Micardis

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/1564/G	This was an application for a group of variations. 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 -	31/10/2022		Annex II and 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).

	Not 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 B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
IA/0123	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	01/04/2022	n/a		
IAIN/0122/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	23/02/2022		Annex II and PL	
WS/2203	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	03/02/2022		PL	
N/0120	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/09/2021	13/12/2021	PL	

WS/1950	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	26/11/2020	13/12/2021	SmPC, Annex II, Labelling and PL	
IG/1261/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 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	16/07/2020	n/a		
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/0988	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the	10/10/2018	n/a		

	relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
IB/0114/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) 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) 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) 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 B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products B.II.b.2.a - Change to importer, batch release	22/05/2018	23/10/2018	Annex II, Labelling and PL	

	arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold				
PSUSA/2882/ 201704	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	30/11/2017	n/a		PRAC Recommendation - maintenance
WS/1288	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	09/11/2017	23/10/2018	SmPC, Annex II, Labelling and PL	
IG/0819	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		
PSUSA/2882/ 201604	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	01/12/2016	n/a		PRAC Recommendation - maintenance
N/0109	Update of the package leaflet with revised contact details of the local representative for Portugal. In addition the MAH took the opportunity to make a	06/06/2016	23/10/2018	PL	

	correction in Section 4 of the Dutch Package Leaflets 20mg, 40mg and 80mg, in line with the EN approved text. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
IG/0678	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	21/04/2016	n/a		
PSUSA/2882/ 201504	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	06/11/2015	n/a		PRAC Recommendation - maintenance
PSUSA/2882/ 201404	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	06/11/2014	n/a		PRAC Recommendation - maintenance
A31/0099	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	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.

	involved in this procedure.				
WS/0570	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 6.0 in order to add "malignancies" as an important potential risk. 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	26/06/2014	n/a		N/A
IG/0432	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	16/04/2014	n/a		
WS/0468	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of the Summary of Product Characteristics, Annex II and Package Leaflet. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure	18/12/2013	04/09/2014	SmPC, Annex II and PL	Update of section 4.8 of the SmPC in order to add dysgeusia as an undesirable effect following CHMP request and assessment of PSUR 12. Furthermore, the PI is updated in line with the latest QRD template version 9.

	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				
PSUSA/2882/ 201304	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	07/11/2013	n/a		PRAC Recommendation - maintenance
N/0100	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/10/2013	04/09/2014	PL	
WS/0362	This was an application for a variation following a 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	25/04/2013	30/05/2013	SmPC, Annex II, Labelling and PL	For Micardis, Micardis Plus, Kinzalmono, kinzalkomb, Pritor, 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/0254	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. In accordance with Article 46 of regulation EC No	15/11/2012	20/12/2012	SmPC, Labelling and PL	For further information please refer to the variation assessment report: H-000209-WS-0254.

	1901/2006, update of sections 4.2, 5.1 and 5.2 of the SmPC in order to include the results of study 0502-0403, a study conducted to evaluate the safety, efficacy and pharmacokinetics of telmisartan in the paediatric population. Furthermore, the PI is being brought in line with the latest QRD template version and minor editorial corrections were implemented in section 4 of the Package Leaflet of Micardis, Pritor and Kinzalmono, in sectIn accordance with Article 46 of regulation EC No 1901/2006, update of sections 4.2, 5.1 and 5.2 of the SmPC in order to include the results of study 0502-0403, a study conducted to evaluate the safety, efficacy and pharmacokinetics of telmisartan in the paediatric population. Furthermore, the Product Information is being brought in line with the latest QRD template version and minor editorial corrections were implemented in section 4 of the Package Leaflet of Micardis, Pritor and Kinzalmono, in section 6.4 of the SmPC of Pritor and Kinzalmono, and in section 9 of the outer labelling of Kinzalmono and Pritor. The requested worksharing procedure proposed amendments to the SmPC, Labelling and Package Leaflet. ion 6.4 of the SmPC of Pritor and Kinzalmono, and in section 9 of the outer labelling of Kinzalmono and Pritor. The requested worksharing procedure proposed amendments to the SmPC, Labelling 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				
IG/0211	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	05/09/2012	n/a		
N/0096	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/07/2012	20/12/2012	PL	
WS/0220	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, 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 has aligned the Annexes with version 8 of the QRD template and updated the list of representatives for Micardis only. The MAH also took the opportunity to make some corrections in the EL Annexes for Micardis, BG, CZ, DA, DE, ES, FI, HU, IS, IT, LV, MT, NL, NO, PL, PT, SE, SK, SL Annexes for Kinzalmono, BG, CZ, DA, DE, ES, FI, HU, IS, IT, LV, MT, NL, NO, PL, PT, SE, SK, SL Annexes for Pritor.	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, 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 aldosterone system, should be added to advise caution also in patients with uncontrolled blood pressure.

	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		
IB/0091/G	This was an application for a group of variations. B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products 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) B.II.b.2.b.2 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing	10/02/2012	25/05/2012	Annex II and PL	
IB/0087/G	This was an application for a group of variations. B.II.e.4.a - Change in shape or dimensions of the	10/05/2011	10/05/2011	SmPC, Labelling and PL	

	container or closure (immediate packaging) - Non-sterile medicinal products B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes				
WS/0102	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	17/02/2011	02/05/2011	SmPC and PL	This type II variation concerns an update of section 4.8 of the SPC to include the ADR 'angioedema (also with fatal outcome)'. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make editorial changes to section 4 in the Package Leaflet and to update the contact details of the Spanish local representative. 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/0040	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	28/02/2011	SmPC 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 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.
IA/0086	To introduce minor changes in the manufacturing process of the finished product 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	17/06/2010	n/a		
IB/0080	IB_26_b_Change in the specification of immediate packaging - addition of new test parameter	12/01/2010	n/a		
IA/0085	IA_09_Deletion of manufacturing site	21/12/2009	n/a		
IA/0084	IA_09_Deletion of manufacturing site	10/12/2009	n/a		
IA/0083	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	07/12/2009	n/a		
IA/0082	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	07/12/2009	n/a		
IA/0081	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	07/12/2009	n/a		
IA/0079	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	03/12/2009	n/a		

II/0073	Extension of Indication	22/10/2009	23/11/2009	SmPC and PL	Please refer to the assessment report for Micardis EMEA/H/C/000209/II/0073.
IA/0078	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	12/08/2009	n/a		
II/0072	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 and Package Leaflet	23/04/2009	29/05/2009	SmPC 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.
II/0074	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	19/03/2009	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 section 4.6 of the SPC and section 2 of the PL. Consequently, the existing contraindication for lactation has been deleted.
IA/0075	IA_05_Change in the name and/or address of a manufacturer of the finished product	10/02/2009	n/a	Annex II and PL	
R/0071	Renewal of the marketing authorisation.	25/09/2008	19/11/2008	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 Micardis continues to be favourable. The CHMP is also of the opinion that the renewal can be granted with unlimited validity. PSURs will continue to be submitted annually until further notice.
II/0067	Changes to the test methods and specifications for the finished product Change(s) to the test method(s) and/or specifications for the finished product	26/06/2008	01/10/2008		
II/0068	Update of Summary of Product Characteristics and Package Leaflet The MAH applied for an update of the SPC sections 4.3, 4.4, and 4.6 as well as PL section 2 to	24/04/2008	03/07/2008	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

	implement the CHMP recommendation on a harmonised labelling relating to the use of ACE inhibitors and Angiotensin II Receptor Antagonists during pregnancy. In addition, linguistic corrections to the Danish Package Leaflet were proposed. Update of Summary of Product Characteristics and Package Leaflet				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/0070	IA_09_Deletion of manufacturing site	23/05/2008	n/a		
IA/0069	IA_05_Change in the name and/or address of a manufacturer of the finished product	23/05/2008	n/a		
N/0066	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/06/2007	n/a	Labelling and PL	
II/0056	Update of Summary of Product Characteristics section 4.4 and 4.5 and update Package Leaflet accordingly with the changes performed on the SPC. Update of Summary of Product Characteristics, Labelling and Package Leaflet	24/01/2007	05/03/2007	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 Micardis.
II/0062	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		

IA/0065	IA_29_b_Change in qual./quant. composition of immediate packaging - all other pharm. forms	10/01/2007	n/a		
II/0057	Update of SPC (4.8) and implementation of MedDRA terminology. Update of Summary of Product Characteristics and Package Leaflet	16/11/2006	04/01/2007	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/0064	IB_33_Minor change in the manufacture of the finished product	18/12/2006	n/a		
IB/0063	IB_10_Minor change in the manufacturing process of the active substance	09/11/2006	n/a		
IA/0061	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/0060	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/0059	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/0058	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/0055	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	12/06/2006	n/a		

IA/0054	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	12/06/2006	n/a		
IA/0053	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	12/06/2006	n/a		
IA/0052	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	07/06/2006	n/a		
IA/0051	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	07/06/2006	n/a		
IA/0050	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	08/05/2006	n/a		
IA/0049	IA_41_a_01_Change in pack size - change in no. of units within range of appr. pack size	06/12/2005	06/12/2005	SmPC, Labelling and PL	
II/0048	Quality changes	17/11/2005	24/11/2005		
IB/0047	IB_31_b_Change to in-process tests/limits during manufacture - addition of new tests/limits	20/12/2004	n/a		
IB/0046	IB_25_a_02_Change to comply with Ph. - compliance with EU Ph. - excipient	20/12/2004	n/a		
II/0044	Update of Summary of Product Characteristics (4.2, 4.3 and 4.4) and Package Leaflet. Update of Summary of Product Characteristics and	21/10/2004	07/12/2004	SmPC and PL	The Marketing Authorisation Holder applied for an update to the SPC (sections 4.2, 4.3, 4.4) and subsequent changes to the PL to remove the contraindication and warnings in patients with severe renal impairment (creatinine clearance

	Package Leaflet				<30ml/min) based on the results of clinical study 502.339, an open-label, placebo run-in, multicentre study of the efficacy and renal safety of telmisartan 40-80mg once daily for 12 weeks, in patients with all degrees of renal impairment, including patients on haemodialysis. In addition, the postal code has been amended in all Annexes.
IB/0045	IB_38_c_Change in test procedure of finished product - other changes	01/10/2004	n/a		
IA/0043	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold IA_11_b_Change in batch size of active substance or intermediate - downscaling	24/06/2004	n/a		
IA/0042	IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	18/03/2004	n/a	Annex II and PL	
IB/0041	IB_14_a_Change in manuf. of active substance without Ph. Eur. certificate - change in manuf. site	16/02/2004	n/a		
R/0040	Renewal of the marketing authorisation.	25/09/2003	09/01/2004	SmPC, Annex II, Labelling and PL	
I/0039	11_Change in or addition of manufacturer(s) of active substance	18/07/2003	23/07/2003		
I/0038	24a_Change in test procedure for starting material/intermediate used in manuf. of active substance	04/07/2003	09/07/2003		

I/0036	12a_Change in specification of starting material/intermediate used in manuf. of the active substance	20/06/2003	27/06/2003		
I/0037	14_Change in specifications of active substance 24_Change in test procedure of active substance	18/06/2003	26/06/2003		
I/0035	24a_Change in test procedure for starting material/intermediate used in manuf. of active substance	18/06/2003	26/06/2003		
I/0034	20a_Extension of shelf-life or retest period of the active substance	18/06/2003	26/06/2003		
I/0031	01_Change in the name of a manufacturer of the medicinal product 11a_Change in the name of a manufacturer of the active substance	16/04/2003	16/05/2003	Annex II and PL	
I/0033	01_Withdrawal of the manufacturing authorisation for a site of manufacture	12/05/2003	n/a		
I/0032	15_Minor changes in manufacture of the medicinal product 16_Change in the batch size of finished product	16/04/2003	23/04/2003		
I/0030	32_Change of imprints/bossing/marking on tablets/printing on capsules, incl. addition/change of inks	12/03/2003	18/03/2003		
N/0029	Minor change in labelling or package leaflet not	08/01/2003	03/02/2003	PL	

	connected with the SPC (Art. 61.3 Notification)				
I/0028	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	11/10/2002	24/10/2002		
N/0027	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/08/2002	30/09/2002	PL	
II/0024	Update of Summary of Product Characteristics and Package Leaflet	21/02/2002	30/05/2002	SmPC and PL	
I/0026	01_Change in the name of a manufacturer of the medicinal product	23/05/2002	24/05/2002		
I/0023	30_Change in pack size for a medicinal product	23/08/2001	19/10/2001	SmPC, Labelling and PL	
I/0022	20_Extension of shelf-life as foreseen at time of authorisation	22/08/2001	19/10/2001	SmPC	
I/0021	04_Replacement of an excipient with a comparable excipient	04/05/2001	n/a		
II/0020	Update of Summary of Product Characteristics and Package Leaflet	19/10/2000	22/01/2001	SmPC and PL	
I/0019	15_Minor changes in manufacture of the medicinal product	22/09/2000	n/a		
I/0018	25_Change in test procedures of the medicinal product	14/08/2000	12/09/2000		

I/0017	13_Batch size of active substance	02/08/2000	12/09/2000		
I/0016	12_Minor change of manufacturing process of the active substance 24a_Change in test procedure for starting material/intermediate used in manuf. of active substance	02/08/2000	12/09/2000		
II/0015	Update of Summary of Product Characteristics and Package Leaflet	12/04/2000	01/08/2000	SmPC, Labelling and PL	
I/0012	24a_Change in test procedure for starting material/intermediate used in manuf. of active substance	15/03/2000	30/03/2000		
I/0011	24a_Change in test procedure for starting material/intermediate used in manuf. of active substance	15/03/2000	30/03/2000		
I/0009	24a_Change in test procedure for starting material/intermediate used in manuf. of active substance	15/03/2000	30/03/2000		
I/0008	14_Change in specifications of active substance 12a_Change in specification of starting material/intermediate used in manuf. of the active substance	15/03/2000	30/03/2000		
I/0006	20_Extension of shelf-life as foreseen at time of authorisation	17/12/1999	09/03/2000	SmPC	

I/0010	24a_Change in test procedure for starting material/intermediate used in manuf. of active substance	20/01/2000	22/02/2000		
N/0014	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/02/2000	30/03/2000	PL	
I/0007	32_Change of imprints/bossing/marking on tablets/printing on capsules, incl. addition/change of inks	17/12/1999	07/01/2000		
I/0005	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	29/10/1999	10/11/1999		
X/0001	X-3-iii_Addition of new strength	20/05/1999	07/09/1999	SmPC, Annex II, Labelling and PL	
N/0004	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/04/1999	11/06/1999	PL	
I/0003	15_Minor changes in manufacture of the medicinal product	19/04/1999	n/a		
I/0002	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	19/04/1999	n/a		