Ozurdex

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
II/0032	C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH	28/03/2019		SmPC and PL	
N/0033	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/03/2019		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).

IB/0031/G	This was an application for a group of variations. B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.5.f - Change to in-process tests or limits applied during the manufacture of the finished product - Addition or replacement of an in-process test as a result of a safety or quality issue B.II.b.5.f - Change to in-process tests or limits applied during the manufacture of the finished product - Addition or replacement of an in-process test as a result of a safety or quality issue B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	05/02/2019	n/a		

PSUSA/985/201801	Periodic Safety Update EU Single assessment - dexamethasone (centrally authorised product indicated in uveitis and macular oedema)	20/09/2018	20/11/2018	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/985/201801.
IB/0030	B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	28/08/2018	n/a		
N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/04/2018	20/11/2018	Labelling and PL	
PSUSA/985/201701	Periodic Safety Update EU Single assessment - dexamethasone (centrally authorised product indicated in uveitis and macular oedema)	14/09/2017	15/11/2017	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/985/201701.
IA/0027	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	01/06/2017	n/a		
II/0025	In line with the RMP commitment, submission of the final report for the Post-Authorisation Safety Study 206207-025 (A Prospective Observational Study to Evaluate Long-Term Safety in Real-World Clinical Practice). C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	23/03/2017	n/a		
PSUSA/985/201601	Periodic Safety Update EU Single assessment - dexamethasone (centrally authorised product	02/09/2016	n/a		PRAC Recommendation - maintenance

	indicated in uveitis and macular oedema)				
IB/0022	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	24/02/2016	n/a		
N/0023	Update of the package leaflet with revised contact details of the local representatives. The MAH also took the opportunity to update section 4 of the package leaflet to add missing asterisks for ADRs that are related to the injection procedure, in line with section 4.8 of the SmPC ADRs. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/02/2016	15/11/2017	PL	
IA/0021	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	28/01/2016	n/a		
PSUSA/985/201501	Periodic Safety Update EU Single assessment - dexamethasone (centrally authorised product indicated in uveitis and macular oedema)	10/09/2015	n/a		PRAC Recommendation - maintenance
IAIN/0020	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	21/05/2015	n/a		
R/0018	Renewal of the marketing authorisation.	22/01/2015	23/03/2015	SmPC, Annex II, Labelling	Based on the review of available information, the CHMP is of the opinion that the quality, safety and efficacy of Ozurdex

				and PL	continues to be adequately and sufficiently demonstrated and considers that the benefit/risk profile of this medicinal product continues to be favourable. The product information has been updated to align with QRD templates. The CHMP recommends that the renewal be granted with unlimited validity.
PSUV/0017	Periodic Safety Update	11/09/2014	n/a		PRAC Recommendation - maintenance
II/0015	Extension of Indication to include a new indication for the treatment of adult patients with visual impairment due to diabetic macular oedema who are pseudophakic or who are considered insufficiently responsive to, or unsuitable for non-corticosteroid therapy. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	24/07/2014	26/08/2014	SmPC, Annex II and PL	Please refer to scientific summary.
IA/0016/G	This was an application for a group of variations. B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.a.3.b.1 - Changes in the composition (excipients) of the finished product - Other excipients - Any minor adjustment of the quantitative composition of the finished product with respect to excipients B.II.e.3.c - Change in test procedure for the immediate packaging of the finished product -	21/05/2014	n/a		

	Deletion of a test procedure if an alternative test procedure is already authorised				
II/0013	Update of Annex II to remove reference to the injection procedure video from the list of elements of the educational material package in the conditions and restrictions for the safe and effective use of the medicinal product. Additional updates to the Risk Management Plan (RMP) were made to consolidate the information in the educational material as well as in response to previous requests following the assessment of RMP version 1.9 and PSUR #4. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	27/06/2013	19/06/2014	Annex II and PL	Following observations of the use of Ozurdex in the clinical practice, the MAH proposed to omit the intravitreal injection procedure video, which was no longer considered necessary to educate treating physicians on the correct application procedure. The CHMP agreed to the removal of the video, and thus the update of Annex II, and considered that the remaining material (consisting of a poster, an injection guide and a copy of the SmPC) was sufficient. In addition, the combination of the educational sets for both indications in uveitis and retinal vein inclusion and streamlining of the information on adverse drug reactions, as proposed by the MAH, was considered by the CHMP to help avoiding the provision of frequent updates and repetitive information to patients and physicians. Other updates to the risk management plan were considered in line with previous requests by the CHMP and PRAC. Minor changes to the package leaflet to better reflect the information in the SmPC and to update the list of local representatives were agreed as well.
IA/0014	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)	10/06/2013	n/a		
T/0012	Tansfer of MA from Allergen Pharmaceuticals Ireland (901969) to Allergen Pharmaceuticals Ireland (514125)	05/02/2013	06/03/2013		

	Transfer of Marketing Authorisation				
IB/0011	B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	15/01/2013	n/a		
IB/0010/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	21/11/2012	n/a		
IAIN/0009	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	29/10/2012	n/a		
IB/0008/G	This was an application for a group of variations. B.II.a.3.b.6 - Changes in the composition (excipients) of the finished product - Other excipients - Replacement of a single excipient with a comparable excipient with the same functional characteristics and at a similar level 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.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	24/09/2012	n/a		

	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) B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
II/0006	Update of sections 4.3, 4.4 and 4.8 of the SmPC in order to: - add two contraindications (section 4.3) • Aphakic eyes with rupture of the posterior lens capsule • Eyes with Anterior Chamber Intraocular Lens (ACIOL) and rupture of the posterior lens capsule; - amend the wording of section 4.4 following the addition of the new contraindications in section 4.3; - add 2 new ADRs (section 4.8) “Hypotony of eye (associated with vitreous leakage due to injection)” and “Complication of device insertion (implant misplacement)” and amend the description of “Device dislocation (migration of implant)” ADR by adding “with or without corneal oedema”. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH	19/07/2012	10/09/2012	SmPC, Annex II, Labelling and PL	Based on post marketing case reports involving device dislocation the MAH updated the description of the following side effect “device dislocation (device migration)” by amending the text as follows “ with or without corneal oedema” in order to better reflect the pathology associated with device migration. In some of the reported cases the eyes were either without lens or were having the natural ocular lens replaced with man-made intraocular lens. The aim of these two contraindications is to minimize the risk of device migration in patients either lacking or having replaced the natural ocular lens. Based on this new safety data the MAH included two new contraindications in patients lacking the crystalline lens or with implanted lens and with rupture of the posterior lens capsule. Based on case reports of complication of device insertion and of decreased intraocular pressure the MAH included in the SmPC the terms ‘complication of device insertion (device misplacement)’ and “Hypotony of eye (associated with vitreous leakage due to the injection)” respectively as side effects.

IB/0007	B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	07/09/2012	n/a		
II/0005	The MAH proposed the update of sections 4.4 and 4.8 of the SmPC in order to add a warning with regards to implant migration to reflect the changes proposed in PSUR 1 (27 July 2010 to 27 January 2011). The MAH also proposed the update of section 4.2 of the SmPC in order to include advice on the use of povidone iodine drops 5% to disinfect the periocular skin, eyelid and ocular surface prior to the injection procedure. The Package Leaflet was proposed to be updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. The requested variation proposed amendments to the SmPC, and Package Leaflet. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH	17/11/2011	22/12/2011		Within this variation the Company has included in the SmPC, sections 4.4 and 4.8, a warning concerning the risk for implant migration from the posterior chamber of the eye into the anterior chamber. The need for such update was identified based on the review of a total of eight medically confirmed cases of device dislocation that have been reported with Ozurdex since the first marketing approval was obtained. The Company, taking advantage of this procedure, has also included in section 4.2 of the SmPC a piece of advice on the use of povidone iodine drops 5% to disinfect the periocular skin, eyelid and ocular surface prior to the injection procedure. The proposed advice regarding the use of povidone-iodine in section 4.2 of the SmPC promotes the safe use of the implant and is in-line with administration in the pivotal clinical trials.
IA/0004/G	This was an application for a group of variations. 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	15/08/2011	n/a		

	B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
II/0001	Extension of indication to include treatment of adults patients with inflammation of the posterior segment of the eye presenting as non-infectious uveitis. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	14/04/2011	16/06/2011	SmPC, Annex II and PL	Please refer to the scientific discussion Ozurdex H-01140-II-001-AR.
N/0002	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/04/2011	n/a	PL	