	06/07/2018	SmPC, Labelling and PL	
IA/0094	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	16/03/2017	n/a		
PSUSA/3110/ 201512	Periodic Safety Update EU Single assessment - verteporfin	07/07/2016	n/a		PRAC Recommendation - maintenance
IA/0093/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for	13/04/2016	n/a		

	the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place				
II/0091	Update of section 4.8 of the SmPC regarding hypersensitivity and vasovagal adverse reactions and the frequencies for retinal oedema and infusion-related chest pain. The Package Leaflet is updated accordingly. The MAH took the opportunity of this procedure to update the Product Information in line with the latest QRD template version 9.1. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/12/2015	19/12/2016	SmPC, Annex II, Labelling and PL	
PSUSA/3110/ 201412	Periodic Safety Update EU Single assessment - verteporfin	23/07/2015	18/09/2015		Please refer to Visudyne-PSUSA/00003110/201412 ePAR: Scientific conclusions and ground recommending the variation to the terms of the marketing authorisation
IA/0089	A.7 - Administrative change - Deletion of manufacturing sites	26/01/2015	n/a		
IAIN/0088	A.1 - Administrative change - Change in the name and/or address of the MAH	10/11/2014	18/09/2015	SmPC, Labelling and PL	

IA/0087	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	13/10/2014	n/a		
IA/0086/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	21/08/2014	n/a		
PSUV/0085	Periodic Safety Update	10/07/2014	n/a		PRAC Recommendation - maintenance
N/0083	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/12/2013	18/09/2015	PL	
IA/0084/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites	08/11/2013	n/a		

	(excluding manufacturer for batch release) A.7 - Administrative change - Deletion of manufacturing sites B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier				
IG/0248	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/12/2012	n/a		
II/0079	Update of sections 4.5, 4.8, 5.2 and 5.3 of the SmPC in order to: - include new text indicating theoretical potential interactions with drugs increasing verteporfin tissue-uptake, free radical scavengers and drugs antagonizing blood vessel occlusion (section 4.5) - include the events of macular edema and retinal edema as adverse drug reactions (section 4.8) - re-word and/or add new wording for the new sub-headings "Distribution", "Linearity/non-linearity", "Special populations", "Hepatic impairment", "Renal impairment", "Ethnic groups/races" and "Effects on gender" (section 5.2) - include new and/or re-worded text under the new sub-headings: "Single and repeated dose toxicity", "Reproductive toxicity", "Carcinogenicity" and "Mutagenicity" (section 5.3) The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to update	20/09/2012	23/10/2012	SmPC, Annex II, Labelling and PL	In order to reflect the up to date available pre-clinical and clinical findings resulting from review of additional literature and already existing data and to bring the PI in line with the latest QRD template (version 8.1), the MAH included new text indicating theoretical potential drug-drug interactions; re-worded and/or added new wording for all new sub-headings under section 5.2 of the SmPC; included new and/or re-worded text under all new sub-headings under section 5.3 of the SmPC. In addition, based on temporal association, increase in annual reporting rates and the possible biological role of Visudyne, the MAH included the events of macular edema and retinal edema as adverse drug reactions.

	the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 8.1. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				
IA/0081/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	07/09/2012	n/a		
IG/0209/G	This was an application for a group of variations. C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	17/08/2012	n/a		

IG/0148/G	This was an application for a group of variations. C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	22/02/2012	n/a		
IB/0077	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	05/01/2012	n/a		
IA/0074/G	This was an application for a group of variations. B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	09/08/2011	n/a	Annex II and PL	
IG/0088/G	This was an application for a group of variations. C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons	11/07/2011	n/a		

	or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
IG/0065	B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing	17/05/2011	n/a		
II/0072/G	This was an application for a group of variations. Replacement of a manufacturer of a starting material used in the manufacture of verteporfin. A.7 - Administrative change - Deletion of manufacturing sites B.I.a.1.d - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New manufacturer of material for which an assessment is required of viral safety and/or TSE risk	14/04/2011	02/05/2011		
IB/0073	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new tests and limits	06/04/2011	n/a		
IG/0032/G	This was an application for a group of variations. To update the Detailed Description of the Pharmacovigilance System (DDPS) to version 9.0, to	21/12/2010	n/a	Annex II	

	include: - a change in the deputy of the Qualified Person for Pharmacovigilance (QPPV); - a change in the major contractual arrangements. - administrative changes not impacting the operation of the pharmacovigilance system. Annex II.B has also been updated with the latest wording as per October 2010 CHMP procedural announcement. C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
IA/0071/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.c - Change in the specification parameters	30/11/2010	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits				
R/0069	Renewal of the marketing authorisation.	18/02/2010	05/05/2010	SmPC, Annex II, Labelling and PL	Based on the review of the available information the CHMP is of the opinion that the quality, the safety and the efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and considers that the benefit/risk profile of Visudyne continues to be favourable. The CHMP therefore recommended that a renewal can be

					granted with unlimited validity. With this procedure the MAH also updated the product information (PI). This update was made so that the PI would be in line with the current QRD requirements.
II/0070	Update of the Detailed Description of the Pharmacovigilance system (DDPS). Changes to QPPV Update of DDPS (Pharmacovigilance)	18/02/2010	23/03/2010	Annex II	With this variation the MAH submitted a new version of the DDPS (core version 8.0 and product specific version 2.0) in accordance with the current Pharmacovigilance guideline. After assessing the documentation the CHMP concluded that the submitted DDPS contained all required elements.
IB/0064	Addition of manufacturer for the active substance. IB_14_b_Change in manuf. of active substance without Ph. Eur. certificate - new manufacturer	10/12/2009	n/a		
IB/0068	IB_33_Minor change in the manufacture of the finished product	03/12/2009	n/a		
IB/0067	IB_37_b_Change in the specification of the finished product - add. of new test parameter	03/12/2009	n/a		
IA/0066	IA_37_a_Change in the specification of the finished product - tightening of specification limits	13/11/2009	n/a		
IA/0065	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	09/11/2009	n/a		
II/0062	To add a Detailed Description of the Pharmacovigilance system (DDPS) to Module 1.8.1. of the Visudyne Marketing Authorisation, in	23/10/2008	04/12/2008	Annex II	With this variation the MAH submitted a first version of the DDPS (version 1.0 dated 30 June, 2008). After assessing the documentation the CHMP concluded that the submitted

	accordance with the current pharmacovigilance guideline. Update of DDPS (Pharmacovigilance)				DDPS contained all required elements. The CHMP therefore accepted an update of Annex II to include an additional paragraph with details of the DDPS under the section "other conditions".
IA/0063	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	18/08/2008	n/a		
IA/0061	IA_05_Change in the name and/or address of a manufacturer of the finished product	08/05/2008	n/a		
II/0059	Inclusion of "retinal pigment epithelial tear" in section 4.8 (Undesirable Effects) of the SPC, further to assessment of data performed by the MAH. Update of Summary of Product Characteristics	19/03/2008	23/04/2008	SmPC	Forty-six cases of 'retinal pigment epithelial tear'(RPET) were retrieved in Novartis' global safety database. In some cases the event took place within the first month of therapy and patients had no previous history of RPET. After analysis of these cases, the relationship between Visudyne and RPE tear cannot be totally excluded. For this reason "retinal pigment epithelial tear" has been included as an adverse reaction to Visudyne treatment in section 4.8 of the SPC.
II/0058	Inclusion of information on excretion of Veterporfin in human milk in section 4.6 (Pregnancy and lactation) of the SPC, further to a re-assessment data performed by the MAH. Update of Summary of Product Characteristics and Package Leaflet	19/03/2008	23/04/2008	SmPC and PL	Based on the assessment of data submitted by the Marketing Authorisation Holder, the information in section 4.6 of the SPC has been updated to include the following statement "Verteporfin and its diacid metabolic are excreted in human milk in low amounts", describing the fact that if Visudyne is taken while breast-feeding, traces of the product are passed on to the nursing mother's milk. Section 2 of the PL has been modified accordingly.
II/0060	Inclusion of safety information on post-marketing reports of Myocardial Infarction in section 4.8 of the	21/02/2008	17/03/2008	SmPC and PL	Based on the assessment of PSUR 9, and the reccomendation from CHMP, the MAH has updated the

	Summary of Product Characteristics (SPC). The Package Leaflet (PL) is being modified accordingly. Update of Summary of Product Characteristics and Package Leaflet				safety information in section 4.8 of the SPC to include the following statement "Myocardial infarction has been reported particularly in patients with a previous cardiovascular history, sometimes within 48 hours after the infusion". Section 4 of the PL is being modified accordingly, to include the following paragraph "Heart attack has been reported, particularly in patients with a history of heart disease, sometimes within 48 hours after treatment with Visudyne". Additionally, 'Slovakia' is being added to the Local representative details for this member state in the PL.
IA/0057	Deletion of manufacturing site IA_09_Deletion of manufacturing site	29/11/2007	n/a		
IA/0056	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	17/08/2007	n/a		
IA/0055	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	17/08/2007	n/a		
II/0053	Update of the Summary of Product Characteristics (SPC) according to the 24 months results of the VIO study conducted in the occult indication as post-approval commitment for Visudyne. As a result, the Therapeutic Indication section (4.1) of the SPC has been amended to delete the indication "treatment of patients with subfoveal occult CNV due to AMD with evidence of recent or ongoing disease progression". Section 5.1 was also updated. The PL (Package	26/04/2007	05/06/2007	SmPC, Labelling and PL	Please refer to the Scientific Discussion H-305-II-53-AR

	Leaflet) has been amended accordingly and the Product Information has also been updated according to the latest QRD template. Furthermore, the contact details of the local representatives for the two new EU Member States, Romania and Bulgaria have been included in the PL. Update of Summary of Product Characteristics and Package Leaflet				
IA/0054	IA_06_a_Change in ATC code: Medicinal products for human use	24/04/2007	n/a	SmPC	
II/0052	Change(s) to the manufacturing process for the finished product Change(s) to the manufacturing process for the finished product	24/01/2007	19/02/2007		
IB/0050	IB_38_c_Change in test procedure of finished product - other changes	11/12/2006	n/a		
IB/0051	IB_37_a_Change in the specification of the finished product - tightening of specification limits	06/12/2006	n/a		
II/0049	Change(s) to the manufacturing process for the active substance Change(s) to the manufacturing process for the active substance	18/10/2006	23/10/2006		

II/0046	Quality changes	23/03/2006	28/03/2006		
N/0047	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/03/2006	n/a	PL	
II/0044	Quality changes	23/02/2006	28/02/2006		
II/0043	Quality changes	23/02/2006	28/02/2006		
IB/0045	IB_24_Change in synthesis or recovery of non-pharmacopoeial excipient (when descr. in dossier)	18/01/2006	n/a		
II/0036	Quality changes	14/12/2005	22/12/2005		
IB/0042	IB_37_b_Change in the specification of the finished product - add. of new test parameter	20/12/2005	n/a		
IB/0041	IB_26_b_Change in the specification of immediate packaging - addition of new test parameter	20/12/2005	n/a		
IB/0035	IB_33_Minor change in the manufacture of the finished product	09/11/2005	n/a		
IA/0040	IA_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	09/11/2005	n/a		
IA/0039	IA_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	09/11/2005	n/a		
IA/0038	IA_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	09/11/2005	n/a		

IA/0037	IA_31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	09/11/2005	n/a		
N/0034	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/09/2005	n/a	PL	
IB/0033	IB_38_c_Change in test procedure of finished product - other changes	18/08/2005	n/a		
IA/0032	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	21/07/2005	n/a		
R/0031	Renewal of the marketing authorisation.	21/04/2005	04/07/2005	SmPC, Annex II, Labelling and PL	
II/0029	This variation relates to an update of SPC section 5.1 (Pharmacodynamic properties) to include the results of the 60 months BPD OCR 002 (TAP) A&B clinical study extension in patients with age-related degeneration with subfoveal choroidal neovascularisation.The Package Leaflet has been amended accordingly. Update of Summary of Product Characteristics and Package Leaflet	17/02/2005	29/03/2005	SmPC and PL	The initial approval for patients with classic-containing, subfoveal choroidal neovascularization due to age-related macular degeneration was based on the 2-year results of the clinical studies BPD OCR 002 A and 002 B (TAP) in which a total of 609 adult patients participated (402 were randomised to verteporfin and 207 to placebo). Study BPD952A2301 was a 3 year open label extension of TAP A and TAP B studies. The TAP Extension study included 476 patients in total. Of these patients 320 were long term verteporfin-treated patients; 134 were "previously placebo" patients treated with verteporfin; 22 "previously placebo" patients not treated with verteporfin.In patients followed from Month 24 onwards and treated with uncontrolled, open-label Visudyne treatment as needed, long-term extension data suggest that Month 24 vision outcomes may

					be sustained for up to 60 Months. In the TAP study in all lesion types, the average number of treatments per year was 3.5 in the first year after diagnosis and 2.4 in the second for the randomised placebo-controlled phase and 1.34 in the third phase, 0.4 in the fourth and 0.1 in the fifth year for the open label extension phase. No additional safety concern was identified.The Package Leaflet has been amended accordingly.
II/0027	The Marketing Authorisation Holder applied to amend SPC sections 4.4 (Special warnings and special precautions for use) and 4.8 (Undesirable effects) following the assessment of the fifth PSUR.The Package Leaflet has been amended accordingly. Update of Summary of Product Characteristics and Package Leaflet	17/02/2005	29/03/2005	SmPC and PL	The CHMP concluded from the assessment of the fifth PSUR that the MAH should provide a safety overview on vision decrease. This overview was submitted in January 2004 and the CHMP requested that the wording concerning visual acuity decrease should be updated. In this variation the MAH applied for an update of the description of visual acuity decrease in section 4.8 of the SPC.Section 4.4 of the SPC provided guidance on precautions to avoid photosensitivity reactions and lists examples of bright light sources which could cause photosensitivity reactions. Two publications document photosensitivity reactions following use of pulse-oximeters, in patients who had undergone photodynamic therapy. For this reason "prolonged exposure to light from light emitting medical devices such as pulse oximeters should also be avoided for 48 hours following Visudyne administration" was added in section 4.4.Infusion related back/ chest pain was evaluated in PSUR 5 and previous PSURs and the MAH proposed a rewording of the description of the infusion related pain.Extravasation of verteporfin can lead to local photosensitivity reactions if the extravasation area is exposed to light. The MAH proposed to add to the warning regarding extravasation in section 4.4 of the SPC "especially if exposed to light". This

					emphasizes the importance of protecting the area from light and is consistent with the already existing guidance to cover the extravasation area to avoid exposure to light.The Package Leaflet has been amended accordingly.
II/0026	This variation relates to an update of SPC section 5.1 (Pharmacodynamic properties) to include the results of the 60 months VIP clinical study extension in patients with pathological myopia.The Package Leaflet has been amended accordingly. Update of Summary of Product Characteristics and Labelling	17/02/2005	29/03/2005	SmPC and PL	The indication of photodynamic therapy (PDT) in myopic eyes with subfoveal choroidal neovascularisation was approved on the basis of the one-year results of the controlled study BPD OCR 003 PM (VIP) in which a total of 120 adult patients participated (81 were randomized to verteporfin and 39 to placebo). In order to confirm the one-year results, a second analysis was performed when all patients had completed 2 years of follow-up. On the basis of the 2-year results provided by the MAH in July 2001 the CHMP concluded that the difference between treatment groups, for visual acuity (mean, median or distribution of changes) examined in its entirety, remained favourable for verteporfin during the 2-year study duration, although, the responder rate was lower than the responder rate at 1 year. The MAH submitted in this variation the results of the 3 year follow up study (BPD952A2302), an open label extension study in patients with subfoveal choroidal neovascularisation due to pathological myopia. The VIP-PM Extension study included 96 (80%) of the 120 patients included in the BPD OCR 003 PM (VIP) study. Of the 81 verteporfin-treated patients, who participated in the BPD OCR 003 PM (VIP) study, 67 (83%) enrolled in the VIP-PM Extension study.In patients followed from Month 24 onwards and treated with uncontrolled, open-label Visudyne treatment as needed, long-term extension data suggest that Month 24 vision outcomes may be sustained for up to 60 months. The average number of treatments

					per year was in the randomised placebo-controlled phase 3.5 in the first year after diagnosis, 1.8 in the second and in the open label extension phase 0.4 in the third year, 0.2 in the fourth and 0.1 in the fifth. No additional safety concern was identified.The Package Leaflet has been amended accordingly.
II/0028	Quality changes	15/12/2004	26/01/2005	SmPC	
IB/0030	IB_10_Minor change in the manufacturing process of the active substance	14/01/2005	n/a		
II/0024	Change(s) to the test method(s) and/or specifications for the finished product	21/10/2004	25/10/2004		
N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/08/2004	n/a	Labelling and PL	
N/0023	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/08/2004	n/a	Labelling	
IB/0022	IB_10_Minor change in the manufacturing process of the active substance	19/05/2004	n/a		
IB/0020	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure IB_12_b_01_Change in spec. of active subst./agent in manuf. of active subst. - test parameter AS	19/05/2004	n/a		
IA/0021	IA_09_Deletion of manufacturing site	16/04/2004	n/a		

IA/0019	IA_13_a_Change in test proc. for active substance - minor change	09/03/2004	n/a		
IA/0018	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	09/03/2004	n/a		
IA/0017	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	09/03/2004	n/a		
N/0016	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/12/2003	14/04/2004	PL	
I/0015	IB_33_Minor change in the manufacture of the finished product	17/11/2003	n/a		
T/0014	Transfer of Marketing Authorisation	04/08/2003	22/09/2003	SmPC, Labelling and PL	
I/0013	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	04/12/2002	14/01/2003	Annex II and PL	
II/0012	Change(s) to the manufacturing process for the finished product	21/11/2002	27/11/2002		
I/0010	15_Minor changes in manufacture of the medicinal product	05/09/2002	24/09/2002		
II/0009	Update of Summary of Product Characteristics	30/05/2002	22/08/2002	SmPC	
II/0005	Extension of Indication	30/05/2002	22/08/2002	SmPC and PL	

II/0008	Update of Summary of Product Characteristics and Package Leaflet	21/02/2002	24/05/2002	SmPC and PL	
I/0006	20a_Extension of shelf-life or retest period of the active substance	07/11/2001	15/02/2002		
II/0007	Change(s) to the manufacturing process for the finished product	17/01/2002	11/02/2002		
I/0004	20_Extension of shelf-life as foreseen at time of authorisation	27/06/2001	n/a		
II/0001	Extension of Indication	14/12/2000	20/03/2001	SmPC and PL	
I/0003	12_Minor change of manufacturing process of the active substance	16/02/2001	11/03/2001		