Rapiscan

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/0041/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.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	30/03/2023		SmPC, Annex II, Labelling and PL	The SmPC section 6.1, 6.3, 6.5 has been updated as follows: • Phosphate salt excipients: hydrates deleted • 7 mL vial added, with the relevant shelf-life (2.5 years) Annex II has been updated as follows: • Addition of GE Healthcare AS ad additional manufacturer responsible for batch release The Labelling and PL have been updated accordingly.

[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).

	B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF				
II/0038	Extension of indication to modify the existing indication to allow use in line with new imaging technologies that have evolved since initial approval of Rapiscan; as a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	11/11/2021	13/12/2021	SmPC and PL	Please refer to Scientific Discussion 'Rapiscan-H-C-001176-II-38'
PSUSA/2616/ 202104	Periodic Safety Update EU Single assessment - regadenoson	02/12/2021	n/a		PRAC Recommendation - maintenance
IAIN/0040/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.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP -	25/10/2021	13/12/2021	Annex II and PL	

	Including batch control/testing A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
IA/0037/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 A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	19/03/2021	13/12/2021	Annex II and PL	
IB/0036/G	This was an application for a group of variations. B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition	07/12/2020	n/a		

II/0034/G	This was an application for a group of variations. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	28/11/2019	24/03/2020	SmPC	
PSUSA/2616/ 201904	Periodic Safety Update EU Single assessment - regadenoson	31/10/2019	n/a		PRAC Recommendation - maintenance
IAIN/0033	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	04/04/2019	24/03/2020	Annex II and PL	
II/0027	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	13/12/2018	23/01/2019	SmPC, Labelling and PL	
PSUSA/2616/ 201804	Periodic Safety Update EU Single assessment - regadenoson	31/10/2018	n/a		PRAC Recommendation - maintenance
IAIN/0030	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	11/12/2017	n/a		
T/0029	Transfer of Marketing Authorisation	23/11/2017	11/12/2017	SmPC, Labelling and	

				PL	
II/0026	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	07/12/2017	20/11/2018	SmPC	The MAH submitted a series of in vitro studies performed to characterise the activity of regadenoson as a substrate or inhibitor of various human transporters. Regadenoson does not significantly inhibit the transporters OAT1, OAT3, OCT1, OATP1B1, OATP1B3, MATE1, MATE2-K, BCRP, P-gp, BSEP, ENT 1 or ENT2 at 1 µM. The data are insufficient to conclude about the risk of interactions at the level of these transporters given that a single concentration was evaluated in most instances. Regadenoson may have a modest inhibitory effect on the active renal transporter, OCT2, and has been found to be likely substrate for BCRP, ENT1 or ENT2 mediated transport. However, given the proposed duration of use, the effects of the drug transporters are unlikely to be clinically relevant.
IB/0028	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	04/12/2017	n/a		
PSUSA/2616/ 201704	Periodic Safety Update EU Single assessment - regadenoson	26/10/2017	n/a		PRAC Recommendation - maintenance
IB/0024/G	This was an application for a group of variations. 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	30/01/2017	n/a		

	data B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
II/0023	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	15/12/2016	n/a		
PSUSA/2616/ 201604	Periodic Safety Update EU Single assessment - regadenoson	27/10/2016	n/a		PRAC Recommendation - maintenance
IA/0021	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	21/12/2015	n/a		
IB/0020/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products 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	21/12/2015	n/a		

PSUSA/2616/201504	Periodic Safety Update EU Single assessment - regadenoson	06/11/2015	n/a		PRAC Recommendation - maintenance
PSUSA/2616/201410	Periodic Safety Update EU Single assessment - regadenoson	21/05/2015	17/07/2015	SmPC and PL	Please refer to Rapuiscan-PSUSA/00002616/201410 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
R/0017	Renewal of the marketing authorisation.	26/02/2015	24/04/2015	SmPC, Annex II and PL	
IA/0016	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	12/11/2014	n/a		
PSUV/0015	Periodic Safety Update	06/11/2014	n/a		PRAC Recommendation - maintenance
PSUV/0014	Periodic Safety Update	22/05/2014	22/07/2014	SmPC and PL	Please refer to Rapiscan EMEA/H/C/1176/PSUV/0014 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
PSUV/0013	Periodic Safety Update	21/11/2013	16/01/2014	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUV/0013.
IAIN/0012	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	28/10/2013	n/a		
IA/0011	A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or	28/10/2013	n/a		

	intermediate used in the manufacture of the AS or manufacturer of a novel excipient				
IB/0010	B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation	11/03/2013	n/a		
IAIN/0009/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in 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.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database 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	16/01/2013	n/a		
II/0006	Update of section 4.8 of the SmPC in order to update the safety information on hypersensitivity reactions following the recommendations from the AR for the second PSUR. The Package Leaflet was updated accordingly. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	15/11/2012	15/11/2013	SmPC and PL	Based on the review of the 2nd periodic safety update report (PSUR), the CHMP recommended an update of the section 4.8 of the SmPC. The MAH proposed and the CHMP agreed to add hypersensitivity reactions including rash, urticaria, angioedema, anaphylaxis and/or throat tightness under category "uncommon" in the adverse drug reactions table and to add the information that signs of hypersensitivity may be immediate or delayed onset.

IAIN/0008	A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release	25/09/2012	29/10/2012	Annex II and PL	
IA/0007	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	08/08/2012	n/a		
II/0005	Update of section 5.1 of the SmPC in order to update the safety information following the results of two clinical studies: 3606-CL-3001 and 3606-CL-3002. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	16/02/2012	21/03/2012	SmPC	Study 3606 CL-3001 was assessing the safety and tolerance of regadenoson in subjects with asthma or chronic obstructive pulmonary disease. In this study dyspnoea was reported more frequently following Rapiscan (18% for patients with COPD; 11% for patients with asthma) than placebo, but at a lower rate than reported during clinical development however the use of bronchodilator therapy for symptoms was not different between Rapiscan and placebo. Section 5.1 of the SmPC was updated accordingly. Study 3606 CL-3002 was assessing the effect of caffeine intake on single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) in subjects administered Regadenoson. The assessment of this study led to a conclusion that caffeine compromised the diagnostic accuracy of detecting reversible perfusion defects and resulted in modifications of section 5.1 of the SmPC.
II/0002	The CHMP considered that the Detailed Description of the Pharmacovigilance System for Rapiscan fulfils the requirements and was acceptable.	22/09/2011	27/10/2011	Annex II	

	C.I.8.a - Introduction of a new Pharmacovigilance system - which has not been assessed by the relevant NCA/EMA for another product of the same MAH				
IB/0004	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	28/06/2011	n/a	SmPC	
IA/0003/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.b.2 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing	27/04/2011	n/a	Annex II and PL	
T/0001	Transfer of Marketing Authorisation	24/11/2010	11/01/2011	SmPC, Labelling and PL	