EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Sprimeo HCT

Procedural steps taken and scientific information after the authorisation

No	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
WS/0173	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	24/05/2012	28/06/2012	SPC, PL	
II/0012/G	This was an application for a group of variations. 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 A 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH C.I.3.b - Implementation of change(s) requested following the assessment of	19/04/2012	25/05/2012	SPC, PL	

[1] Notifications are issued for type I variations (unless part of a group or a worksharing application). Opinions are issued for all other procedures.
[2] No Commission Decision is issued for type A and type IB variations or for type II variations and annual re-assessments that do not affect the annexes.
[3] SPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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	an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				
WS/0189	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	19/04/2012	25/05/2012	SPC	
A20/0011	Article 20 Review On 20 December 2010, the European Commission initiated a procedure under Article 20 of Regulation (EC) No 726/2004 for all aliskiren-containing medicinal products authorised in the centralised procedure and requested the CHMP to assess all the available data and its impact on the risk benefit balance for aliskiren-containing medicinal products and to give its opinion on whether the marketing authorisations for these products should be maintained, varied, suspended or revoked. The scope of the review was to assess the risk benefit balance of all aliskiren-containing medicinal products in the approved indication of hypertension in	16/02/2012	20/04/2012	SPC, Annex II, PL	Please refer to the Assessment Report: Sprimeo HCT-H-2421-A20-11-Assessment Report-Article 20

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	light of the emerging safety data from the ALTITUDE study in patients with diabetes at high risk for cardiovascular and renal events which lead to the premature study termination.				
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		
WS/0191/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. The specification of the active substance aliskiren has been tightened. The test procedures used for aliskiren have been updated. In addition, typographic errors have been corrected in the dossier. All those changes apply to both routes of synthesis of aliskiren (Synthesis B and synthesis C) where applicable.	16/02/2012	16/02/2012		

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	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.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure, 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.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/0165	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.2 and 5.1 of the SmPC to include information about the efficacy and safety of aliskiren in elderly and very elderly hypertensive patients based on data from the AGELESS study. This application is submitted in fulfilment of the FUM 002	22/09/2011	27/10/2011	SPC	AGELESS study was conducted in order to specifically evaluate the safety and efficacy of aliskiren and aliskiren/HCT in elderly (>65ys) and very elderly (>75 ys) hypertensive patients. Overall the results of this clinical study support the conclusion of a positive benefit/risk ratio in the use of the aliskiren+HCTZ as antihypertensive treatment of elderly and very elderly patients. However, the review of available data also suggests different response to the treatment of elderly and very elderly demonstrating no clinically meaningful additional blood pressure reduction by increasing the

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	for Riprazo HCT, Sprimeo HCT and Rasilamlo. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				dose to 300 mg in the majority of elderly patients. Section 4.2 has been updated with this information. Furthermore, section 5.1 has been updated by including information about the efficacy and safety of aliskiren in elderly and very elderly hypertensive patients.
WS/0168	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.8 of the SmPC to add the Adverse Drug Reaction 'hypersensitivity reactions' under post-marketing experience as requested by CHMP following PSUR review. The Package Leaflet has been updated accordingly. In addition, minor changes have been made in the Section 2 of the Package Leaflet with regards to angioedema. This application is submitted in fulfilment of the FUM 004 for Riprazo HCT and FUM 003 for Sprimeo HCT. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	22/09/2011	27/10/2011	SPC, PL	Following the review of PSUR 5 for aliskiren MAH conducted review of all cases of severe cutaneous adverse reactions (SCARs) and of arthralgia. The analysis revealed a possible relationship between these events and hypersensitivity. The evidence presented has resulted in an update to the Summary of Product Characteristics (SmPC) for Rasilez, Sprimeo, Riprazo and Rasilez HCT to add hypersensitivity as a post-marketing adverse event in the section 4.8 of the SmPC. Corresponding amendments were also introduced into the Package Leaflet. The present application is submitted to introduce the same changes to the Product Information of Rasilamlo, Riprazo HCT and Sprimeo HCT. In addition, minor changes have been made in the Section 2 of the Package Leaflet in regards to angioedema.
WS/0169	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	22/09/2011	27/10/2011	SPC, PL	Contraindication with regards to concomitant use of aliskiren and the highly potent P-gp inhibitor ciclosporin and other potent P-gp inhibitors (verapamil, quinidine) was introduced on the basis of results from drug-drug

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	Update of section 4.3 of the Summary Product Characteristics (SmPC) to remove verapamil from the contraindications, and sections 4.4 and 4.5 of the SmPC, following the CHMP assessment of the data regarding the potential for interaction of aliskiren with verapamil, and the impact of Pgp inhibition on the distribution of aliskiren. The Package Leaflet has been updated accordingly. In addition, MAH took opportunity to update the contact details of local representatives in the PIL for Riprazo, Sprimeo and Riprazo HCT. This application is submitted in fulfilment of the FUM001 for Riprazo HCT and Sprimeo HCT. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				interaction study. Subsequently, as a part of Rasilez FUM 015 MAH was requested to provide additional preclinical data evaluating the potential mechanism of the ciclosporin and other potent P-gp inhibitor interaction with aliskiren. A type II variation was approved to remove the contraindication against concomitant use of verapamil and aliskiren from the Summary of Product Characteristics of Rasilez and RasilezHCT (II/41 and II/05-G, approved in March 2011) and to include a statement with regard to potential for interaction with organic anionic transporting polypeptide (OATP) inhibitors and with rifampicin. Corresponding amendments were also introduced into the Patient leaflet. The present variation application is submitted to introduce the same changes to the Product Information for all aliskiren-containing medicinal products. The proposed changes to the product information are acceptable.
IA/0001/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	26/08/2011	n/a		

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	operation of the pharmacovigilance system				
IG/0101	B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the currently approved batch size	18/08/2011	n/a		
IG/0102	B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the currently approved batch size	18/08/2011	n/a		