Irbesartan Zentiva

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
IB/0099	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	25/08/2023	n/a		
IB/0098/G	This was an application for a group of variations.	09/03/2023	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).

	B.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition) 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 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				
IAIN/0097	C.I.11.a - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of wording agreed by the competent authority	27/09/2022	11/09/2023	Annex II	To update Annex II in line with the outcome of the Article 31 referral on angiotensin-II-receptor antagonists (sartans) containing a tetrazole group (EMEA/H/A-31/1471) and Article 5(3) assessment on nitrosamines (EMEA/H/A-5(3)/1490).
N/0096	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	25/07/2022	11/09/2023	Labelling	
IB/0095/G	This was an application for a group of variations. 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	21/07/2022	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				
PSUSA/10601 /202108	Periodic Safety Update EU Single assessment - irbesartan, irbesartan / hydrochlorothiazide	07/04/2022	n/a		PRAC Recommendation - maintenance
IB/0094/G	This was an application for a group of variations. 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 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	17/02/2022	n/a		
IB/0092	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	04/08/2021	18/07/2022	Annex II and PL	
IB/0090	B.III.1.a.1 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from an already approved manufacturer	14/07/2021	n/a		

IB/0091	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	16/06/2021	16/07/2021	SmPC, Labelling and PL	Update to add information on hypoglycaemia, on a drug-drug interaction with irbesartan and repaglinide and to add anaemia to the list of adverse drug reactions with frequency unknown.
IAIN/0089	C.I.11.a - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of wording agreed by the competent authority	12/05/2021	16/07/2021	Annex II	
IB/0088/G	This was an application for a group of variations. 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 B.III.1.a.3 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from a new manufacturer (replacement or addition)	22/04/2021	n/a		
A31/0080	The European Commission triggered a referral under Article 31 of Directive 2001/83/EC and requested the CHMP to assess the impact of nitrosamine impurities on the benefit-risk balance of valsartan-containing medicinal products and to issue a recommendation on whether the relevant marketing authorisations should be maintained, varied, suspended or revoked. During the CHMP plenary meeting in September	12/11/2020	19/02/2021	Annex II	Please refer to the assessment report: Irbesartan Zentiva EMEA/H/A-31/1471/C/785/0080

	2018, the scope of the referral has been widened to include all sartans with a tetrazole group in their molecular structure (candesartan, irbesartan, losartan, olmesartan and valsartan). The CHMP Opinion was issued on 31 January 2019 and the Commission Decision was issued on 2 April 2019. In a letter dated 29 July 2020, the European Commission requested the EMA to assess the impact of the outcome of the Article 5(3) assessment on nitrosamines adopted on 25 June 2020 on the CHMP's opinion of 31 January 2019 for the scientific assessment and review under Article 31 of Directive 2001/83/EC regarding angiotensin-II-receptor antagonists (sartans) containing a tetrazole group (EMEA/H/A-31/1471). The CHMP was requested to give its recommendation whether the conditions of the Marketing Authorisations should be varied.				
IB/0087/G	This was an application for a group of variations. B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) 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	16/12/2020	16/07/2021	Annex II and PL	

	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 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 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.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)				

	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.e - Change in test procedure for the finished product - Update of the test procedure to comply with the updated general monograph in the Ph. Eur. B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material				
IA/0086	A.7 - Administrative change - Deletion of manufacturing sites	24/09/2020	16/07/2021	SmPC, Annex II and PL	
IA/0085/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.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	07/09/2020	n/a		

	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				
IB/0084/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.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters	27/05/2020	16/07/2021	Annex II	

	and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) 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 B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State				
IB/0083/G	This was an application for a group of variations. B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF 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 originally approved batch size	14/10/2019	n/a		
IG/1065	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the	28/03/2019	n/a		

	relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer				
IG/1027	B.III.1.a.1 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from an already approved manufacturer	05/12/2018	n/a		
T/0079	Transfer of Marketing Authorisation	18/09/2018	10/10/2018	SmPC, Labelling and PL	
WS/1346	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 'anaphylactic reaction including anaphylactic shock' to the list of adverse drug reactions. The PL is updated accordingly. In addition, the MAH took the opportunity to update the information on local representatives in Bulgaria and Germany and to update the product information in line with the latest QRD template (version 10). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/07/2018	10/10/2018	SmPC, Labelling and PL	
IB/0077/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a	02/08/2017	19/07/2018	Annex II and PL	

	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.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
IG/0814	A.7 - Administrative change - Deletion of manufacturing sites	28/07/2017	n/a		
IB/0075	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	25/07/2017	n/a		
IB/0074/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient B.I.a.2.e - Changes in the manufacturing process of	02/06/2017	n/a		

	the AS - Minor change to the restricted part of an ASMF 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 originally approved batch size				
IB/0073/G	This was an application for a group of variations. B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF 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 originally approved batch size B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	05/01/2017	n/a		
PSUSA/1782/ 201508	Periodic Safety Update EU Single assessment - irbesartan	28/04/2016	21/06/2016	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1782/201508.
N/0071	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/09/2015	21/06/2016	PL	
N/0070	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/03/2015	21/06/2016	PL	
IB/0069	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other	19/02/2015	n/a		

	changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
A31/0063	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.
IG/0454	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	17/07/2014	n/a		
IA/0067	B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	14/05/2014	n/a		

N/0066	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/03/2014	04/09/2014	PL	
IA/0065	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	26/09/2013	n/a		
IG/0327	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	02/08/2013	n/a		
II/0057	Update of SmPC sections 4.3, 4.4 and 4.5 to reflect that the concomitant use of Angiotensin II Receptor Blockers (ARBs) with aliskiren is contraindicated in patients with renal impairment and in patients with diabetes mellitus. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to align the annexes with the latest QRD template, to make editorial changes in the annexes and to introduce the contact details of the local representative in Croatia in the 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	27/06/2013	31/07/2013	SmPC, Annex II, Labelling and PL	Please refer to the Scientific Discussion "Irbesartan Zentiva-EMEA-H-C-0785-II-57".
IA/0062	A.7 - Administrative change - Deletion of manufacturing sites	05/06/2013	31/07/2013	Annex II and PL	

IB/0060	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	06/05/2013	n/a		
IA/0061	B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter	26/04/2013	n/a		
II/0058	Change in the specifications limits range for the active substance Irbesartan. B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS	25/04/2013	n/a		
IA/0059	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	22/04/2013	n/a		
IAIN/0056	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	03/01/2013	n/a		
IA/0055	A.7 - Administrative change - Deletion of manufacturing sites	03/12/2012	n/a		
IA/0054	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	09/11/2012	n/a		

IAIN/0053	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	30/10/2012	n/a		
IB/0052/G	This was an application for a group of variations. B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS 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	15/10/2012	n/a		
T/0051	Transfer of Marketing Authorisation	10/09/2012	28/09/2012	SmPC, Labelling and PL	
IA/0050	B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products	26/07/2012	30/08/2012	SmPC	
N/0048	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/05/2012	30/08/2012	Labelling	
IAIN/0049	A.1 - Administrative change - Change in the name and/or address of the MAH	03/04/2012	30/08/2012	SmPC, Labelling and PL	

IA/0047	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	22/02/2012	n/a		
IAIN/0046/G	This was an application for a group of variations. A.2.a - Administrative change - Change in the (invented) name of the medicinal product for CAPs B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	06/02/2012	30/08/2012	SmPC, Annex II, Labelling and PL	

R/0041	Renewal of the marketing authorisation.	20/10/2011	20/01/2012		Based on the CHMP review of the available information and on the basis of a re-evaluation of the benefit risk balance, the CHMP was 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 Irbesartan Winthrop continues to be favourable. The CHMP recommended the renewal of the Marketing Authorisation for Irbesartan Winthrop, subject to the conditions as laid down in Annex II to the Opinion. The CHMP was also of the opinion that the renewal can be granted with unlimited validity. The renewal required no amendments to the terms of the Community Marketing Authorisation.
IB/0044	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	13/01/2012	n/a		
IB/0043	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	11/01/2012	n/a		
IB/0045	B.I.a.3.z - Change in batch size (including batch size ranges) of AS or intermediate - Other variation	04/01/2012	n/a		
II/0035	Update of the Summary of Product Characteristics. Update of SmPC sections 4.6 and 5.3 with wording related to fertility.	19/05/2011	05/07/2011	SmPC	It is unknown whether irbesartan or its metabolites are excreted in human milk. Available pharmacodynamic/toxicological data in rats have shown excretion of irbesartan or its metabolites in milk.

	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				Fertility and reproductive performance were not affected in studies of male and female rats even at oral doses of irbesartan causing some parental toxicity (from 50 to 650 mg/kg/day), including mortality at the highest dose. No significant effects on the number of corpora lutea, implants, or live fetuses were observed. Irbesartan did not affect survival, development, or reproduction of offspring. Studies in animals indicate that the radiolabeled irbesartan is detected in rat and rabbit fetuses.
WS/0074	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	14/04/2011	07/06/2011	SmPC and PL	This type IB variation concerns an update of section 4.8 of the SmPC with the ADR 'jaundice', upon request by the CHMP following the assessment of irbesartan PSUR 15 and FU2 020.1. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to make some editorial changes in the SmPC and Package Leaflet. This application was submitted following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.
IA/0040	A.7 - Administrative change - Deletion of manufacturing sites	27/05/2011	n/a		
IA/0039	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	04/05/2011	n/a		
IA/0037	C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the	08/04/2011	n/a	Annex II	

	major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD				
IA/0036/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS	08/04/2011	n/a		
IB/0038	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	06/04/2011	n/a		
T/0034	Transfer of Marketing Authorisation	24/11/2010	06/01/2011	SmPC, Labelling and PL	
II/0028	This type II variation concerns an update of section 4.8 of the SPC, upon request by the CHMP following the assessment of the irbesartan PSUR covering 12 Aug 2006 - 11 Aug 2009, to add the ADR "Vertigo" with the frequency of "not known" under 'post-marketing experience'. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to align	23/09/2010	05/11/2010	SmPC and PL	This type II variation concerns an update of section 4.8 of the SPC, upon request by the CHMP following the assessment of the irbesartan PSUR covering 12 Aug 2006 - 11 Aug 2009, to add the ADR "Vertigo" with the frequency of “not known” under ‘post-marketing experience’. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to align the product information with the latest QRD template (version

	the product information with the latest QRD template (version 7.3) and the Guideline on Summary of Product Characteristics (September 2009). 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				7.3) and the Guideline on Summary of Product Characteristics (September 2009).
IA/0033/G	This was an application for a group of variations. 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.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV	28/10/2010	n/a	Annex II	
IB/0032	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	26/08/2010	n/a		
IA/0031	B.III.2.a.1 - Change of specification('s) of a former non Pharmacopoeial substance to comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - AS	06/07/2010	n/a		
IB/0030	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an	10/06/2010	n/a		

	ASMF				
IB/0029	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	19/05/2010	n/a		
N/0027	To change the phone number of the Slovak local representative in the Package Leaflet. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/03/2010	n/a	PL	
IA/0026/G	This was an application for a group of variations. C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV 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	22/03/2010	n/a	Annex II	
IB/0025	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition)	02/12/2009	n/a		
II/0024	Change of the manufacturing site of irbesartan and as a consequence a change in the batch size of this active substance. Change(s) to the manufacturing process for the	24/09/2009	05/10/2009		

	active substance				
IA/0023	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	08/07/2009	n/a		
IA/0022	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	22/06/2009	n/a		
N/0021	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/05/2009	n/a	PL	
IA/0020	IA_32_a_Change in batch size of the finished product - up to 10-fold	27/04/2009	n/a		
IB/0019	IB_10_Minor change in the manufacturing process of the active substance	17/04/2009	n/a		
II/0018	Update of SPC sections 2, 4.2, 4.3, 4.8, 5.1 and 6.5 in order to align the Product Information of Irbesartan Winthrop with the Product Information of the reference product Aprovel. Update of Summary of Product Characteristics	19/03/2009	08/04/2009	SmPC	The SPC of Irbesartan Winthrop has been aligned with the Product Information of the reference product Aprovel as approved with the renewal procedure.
II/0017	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.	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

	Update of Summary of Product Characteristics and Package Leaflet				recommending an alternative treatment with better 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/0016	Update of Detailed Description of the Pharmacovigilance System Changes to QPPV Update of DDPS (Pharmacovigilance)	22/01/2009	25/02/2009	Annex II	The Detailed Description of the Pharmacovigilance System has been updated (Version 3.0) to reflect the change of the Qualified Person for Pharmacovigilance (QPPV) as well as to notify other changes to the DDPS performed since the last approved version. Consequently, Annex II has been updated using the standard text including the new version number of the agreed DDPS.
IB/0015	IB_10_Minor change in the manufacturing process of the active substance IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	18/08/2008	n/a		
N/0013	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/08/2008	n/a	PL	
IA/0014	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	29/07/2008	n/a		
II/0010	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.	24/04/2008	11/06/2008	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

	Update of Summary of Product Characteristics and Package Leaflet				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.
IB/0012	IB_10_Minor change in the manufacturing process of the active substance IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	25/04/2008	n/a		
IA/0011	IA_09_Deletion of manufacturing site	03/04/2008	n/a		
IA/0009	IA_09_Deletion of manufacturing site	13/02/2008	n/a		
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/12/2007	n/a	PL	
IB/0006	IB_42_b_Change in storage conditions of the finished/diluted/reconstituted product	20/12/2007	n/a	SmPC, Labelling and PL	
IA/0008	IA_09_Deletion of manufacturing site	14/12/2007	n/a		

IB/0004	IB_10_Minor change in the manufacturing process of the active substance	21/09/2007	n/a		
IA/0005	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	20/09/2007	n/a		
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/05/2007	n/a	PL	
IA/0003	IA_32_a_Change in batch size of the finished product - up to 10-fold	23/03/2007	n/a		
IA/0002	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	23/03/2007	n/a		