



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Tolura

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
IA/0045	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	05/08/2024	n/a		
IA/0044	B.II.b.3.a - Change in the manufacturing process of	20/11/2023	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).



	the finished or intermediate product - Minor change in the manufacturing process				
IAIN/0043/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 - Not including batch control/testing B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	20/11/2023		Annex II and PL	
IA/0042	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	19/07/2023	n/a		
IAIN/0041	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	12/04/2023	n/a		
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/01/2023		PL	
IA/0039	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	09/12/2022	n/a		

IAIN/0038/G	This was an application for a group of variations. 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 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 A.7 - Administrative change - Deletion of manufacturing sites	11/07/2022	n/a		
N/0037	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/01/2022		PL	
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 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.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	16/12/2020	n/a		
IB/0035	C.I.7.b - Deletion of - a strength	21/08/2020	02/08/2021	SmPC, Annex II, Labelling and PL	

IA/0034	B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	11/05/2020	n/a		
IB/0033/G	This was an application for a group of variations. 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.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	09/03/2020	n/a		
IA/0032	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	16/12/2019	n/a		
IAIN/0031/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 A.7 - Administrative change - Deletion of manufacturing sites B.III.1.a.1 - Submission of a new/updated or	14/05/2019	n/a		

	deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - New certificate from an already approved manufacturer				
IA/0030/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place 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	12/12/2018	n/a		
IB/0029	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	17/09/2018	23/09/2019	SmPC	
N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/02/2018	23/09/2019	Labelling and PL	
IA/0027/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	26/07/2017	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				
IA/0026	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	24/02/2016	n/a		
IA/0025	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	09/12/2015	n/a		
IB/0024	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	29/06/2015	24/06/2016	SmPC, Labelling and PL	
IA/0023	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	04/05/2015	n/a		
R/0022	Renewal of the marketing authorisation.	22/01/2015	19/03/2015		Based on the CHMP review of data on quality, safety and efficacy, including all variations introduced since the marketing authorisation was granted, the CHMP considered that the risk-benefit balance of Tolura in the treatment of essential hypertension in adults and reduction of

					cardiovascular morbidity in adults with manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke, or peripheral arterial disease) or type 2 diabetes mellitus with documented target organ damage remains favourable, and therefore recommends the renewal of the marketing authorisation. The CHMP recommended that the renewal be granted with unlimited validity.
IA/0021	A.7 - Administrative change - Deletion of manufacturing sites	17/09/2014	n/a		
A31/0013	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.
IB/0020/G	This was an application for a group of variations.	06/06/2014	n/a		

	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				
IB/0019/G	This was an application for a group of variations. 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 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	22/05/2014	04/09/2014	SmPC and PL	
IB/0018/G	This was an application for a group of variations. 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	13/12/2013	04/09/2014	SmPC, Labelling and PL	

	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				
IAIN/0017	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	12/11/2013	n/a		
PSUSA/2882/201304	Periodic Safety Update EU Single assessment - hydrochlorothiazide / telmisartan, telmisartan	07/11/2013	n/a		PRAC Recommendation - maintenance
IA/0015	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	18/10/2013	n/a		
IB/0014/G	This was an application for a group of variations. 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 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	24/09/2013	04/09/2014	SmPC, Annex II and PL	

N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/07/2013	04/09/2014	PL	
II/0010/G	This was an application for a group of variations. -To introduce changes to the manufacturing process of the active substance. -To introduce changes to the specification parameters and/or limits of the active substance. B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product 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.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.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.c - Change in the specification parameters	30/05/2013	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method				
IB/0011	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	11/12/2012	n/a		
IA/0009	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	21/11/2012	n/a		
IB/0008	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 are submitted by the MAH	26/07/2012	31/10/2012	SmPC, Annex II, Labelling and PL	
IA/0007	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	31/05/2012	n/a		
IA/0006	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	31/05/2012	n/a		
IA/0005	B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur.	16/05/2012	n/a		

	Monograph - Updated certificate from an already approved manufacturer				
IB/0004/G	This was an application for a group of variations. Update of SmPC section 4.8 upon request by CHMP following the assessment of PSUR 9 to add the ADR 'hypoglycaemia' under postmarketing experience. The same section was also update to include the ARD angiodema (also with fatal outcome) as requested by CHMP to bring the Annex in line with the Reference Medicinal Product Information. The Package Leaflet has been updated accordingly. Additionally, the MAH took the opportunity to update Annex IIB with regards to Pharmacovigilance system. Furthermore, in the Package Leaflet the contact details of the Dutch, Estonian, Latvian and Lithuanian local representatives have been updated. 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 are submitted by the MAH 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 are submitted by the MAH	10/08/2011	n/a	SmPC, Annex II and PL	
IB/0003	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an	12/04/2011	n/a		

	ASMF				
IB/0002	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	01/02/2011	n/a		
IB/0001	To add "Reduction of cardiovascular morbidity in patients with (i) manifest atherothrombotic cardiovascular disease (history of coronary heart disease, or peripheral arterial disease) or (ii) type 2 diabetes mellitus with documented target organ damage" based on the results of 3 clinical trials (ONTARGET, TRANSCEND, PRoFESS). Consequently SPC sections 4.1, 4.2, 4.4, 4.8 and 5.1 have been amended. The Package Leaflet has been updated accordingly. 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 are submitted by the MAH	05/10/2010	n/a	SmPC and PL	