PritorPlus

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/1812	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	07/01/2025		SmPC and PL	
WS/2611	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	16/05/2024	n/a		

[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).

	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required				
WS/2573/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. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation 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 C.I.3.a - 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 - Implementation of wording agreed by the competent authority	25/01/2024		SmPC, Annex II, Labelling and PL	
PSUSA/2882/ 202203	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	01/12/2022	n/a		PRAC Recommendation - maintenance
IG/1549	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/08/2022	24/07/2023	SmPC and PL	To update sections 4.4 and 4.8 of the SmPC and sections 2 and 4 of the PL to implement the wording regarding the

					adverse event Acute Respiratory Distress Syndrome (ARDS) affecting the medicinal products that contain hydrochlorothiazide.
N/0128	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/12/2021	29/06/2022	PL	
IG/1448	A.7 - Administrative change - Deletion of manufacturing sites	04/10/2021	n/a		
WS/2077	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To update the PI to align the wording for the excipients lactose, sodium and sorbitol to the "Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' (SANTE-2017-11668, Rev. 1)", published in Nov. 2019. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/06/2021	29/06/2022	SmPC, Annex II and PL	
IG/1262/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/importer of the finished product, including quality control sites (excluding manufacturer for batch release) B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the	16/07/2020	n/a		

	relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer 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				
IG/1259	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/06/2020	09/03/2021	SmPC and PL	
IG/1218	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	10/04/2020	n/a		
WS/1768	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/03/2020	09/03/2021	SmPC and PL	
PSUSA/2882/201904	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	28/11/2019	n/a		PRAC Recommendation - maintenance
PSUSA/2882/201804	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	29/11/2018	n/a		PRAC Recommendation - maintenance
IG/1011	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	27/11/2018	04/11/2019	SmPC and PL	

IG/1002/G	This was an application for a group of variations. B.II.d.1.i - Change in the specification parameters and/or limits of the finished product - Ph. Eur. 2.9.40 uniformity of dosage units is introduced to replace the currently registered method, either Ph. Eur. 2.9.5 or Ph. Eur. 2.9.6 B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation 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 B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	16/11/2018	n/a		
IG/0989	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	10/10/2018	n/a		
T/0115	Transfer of Marketing Authorisation	16/03/2018	13/04/2018	SmPC, Labelling and PL	
IG/0904	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	06/02/2018	07/03/2018	Annex II and PL	

PSUSA/2882/ 201704	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	30/11/2017	n/a		PRAC Recommendation - maintenance
IG/0820	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	29/06/2017	n/a		
WS/1110	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 4.5 and 4.8 to align the hydrochlorothiazide component information with that of the originator. The Package Leaflet is updated accordingly. In addition, Worksharing applicant (WSA) took the opportunity of this procedure to bring the PI in line with the latest QRD template, including combining the SmPC of the different strengths, as well as implement minor editorial changes and reformatting of some sections of the SmPC. The details of local representative (Portugal for MicardisPlus and United Kingdom for PritorPlus and Kinzalkomb) in the PL have been updated. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	06/04/2017	07/03/2018	SmPC, Annex II, Labelling and PL	In order to align the information for the Hydrochlorothiazide component with the information from the competitor/originator labels, section 4.8 of MicardisPlus, PritorPlus, and Kinzalkomb SmPCs has been updated with addition of the side effects thrombocytopenia (sometimes with purpura), hypomagnesaemia, hypercalcaemia, hypochloraemic alkalosis, headache, nausea and erythema multiforme. Wording on interaction with Calcium salt in section 4.5 was also updated. The Package Leaflet is updated accordingly.
IG/0781	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the	06/03/2017	n/a		

	relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
PSUSA/2882/ 201604	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	01/12/2016	n/a		PRAC Recommendation - maintenance
N/0108	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/07/2016	07/03/2018	PL	
IG/0684/G	This was an application for a group of variations. 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.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	25/04/2016	n/a		
PSUSA/2882/ 201504	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	06/11/2015	n/a		PRAC Recommendation - maintenance
N/0105	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	25/08/2015	07/03/2018	PL	
IG/0502	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	13/11/2014	n/a		

PSUSA/2882/ 201404	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	06/11/2014	n/a		PRAC Recommendation - maintenance
A31/0093	On 17 April 2013, further to the emergence of new evidence from the scientific literature on dual RAS blockade therapy and given the seriousness of the identified safety concerns, the Italian Medicines Agency (AIFA) initiated a review under Article 31 of Council Directive 2001/83/EC, requesting the Pharmacovigilance Risk Assessment Committee (PRAC) to issue a recommendation on the benefit-risk of dual RAS blockade therapy through the combined use of angiotensin-converting enzyme inhibitors (ACE-inhibitors), angiotensin II receptor blockers (ARBs) or aliskiren and to determine whether any regulatory measures should be taken on the marketing authorisations of the products involved in this procedure.	22/05/2014	04/09/2014	SmPC and PL	For further information please refer to the Renin-angiotensin-system (RAS)-acting agents Article 31 referral - Assessment report.
N/0102	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/07/2014	07/03/2018	PL	
WS/0569	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of a revised RMP version 9.0 in order to align the RMP with that of telmisartan monotherapy products to ensure consistency. In addition, the RMP was reformatted according to the current	26/06/2014	n/a		N/A

	requirements of the Guidelines on Good Pharmacovigilance Practice. The requested variation worksharing procedure proposed no amendments to the PI. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				
IG/0388	A.7 - Administrative change - Deletion of manufacturing sites	11/12/2013	04/09/2014	Annex II and PL	
PSUSA/2882/ 201304	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	07/11/2013	n/a		PRAC Recommendation - maintenance
WS/0436	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 5.1 of the SmPC to add information related to the cardiovascularmorbidity based on the ONTARGET and TRANSCEND trials following the outcome of the Article 20 procedure for MicardisPlus /PritorPlus /Kinzalkomb (telmisartan/HCTZ). In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is being brought in line with the latest QRD template version 9. The requested worksharing variation procedure proposed amendments to the Summary of Product Characteristics and Package Leaflet.	24/10/2013	04/09/2014	SmPC and PL	In this type II variation, information related to the cardiovascular morbidity and the ONTARGET and TRANSCEND trials following the Article 20 procedure is provided. The objective was to bring consistent information on the properties of telmisartan regarding cardiovascular prevention for the SmPC of the telmisartan + hydrochlorothiazide medicinal products. The section 5.1 is now in line with the current approved text of the EU SmPC section 5.1 of the telmisartan monocomponent products.

	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				
N/0095	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/10/2013	04/09/2014	PL	
IG/0356	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	23/09/2013	n/a		
IG/0322	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/07/2013	n/a		
WS/0372	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 in order to add a new adverse reaction "acute myopia". The package leaflet is amended accordingly. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	25/04/2013	29/05/2013	SmPC and PL	In a recent procedure WS288, "acute angle-closure glaucoma" was added as a new side effect in section 4.8. Since "acute angle-closure glaucoma" can cause "acute myopia, the WSA is proposing to add this adverse reaction accordingly. The Package Leaflet is proposed to be updated accordingly. Furthermore, the WSA proposed this opportunity to sort out an inconsistency in section 2 of the PILs of MicardisPlus compared to PritorPlus and Kinzalkomb as a different term is used to describe symptoms of acute myopia and acute angle closure glaucoma. The requested variation worksharing procedure proposed amendments to the Summary of Product Characteristics and Package Leaflet.
WS/0362	This was an application for a variation following a	25/04/2013	29/05/2013	SmPC, Annex	For Micardis, Micardis Plus, Kinzalmono, kinzalkomb, Pritor,

	worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. The requested variation worksharing procedure proposed amendments to the Summary of Product Characteristics, Annex II, Labelling 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			II, Labelling and PL	Pritor Plus Update of sections 4.2, 4.3, 4.4 and 4.5 of the SmPC to implement recommendations regarding the use of telmisartan with aliskiren as requested by the CHMP in the PSUR following the outcome of Article 20 related to aliskiren. In addition, information related to interaction with digoxin is added in section 4.5 of the SmPC. The Package leaflet is updated accordingly. Furthermore, the WSA took the opportunity to sort out a number of inconsistencies in content between SmPCs and PILs for the different products as follows: For Micardis, Micardis Plus, Kinzalmono, kinzalkomb, Pritor, Pritor Plus - Inconsistency between SmPC section 4.5 and PIL regarding interaction with alcohol, barbiturates, narcotics or antidepressants - Inconsistency between SmPC section 4.2 and PIL regarding the storage recommendation. For Twynsta, Onduarp PIL section 4 will be brought in line with SmPC section 4.8 with regard to the side effect hyperglycaemia (amlodipine component) For Micardis Plus, Kinzalkomb, Pritor Plus In the PIL section 2, there is a different wording of telmisartan mono products compared to the telmisartan/HCTZ products for the explanation of cholestasis or biliary obstruction. The MAH proposes to align the wording in the PIL of the telmisartan/HCTZ products so that it is identical with telmisartan mono products.

					Besides, editorial changes are proposed for Twynsta, Onduarp, Micardis, MicardisPlus, Pritor, PritorPlus, Kinzalmono and Kinzalkomb regarding storage recommendations in Annex IIIA in bold characters to bring them in line with the printing style on the actual, marketed products. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Micardis and Micardis Plus: (Belgium, Bulgaria and Luxembourg, Estonia, Lithuania) Twynsta/Onduarp (Estonia, Belgium and Luxembourg) Furthermore, the WSA proposed this opportunity to bring the PI in line with the latest QRD template (Version 9).
WS/0288	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 4.4 of the SmPC in order to add a new warning on acute myopia and angle-closure glaucoma with hydrochlorothiazide and to include acute angle-closure glaucoma as a new ADR in section 4.8 of the SmPC. Sections 2 and 4 of the Package Leaflet are updated accordingly. In addition the MAH is taking the opportunity to make some corrections in the DE, ES, FR, IT and LT Annexes for MicardisPlus, DE and IT Annexes for PritorPlus and Kinzalkomb. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-	20/09/2012	24/10/2012	SmPC and PL	This type II variation concerns an update of section 4.4 of the telmisartan/HCT SmPC to include a new warning on acute myopia and angle-closure glaucoma with HCT and to include acute angle-closure glaucoma as a new ADR in section 4.8 of the telmisartan/HCT SmPC, with consequential changes to the PL.

	clinical, clinical or pharmacovigilance data				
IG/0208	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	22/08/2012	n/a		
WS/0247	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of Summary of Product Characteristics and Package Leaflet. C.I.3.a - 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 - Changes with NO new additional data are submitted by the MAH	24/05/2012	28/06/2012	SmPC and PL	This type IB variation concerns an update of section 4.6 of the SmPC and package leaflet. The present worksharing variation application is submitted to update the relevant sections of SmPC and PL according to a harmonised wording concerning the use of hydrochlorothiazide in combination with angiotensin II receptor antagonists during pregnancy and breast-feeding as per the recommendation and wording agreed by PhVWP and CHMP in June 2011. In particular, with this variation the MAH added information on the limited experience with hydrochlorothiazide during pregnancy, especially during the first trimester. In addition the MAH added that hydrochlorothiazide crosses the placenta and its use during the second and third trimester may compromise foeto-placental perfusion and may cause foetal and neonatal effects like icterus, disturbance of electrolyte balance and thrombocytopenia. The updated of the SmPC includes that hydrochlorothiazide should not be used for essential hypertension in pregnant women except in rare situations where no other treatment could be used.
IG/0181/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	25/05/2012	n/a		

	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 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				
WS/0221	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Following the assessment of PSUR 10 and PSUR 11 for telmisartan, update to section 4.4 of the SmPC to include a warning for diabetic patients when treated with insulin or oral antidiabetics and to include a warning on RAAS blockage in patients with uncontrolled blood pressure, and update to section 4.8 of the SmPC to include "cough", "somnolence" and “interstitial lung disease” as new ADR and consequential changes to section 4 of the PL. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet for MicardisPlus only. Furthermore, the PI is being brought in line with the latest QRD template version 8. Finally the MAH took the opportunity to make some corrections in the BG, CZ, DA, DE, ES, ET, FI, FR, HU, IS, IT, LV, MT, NL, NO, PL, PT, SE, SK, SL	19/04/2012	25/05/2012	SmPC, Annex II, Labelling and PL	This type II variation concerns an update of sections 4.4 and 4.8 of the SmPC, upon request by CHMP following the assessment of PSUR 10 and 11 for telmisartan, to include a warning for diabetic patients when treated with insulin or oral antidiabetics and to include a warning on RAAS blockage in patients with uncontrolled blood pressure, and to add "cough", "somnolence" and “interstitial lung disease” as new ADR. Post-marketing experience with telmisartan has identified “somnolence”, “cough” and “interstitial lung disease” as new side effects. Regarding “diabetic patients”, as several patients that developed hypoglycemia were treated with antidiabetics or insulin, the MAH was requested to include a warning to be added in section 4.4 of SmPC in order to advise caution in patient diabetic treated with antidiabetics or insulin. Based on the cases from post marketing experience, the MAH was requested to discuss if an additional recommendation, regarding the dual blockade of the renin angiotensin.

	Annexes for PritorPlus and BG, CZ, DA, DE, ES, ET, FI, HU, IS, IT, LV, MT, NL, NO, PL, PT, SE, SK, SL Annexes for Kinzalkomb. 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				
IG/0165	B.III.1.a.1 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from an already approved manufacturer	10/04/2012	n/a		
WS/0175	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. To tighten the specification limits of the finished product. B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	15/12/2011	n/a		
IG/0105	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	06/10/2011	n/a		

IG/0094/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	25/08/2011	n/a	SmPC, Annex II, Labelling and PL	
WS/0104	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of Summary of Product Characteristics, Annex II and Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	17/02/2011	02/05/2011	SmPC, Annex II and PL	This type II variation concerns an update of section 4.8 of the SPC to include the ADRs 'angioedema (also with fatal outcome)' and 'Exacerbation of activation of Systemic Lupus erythematosus'. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes to the SPC and section 4 of the Package Leaflet, to update the contact details of the Spanish local representative in the Package Leaflet and to update annex II with standard wording concerning the pharmacovigilance system. This application was submitted as a Type II variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.
WS/0087/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. To add a new alternative manufacturer for the active substance. To increase the batch size of the active substance.	14/04/2011	14/04/2011		

	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation 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				
WS/0039	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of Summary of Product Characteristics and Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	20/01/2011	21/02/2011	SmPC, Annex II and PL	This type II variation concerns an update of section 4.8 of the SPC, upon request by CHMP following the assessment of PSUR 9, to add further information about 'liver disorder' and to add the ADR 'hypoglycaemia' under post-marketing experience. Most cases of abnormal liver function / liver disorder from post-marketing experience occurred in Japanese patients. The product information has now been updated to reflect the fact that Japanese patients are more likely to experience these adverse reactions. Post-marketing experience with telmisartan has identified hypoglycaemia as a new side effect which occurs mainly in diabetic patients and patients with abnormal glucose tolerance. Based on the statistically significant number of hypoglycaemia reports from pooled clinical trials in hypertensive patients suffering from diabetes, and the cardiovascular outcome trial TRANSCEND, a direct causal relationship between the occurrence of hypoglycaemia in diabetic patients and the therapeutic use of telmisartan cannot be excluded. In addition, the MAH took the opportunity to update Annex II with the standard DDPS wording and to make changes to the SPC to bring it in line with the latest version of the SPC guideline. The Package Leaflet has been updated

					accordingly. This application was submitted as a Type II variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.
IG/0045/G	This was an application for a group of variations. 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	08/02/2011	n/a		
IG/0010/G	This was an application for a group of variations. 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 currently approved batch size B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions B.II.b.5.c - Change to in-process tests or limits	30/06/2010	n/a		

	applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.III.1.a.3 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)				
IA/0076	To adjust the net weights of active pharmaceutical ingredients Telmisartan, Hydrochlorothiazide and Telmisartan Spray Dried Granulate intermediate. B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions	04/06/2010	n/a		
II/0074	Update of Summary of Product Characteristics and Package Leaflet This type II variation concerns an update of section 4.4 of the SPC to include a warning on the use of dual RAAS blockade and section 4.5 of the SPC to include information on the interaction with ramipril. Further, a minor change has been made to section 4.8 of the SPC to delete the term 'ineffectiveness of telmisartan'. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes to the SPC and Package Leaflet and to update the list of local representatives in the Package Leaflet. Update of Summary of Product Characteristics and Package Leaflet	18/03/2010	29/04/2010	SmPC and PL	Dual blockade of the renin-angiotensin-aldosterone system: As a consequence of inhibiting the renin-angiotensin-aldosterone system, hypotension, syncope, hyperkalaemia, and changes in renal function (including acute renal failure) have been reported in susceptible individuals, especially if combining medicinal products that affect this system. Dual blockade of the renin-angiotensin-aldosterone system (e.g. by adding an ACE-inhibitor to an angiotensin II receptor antagonist) is therefore not recommended in patients with already controlled blood pressure and should be limited to individually defined cases with close monitoring of renal function. Inteaction with ramipril: In one study the co-administration of telmisartan and ramipril led to an increase of up to 2.5 fold in the AUC0-24

					and Cmax of ramipril and ramiprilat. The clinical relevance of this observation is not known. The term 'drug ineffective' currently labelled as an adverse drug reaction observed with telmisartan mono therapy is not substantiated from clinical trial data or from post marketing experience, and has therefore been deleted from section 4.8 of the SPC.
IA/0075/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.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	26/03/2010	n/a		
IA/0073	To delete a manufacturing site for an intermediate product. IA_09_Deletion of manufacturing site	08/12/2009	n/a		
IA/0072	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	03/12/2009	n/a		
IA/0071	IA_09_Deletion of manufacturing site	03/12/2009	n/a		
IB/0070	IB_27_b_Change to test proc. of immediate packaging - other changes (incl. replacement/addition)	02/12/2009	n/a		

IA/0069	IA_15_a_Submission of Ph. Eur. certificate for active substance - approved manufacturer	19/10/2009	n/a		
II/0064	Update of Detailed Description of the Pharmacovigilance System Update of DDPS (Pharmacovigilance)	24/09/2009	14/10/2009	Annex II	The Detailed Description of the Pharmacovigilance System has been updated (Version 9.7) to notify changes to the DDPS performed since the last approved version, e.g. introduction of a safety management team. Consequently, Annex II has been updated with the new version number of the agreed DDPS.
IA/0068	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	01/09/2009	n/a		
IA/0067	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	01/09/2009	n/a		
IA/0066	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	12/08/2009	n/a		
II/0057	Update of SPC section 4.8 and 5.1 as well as PL section 4 to add information regarding "sepsis" as new side effect. In addition, the MAH took the opportunity to update the List of Local Representatives. Update of Summary of Product Characteristics, Labelling and Package Leaflet	23/04/2009	27/05/2009	SmPC, Labelling and PL	In the "Prevention Regimen For Effectively avoiding Second Strokes" (PRoFESS) trial in patients 50 years and older, who recently experienced stroke, an increased incidence of sepsis was noted for telmisartan compared with placebo, 0.70 % vs. 0.49 % [RR 1.43 (95 % confidence interval 1.00 - 2.06)]; the incidence of fatal sepsis cases was increased for patients taking telmisartan (0.33 %) vs. patients taking placebo (0.16 %) [RR 2.07 (95 % confidence interval 1.14 - 3.76)]. The observed increased

					occurrence rate of sepsis associated with the use of telmisartan may be either a chance finding or related to a mechanism not currently known. The term "sepsis including fatal outcome" was therefore added to SPC section 4.8 with the frequency unknown and the package leaflet was updated accordingly.
T/0061	Transfer of Marketing Authorisation	17/04/2009	06/05/2009	SmPC, Annex II, Labelling and PL	The MAH applied for the transfer of the Marketing Authorisation of PritorPlus from Bayer Healthcare AG to Bayer Schering Pharma AG. The transfer will take place on 15 August 2009.
IA/0062	IA_05_Change in the name and/or address of a manufacturer of the finished product	17/04/2009	n/a	Annex II and PL	
IA/0063	IA_05_Change in the name and/or address of a manufacturer of the finished product	15/04/2009	n/a		
II/0058	Update of Detailed Description of the Pharmacovigilance System Update of DDPS (Pharmacovigilance)	19/03/2009	07/04/2009	Annex II	The Detailed Description of the Pharmacovigilance System has been updated (Version 9.5) to reflect the integration of the companies' pharmacovigilance systems (Bayer and Schering AG). Consequently, Annex II has been updated with the new version number and date of the agreed DDPS.
II/0059	The MAH applied for an update of the SPC sections 4.3 and 4.6 as well as PL section 2 to implement the CHMP recommendation on a harmonised labelling relating to the use of Angiotensin II Receptor Antagonists during pregnancy and lactation. Furthermore, minor typographical changes have been introduced to SPC section 4.4. Update of Summary of Product Characteristics and	19/02/2009	17/03/2009	SmPC and PL	Available data regarding use of AIIRAs during lactation have been assessed. There are no concrete data to support the contraindication of use of AIIRAs during breast-feeding. All AIIRA agents were found in the milk of lactating rats but no human data about their transfer into breast milk are available. There is only a theoretical presumption of low transport according to their high plasma protein binding and low oral availability. A harmonised wording recommending an alternative treatment with better

	Package Leaflet				established safety profiles during breast-feeding, especially while nursing a newborn or preterm infant, has been included in the section 4.6 of the SPC and section 2 of the PL. Consequently, the existing contraindication for lactation has been deleted.
II/0054	Update of the SPC section 4.8 in order to update the information based on a re-calculation of the frequencies for the undesirable effects taking into account adverse drug reactions instead of adverse events. In addition, SPC section 4.9 is proposed to be updated with regard to the information on overdose and information regarding photosensitivity with the component hydrochlorothiazide has been included in SPC section 4.4. The respective sections of the PL have been amended accordingly. Furthermore, the MAH took the opportunity to introduce minor revisions to the PI including an update of the list of local representatives. Update of Summary of Product Characteristics and Package Leaflet	18/12/2008	27/01/2009	SmPC and PL	The revision of the EU SPC Guideline in October 2005 necessitated a re-calculation of the frequencies of undesirable effects taking into account adverse drug reactions instead of adverse events. Furthermore, the basis for the frequency estimation (i.e. the number of patients treated in eligible clinical trials with telmisartan/hydrochlorothiazide) has continuously grown since 2005. For the calculation of frequencies clinical trials have been included with a minimum treatment duration of 8 weeks. Therefore all randomised and double-blind clinical trials (placebo or active controlled) meeting this pre-requisite and which listed adverse events and reactions by individual patients (i.e. patient by patient basis) were identified and 9 clinical trials served as the basis for the frequency estimation of side effects of telmisartan + hydrochlorothiazide. Regarding SPC section 4.9 the information so far stated that "no data are available for telmisartan with regard to overdose in humans". However, several mostly spontaneous reports of overdoses had been received by the MAH, and consequently SPC section 4.9 has been revised.
IA/0056	IA_39_Change/addition of imprints, bossing or other markings	25/11/2008	n/a	SmPC and PL	

IA/0055	IA_39_Change/addition of imprints, bossing or other markings	25/11/2008	n/a	SmPC and PL	
N/0053	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/08/2008	n/a	PL	
II/0047	The MAH applied for an update of the SPC sections 4.3, 4.4, and 4.6 as well as PL section 2 to implement the CHMP recommendation on a harmonised labelling relating to the use of ACE inhibitors and Angiotensin II Receptor Antagonists during pregnancy. Update of Summary of Product Characteristics and Package Leaflet	24/04/2008	02/07/2008	SmPC and PL	Cooper's study published in the NEJM in June 2006 identified a signal of increased risk of congenital malformations, particularly cardiac defects after exposure to ACE inhibitors during the first trimester of pregnancy. Since the role of confounding factors such as diabetes and hypertension cannot be accurately defined based on the available data, the teratogenic potential of ACE inhibitors is not demonstrated, even though data suggest that such exposure cannot be considered as safe and should be avoided. There are fewer data regarding the risks associated with first trimester exposure to Angiotensin II receptor antagonists (AIIRAs) than for ACE inhibitors. Nevertheless, there is no evidence that the risk is lower for AIIRAs, and it is considered that any conclusions on ACE inhibitors are also valid for AIIRAs. Therefore, the existing contraindication for the 2nd and 3rd trimester of pregnancy remained, but a harmonised wording regarding pregnancy across the class was introduced
IA/0052	IA_09_Deletion of manufacturing site	28/05/2008	n/a		
IA/0051	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	28/05/2008	n/a		

IA/0050	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	28/05/2008	n/a		
IA/0049	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	28/05/2008	n/a		
IA/0048	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	09/04/2008	n/a		
X/0042	Annex I_2.(c) Change or addition of a new strength/potency	24/01/2008	01/04/2008	SmPC, Labelling and PL	
II/0045	Changes to the manufacturing process for the finished product Change(s) to the manufacturing process for the finished product	24/01/2008	29/01/2008		
IB/0046	IB_38_c_Change in test procedure of finished product - other changes	07/01/2008	n/a		
N/0043	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/08/2007	n/a	Labelling and PL	
IA/0044	IA_05_Change in the name and/or address of a manufacturer of the finished product	10/08/2007	n/a		
R/0040	Renewal of the marketing authorisation.	22/02/2007	14/05/2007	SmPC, Labelling and PL	Based on the CHMP 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 profile of PritorPlus continues to be favourable. The CHMP is of the opinion that the renewal can be granted with unlimited validity.
II/0033	Update of Sections 4.4 and 4.5 of the SPC further to a follow-up measure requested by CHMP. The Package Leaflet has been updated accordingly. Furthermore, the MAH has taken the opportunity to implement the latest QRD template (7.2). Update of Summary of Product Characteristics, Labelling and Package Leaflet	24/01/2007	28/02/2007	SmPC, Annex II, Labelling and PL	The following statement with regards to interaction between NSAIDs and angiotensin II antagonists has been added to section 4.5 of the SPC: "NSAIDs (i.e. acetylsalicylic acid at anti-inflammatory dosage regimens, COX-2 inhibitors and non-selective NSAIDs) may reduce the diuretic, natriuretic and antihypertensive effects of thiazide diuretics and the antihypertensive effects of angiotensin II antagonists. In some patients with compromised renal function (eg dehydrated patients or elderly patients with compromised renal function) the co-administration of angiotensin II antagonists and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration shoul be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter." In addition, minor changes have been introduced in the wording of the subsections on "lithium", "medicinal products that may increase potassium levels or induce hyperkalaemia", "alcohol and antidepressants.

					Regarding section 4.4, a number of cross-references have been introduced, as well as the following sentence on fructose intolerance, in line with the Guideline on Excipients: Sorbitol: Patients with hereditary problems of fructose intolerance should not take PritorPlus.
II/0038	Change(s) to the manufacturing process for the active substance Change(s) to the manufacturing process for the active substance	24/01/2007	31/01/2007		
II/0034	Update of SPC (4.8) and implementation of MedDRA terminology. Update of Summary of Product Characteristics and Package Leaflet	16/11/2006	08/01/2007	SmPC and PL	Update Section 4.8 of the SPC to add "acute renal failure, blood creatine phosphokinase increased and hyperkalaemia". The changes are based either on pharmacological mechanisms and/or on data mining of the company safety database.
IB/0041	IB_33_Minor change in the manufacture of the finished product	15/12/2006	n/a		
IB/0039	IB_10_Minor change in the manufacturing process of the active substance	09/11/2006	n/a		
IA/0037	IA_41_a_01_Change in pack size - change in no. of units within range of appr. pack size	17/10/2006	17/10/2006	SmPC, Labelling and PL	
IA/0036	IA_41_a_01_Change in pack size - change in no. of units within range of appr. pack size	17/10/2006	17/10/2006	SmPC, Labelling and	

				PL	
IA/0035	IA_29_b_Change in qual./quant. composition of immediate packaging - all other pharm. forms	15/10/2006	n/a		
N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/06/2006	n/a	PL	
IA/0031	IA_15_a_Submission of Ph. Eur. certificate for active substance - approved manufacturer	12/06/2006	n/a		
N/0029	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/05/2006	n/a		
IA/0030	IA_15_a_Submission of Ph. Eur. certificate for active substance - approved manufacturer	12/05/2006	n/a		
IA/0028	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	05/05/2006	n/a		
IA/0027	IA_36_ b_Change in shape or dimensions of the container/closure - other pharm. forms	28/03/2006	n/a		
T/0025	Transfer of Marketing Authorisation	24/02/2006	22/03/2006	SmPC, Labelling and PL	Transfer of MAH from Glaxo Group Limited to Bayer HealthCare AG.
IA/0026	IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	20/03/2006	n/a	Annex II and PL	
II/0022	Quality changes	23/02/2006	28/02/2006		

IA/0023	IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	06/02/2006	n/a	Annex II and PL	
IA/0024	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	03/02/2006	n/a		
IA/0021	IA_41_a_01_Change in pack size - change in no. of units within range of appr. pack size	29/11/2005	29/11/2005	SmPC, Labelling and PL	
IA/0019	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	11/10/2005	n/a		
II/0018	Quality changes	23/06/2005	30/06/2005		
II/0015	Quality changes	26/05/2005	30/06/2005		
IB/0017	IB_25_a_02_Change to comply with Ph. - compliance with EU Ph. - excipient	13/04/2005	n/a		
IB/0016	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	13/04/2005	n/a	SmPC	
IB/0013	IB_31_b_Change to in-process tests/limits during manufacture - addition of new tests/limits	10/11/2004	n/a		
IA/0014	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	08/11/2004	n/a		

	IA_11_b_Change in batch size of active substance or intermediate - downscaling				
N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/07/2004	n/a	PL	
IB/0011	IB_14_a_Change in manuf. of active substance without Ph. Eur. certificate - change in manuf. site	02/04/2004	n/a		
I/0010	11_Change in or addition of manufacturer(s) of active substance	18/07/2003	22/07/2003		
I/0008	14_Change in specifications of active substance 24_Change in test procedure of active substance	21/07/2003	22/07/2003		
I/0009	24a_Change in test procedure for starting material/intermediate used in manuf. of active substance	04/07/2003	08/07/2003		
I/0007	12a_Change in specification of starting material/intermediate used in manuf. of the active substance	20/06/2003	26/06/2003		
I/0006	24a_Change in test procedure for starting material/intermediate used in manuf. of active substance	20/06/2003	26/06/2003		
I/0005	01_Change in the name of a manufacturer of the medicinal product 11a_Change in the name of a manufacturer of the active substance	20/05/2003	26/05/2003		

I/0002	11_Change in or addition of manufacturer(s) of active substance	04/03/2003	13/03/2003		
N/0003	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/01/2003	06/03/2003	PL	
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/07/2002	22/08/2002	PL	