EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Opgenra

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
IG/0474	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	02/09/2014	n/a		
IG/0473/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH	22/08/2014		SmPC, Annex II, Labelling 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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

	A.7 - Administrative change - Deletion of manufacturing sites				
WS/0421/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised	25/04/2014	n/a		
WS/0452	This was an application for a variation following a	20/02/2014		Annex II and PL	

	worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. New manufacturing site for quality control and release testing of the finished product. B.II.b.2.c.3 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing for a biol/immunol product and any of the test methods is a biol/immunol/immunochemical method				
IG/0411/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH A.1 - Administrative change - Change in the name and/or address of the MAH	18/02/2014		SmPC, Labelling and PL	
R/0033	Renewal of the marketing authorisation.	19/09/2013	20/11/2013	SmPC, Annex II, Labelling and PL	Based on the review of the available information and on the basis of a re-evaluation of the benefit risk balance, the CHMP is of the opinion that the quality, safety and efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and, therefore, considered that the benefit risk of Opgenra continues to be favourable. The CHMP recommends that one additional five-year renewal be required. This is based on the following pharmacovigilance grounds: the clinical experience with the product in the designated indication has been very limited in the EU during the first 5-year period of marketing authorisation. Indeed, there has been a limited exposure due to a recent and limited marketing of the product (launched in the EU only in August 2011 and marketed in only few Member States). In addition,

					results of the post-authorisation studies to investigate the long term safety and efficacy of Opgenra and also investigate the actual drug utilisation in 'real life' are needed to further characterise the safety and efficacy profile.
IAIN/0035/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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	01/10/2013	n/a		
WS/0364/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change to drug substance and finished product quality control methods. Approval of additional drug substance control testing site. 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.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	19/09/2013	n/a		

	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
WS/0406	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Extension of drug substance shelf life. B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	25/07/2013	n/a		
WS/0395/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Deletion of manufacturing site. Changes to manufacturing process. A.7 - Administrative change - Deletion of manufacturing sites B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation	27/06/2013	n/a		
WS/0387/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Addition of quality control testing laboratory.	27/06/2013	n/a		

	Changes to test method and acceptance criteria. Extension of excipient shelf life. B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation B.II.e.3.b - Change in test procedure for the immediate packaging of the finished product - Other changes to a test procedure (including replacement or addition)				
IB/0028	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/03/2013	20/11/2013	SmPC, Annex II, Labelling and PL	Update of the product information to bring it in line with the latest version of the QRD template (version 8 rev. 2), including update of the MAH contact details. Section 6.6 of the SmPC is also updated to clarify the instructions for reconstitution to avoid tapping of glass vial.
IAIN/0030	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	13/03/2013	n/a		
IB/0027	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	08/01/2013	20/11/2013	SmPC	
IA/0026/G	This was an application for a group of variations.	15/10/2012	n/a		

	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.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.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer				
IB/0025/G	This was an application for a group of variations. B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	02/08/2012	n/a		
IAIN/0024/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.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	12/07/2012	n/a		

	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.f - Changes to an existing pharmacovigilance system as described in the DDPS - Deletion of topics covered by written procedure(s) describing pharmacovigilance activities C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities 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/0023/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 of the finished product, including quality control sites (excluding manufacturer for batch release) 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)	27/04/2012	n/a		
WS/0224/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any	15/03/2012	n/a		

	manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for biological/immunological medicinal products. B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation				
IA/0022/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS 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) A.7 - Administrative change - Deletion of manufacturing sites B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information B.II.c.z - Change in control of excipients in the Finished Product - Other variation	29/02/2012	n/a	Annex II	
WS/0203/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.c.2.d - Change in test procedure for an excipient -	16/02/2012	16/02/2012		

	Other changes to a test procedure (including replacement or addition) B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)				
IA/0014/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	28/10/2011	n/a		
IA/0013/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release	16/09/2011	n/a	SmPC, Annex II, Labelling and PL	
T/0012	Transfer of Marketing Authorisation	20/04/2011	14/06/2011	SmPC, Labelling and PL	
IA/0011	A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release	23/03/2011	n/a	Annex II and PL	
WS/0077/G	This was an application for a group of variations	17/03/2011	17/03/2011		

	following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Minor changes to an approved test procedures for an excipient and of the finished product. B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
WS/0064/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Changes in the manufacturing process of the active substance. Change in the specification parameters of the active substance. Minor changes in test procedure for active substance. Submission of an updated Ph. Eur. Certificate of suitability. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol	17/03/2011	17/03/2011		

	B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer				
WS/0057	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change in test procedure for active substance - Addition of new reference standards. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to a biological/immunological/ immunochemical test method or a method using a biological reagent for a biological AS	20/01/2011	20/01/2011		
WS/0050	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change to the in-process limits during the manufacture of the active substance. B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of	21/10/2010	21/10/2010		

	in-process limits				
II/0004	Update of Annex II and IV of the product information to reflect that the training DVD now contains animated images of an operation rather then images recorded during a live surgery on a patient. Annex II has also been updated with the current version number of the RMP (version 2.1). The MAH has also taken the opportunity to amend Annex IIIA to include the full set of particulars on the outer blister containing the vial and to have a simplification of the vial label. Update of Summary of Product Characteristics, Labelling and Package Leaflet	18/03/2010	10/06/2010	Annex II and Labelling	The conditions for marketing authorization, as detailed in Annex II and Annex IV of the Opgenra Product Information, require the DVD to contain images recorded during a live surgery on a patient. The MAH has requested a change to this requirement and presented a DVD for review which contains animated images of an operation on a patient. This change was agreed by the CHMP and Annex II and IV have been updated accordingly. An extended user testing should however be performed and assessed before placing the product on the market.
II/0009	Updates to release specifications and changes to end-of-shelf-life specifications. Change(s) to the test method(s) and/or specifications for the finished product	22/04/2010	30/04/2010		
II/0007	Updates to the excipient (collagen matrix) including a new manufacturing suite and a scaled up process. Change(s) to the manufacturing process for the finished product	18/03/2010	01/04/2010		
II/0005	Updates to the auditing of the sterilization process. The terminal sterilisation process used during routine production remains unchanged. Change(s) to the manufacturing process for the	22/10/2009	10/11/2009		

	finished product				
IB/0006	IB_36_a_Change in shape or dimensions of the container/closure - sterile ph. forms/biologicals	20/07/2009	n/a		
II/0001	Changes to the quality documentation Update of or change(s) to the pharmaceutical documentation	29/05/2009	16/07/2009	SmPC, Labelling and PL	
II/0003	Changes to module 3 (analytical methods, specifications, stability protocol) in order to comply with post-authorisation commitments. Update of or change(s) to the pharmaceutical documentation	25/06/2009	13/07/2009		
IB/0002	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	24/04/2009	24/04/2009	SmPC, Labelling and PL	