



Optimark

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
T/0037	Transfer of Marketing Authorisation	14/03/2017	11/04/2017	SmPC, Labelling and PL	
PSUSA/1508/201601	Periodic Safety Update EU Single assessment - gadoversetamide	02/09/2016	n/a		PRAC Recommendation - maintenance
IB/0036	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing	20/07/2016	16/02/2017	Annex II	

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).



	authorisation, including the RMP - Other variation				
II/0031	<p>Update of section 4.4 of the SmPC in order to add a warning on acute kidney injury based on information derived from post-marketing reports. The Package Leaflet is updated accordingly.</p> <p>In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce some editorial changes and to bring the PI in line with the latest QRD template version 9.1.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>	10/03/2016	16/02/2017	SmPC, Annex II and PL	In patients with baseline renal impairment, acute kidney injury requiring dialysis has occurred with the use of Optimark. The risk of acute kidney injury may increase with an increased dose of the contrast agent. Administer the lowest dose possible for adequate imaging.
IAIN/0033	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	08/12/2015	n/a		
PSUSA/1508/201501	Periodic Safety Update EU Single assessment - gadoversetamide	24/09/2015	19/11/2015	SmPC	Please refer to Optimark PSUSA/00001508/201501 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IB/0030	B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue	22/10/2015	n/a		
IA/0029/G	This was an application for a group of variations.	24/06/2015	n/a		

	A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites				
IB/0027	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/04/2015	02/06/2015	SmPC and PL	
IB/0026	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	30/03/2015	n/a		
IB/0025	To postponing the due date for the submission of the final study report evaluating the potential for long-term retention of gadolinium in bone (bone study) from September 2014 to June 2016 C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	15/12/2014	02/06/2015	Annex II	
IA/0024	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)	27/10/2014	n/a		
IB/0023/G	This was an application for a group of variations. B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	08/10/2014	n/a		

	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
II/0021	<p>Update of section 6.6 of the Summary of Product Characteristics (SmPC) on the implementation of traceability measures in context with Electronic Health Records and corresponding updates to Package Leaflet (PL) and Labelling as requested per PRAC and CHMP.</p> <p>C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation</p>	25/09/2014	01/12/2014	SmPC, Labelling and PL	<p>As per PRAC/CHMP request, the MAH adapted the traceability measures in light of the increasing use of Electronic Health Records by Healthcare Professionals and Institutions in the Product Information (PI). The PI has been updated to include the following information:</p> <ul style="list-style-type: none"> - SmPC, Package Leaflet: If electronic patient records are used, the name of the product, the batch number and the dose should be entered into the patient record. - Labelling (intermediate and outer packaging): For recording: stuck the peel-off tracking label onto the patient record; for electronic records: enter product name, batch no and dose. - Labelling (inner packaging): This sticky label should be stuck on patient records. <p>For electronic records: enter product name, batch no. and dose.</p>
PSUV/0022	Periodic Safety Update	11/09/2014	n/a		PRAC Recommendation - maintenance
IAIN/0020	C.I.12 - Inclusion or deletion of black symbol and explanatory statements for medicinal products in the list of medicinal products that are subject to additional monitoring	13/02/2014	01/12/2014	SmPC and PL	
IB/0019	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	13/12/2013	01/12/2014	Annex II	
IAIN/0018	B.II.b.1.a - Replacement or addition of a	23/09/2013	n/a		

	manufacturing site for the FP - Secondary packaging site				
IAIN/0017	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	29/07/2013	n/a		
IB/0016	B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation	05/07/2013	n/a		
T/0015	Transfer of Marketing Authorisation	15/02/2013	13/03/2013	SmPC, Labelling and PL	Transfer of MA from Covidien Deutschland GmbH to Mallinckrodt Deutschland GmbH.
IA/0014	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	12/09/2012	n/a		
R/0012	Renewal of the marketing authorisation.	19/04/2012	15/06/2012	SmPC, Annex II, Labelling and PL	<p>Based upon the data that have become available since the granting of the initial Marketing Authorisation, the CHMP considers that the benefit-risk balance of Optimark remains positive, but considers that its safety profile is to be closely monitored for the following reasons:</p> <ul style="list-style-type: none"> Optimark is a linear non-ionic chelates gadolinium contrast agent, classified among the High Risk category for Nephrogenic Systemic Fibrosis (NSF). Two further annual cumulative reviews on NSF cases are to be submitted; in addition a study to investigate the long-term gadolinium retention in human bone is to be performed. NSF is a serious safety issue and the results of this further awaited data could have an impact on the benefit-risk balance of the product. <p>The CHMP decided that the MAH should continue to submit yearly PSURs.</p>

					Therefore, based upon the safety profile of Optimark, which requires the submission of yearly PSURs, the CHMP concluded that the MAH should submit one additional renewal application in 5 years time.
II/0013	<p>to replace the currently used resin for the manufacturing of the syringe barrels with a new resin material.</p> <p>B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products</p>	24/05/2012	24/05/2012		
II/0010	<p>Update of section 4.8 of the SmPC further to a review of the safety database conducted by the MAH and in order to also bring the SmPC in line with the SmPC guideline. The Package leaflet has been updated accordingly. The MAH also took the opportunity to update the product information in line with the QRD template (version 8, revision 1).</p> <p>C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data</p>	15/03/2012	20/04/2012	SmPC, Annex II, Labelling and PL	Further to a review of the MAH's safety database conducted by the MAH and also in line with the SmPC guideline, changes were made to the 'Undesirable effects' section of the Summary of Product Characteristics (SmPC). Overall, the frequency of several adverse reactions was revised and the adverse reactions "conjunctivitis", "vertigo", "laryngeal oedema", "chills" and "albumin in urine" were added to the SmPC. The Package Leaflet has been revised in accordance.
IA/0011/G	<p>This was an application for a group of variations.</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor</p>	17/10/2011	n/a		

	changes to an approved test procedure				
IA/0009/G	<p>This was an application for a group of variations.</p> <p>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</p> <p>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</p> <p>C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database</p> <p>C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV</p> <p>C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV</p>	30/09/2011	n/a	Annex II	
IB/0007/G	<p>This was an application for a group of variations.</p> <p>B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer</p> <p>B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling</p>	11/02/2011	n/a		

Medicinal product no longer authorised

IA/0006	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	12/11/2010	n/a		
A20/0004	Pursuant to Article 20 of Regulation (EC) No 726/2004, the European Commission requested on 19 November 2008, the opinion of Committee for Medicinal Products for Human Use (CHMP) on measures necessary to ensure the safe and effective use of Optimark and on whether the marketing authorisation should be varied in relation to its use in special patient's population more at risk to develop nephrogenic systemic fibrosis (NSF).	19/11/2009	10/05/2010	SmPC, Annex II and PL	Please refer to the assessment report published after deletion of commercially confidential information: EMEA/H/C/0745/A20/0004.
IA/0005	IA_13_a_Change in test proc. for active substance - minor change	10/11/2009	n/a		
II/0003	Update of DDPS (Pharmacovigilance)	19/03/2009	03/04/2009	Annex II	Update the Detailed Description of the Pharmacovigilance System (DDPS) as consequence of corrective and preventive actions following a pharmacovigilance inspection and to be in compliance with Volume 9A of the Rules Governing Medicinal Products in the European Union. Consequently, Annex II of the product information was updated with the agreed version number of the DDPS (2009/02).
IA/0002	IA_01_Change in the name and/or address of the marketing authorisation holder	29/04/2008	n/a	SmPC, Labelling and PL	
II/0001	Quality changes	21/02/2008	27/03/2008	SmPC, Annex II, Labelling and PL	