Clopidogrel Krka

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/0040/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	23/11/2023	01/12/2023	SmPC 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).

	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				
IB/0039	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	09/06/2022	04/07/2023	SmPC and PL	
IA/0038	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)	09/11/2021	n/a		
IB/0037	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	07/10/2021	28/10/2021	SmPC and PL	
IB/0036	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	30/04/2021	19/05/2021	SmPC and PL	

	product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH				
IB/0035	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	04/12/2020	19/05/2021	SmPC and PL	
IB/0034	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	24/02/2020	12/05/2020	SmPC and PL	
IB/0033	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	25/09/2019	12/05/2020	SmPC, Annex II, Labelling and PL	
IB/0032/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	05/06/2019	12/05/2020	SmPC, Labelling and PL	

	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				
IB/0031	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	17/04/2018	28/03/2019	SmPC, Labelling and PL	
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.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.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	16/04/2018	n/a		
IB/0029/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	22/06/2017	19/07/2017	SmPC, Labelling and PL	

	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 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 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				
IAIN/0028	B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g.	19/10/2016	19/07/2017	SmPC, Labelling and	

	tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes			PL	
IB/0027/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 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	08/12/2015	02/06/2016	SmPC, Annex II and PL	
IB/0026	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	01/06/2015	02/06/2016	SmPC and PL	

PSUSA/820/201311	Periodic Safety Update EU Single assessment - acetylsalicylic acid / clopidogrel, clopidogrel	10/07/2014	n/a		PRAC Recommendation - maintenance
R/0022	Renewal of the marketing authorisation.	20/03/2014	14/05/2014		The safety and efficacy of clopidogrel have been demonstrated by several large clinical studies. The MAH has submitted an Addendum to Clinical Overview (ACO) to provide details of the efficacy and safety of Clopidogrel Krka since its approval. In the CHMP's view the provided data do not change the overall knowledge about the beneficial effect and safety profile of clopidogrel when used in the approved indications. The beneficial effect of Clopidogrel Krka remains in line with that of the originator product (Plavix), and is considered positive. The CHMP therefore recommended that Clopidogrel Krka Marketing Authorisation can be renewed with unlimited validity.
IB/0025/G	This was an application for a group of variations. To update sections 4.4 and 4.5 of the SmPC to add information on an interaction with the selective serotonin reuptake inhibitors (SSRIs) in section 4.5 and consequential information concerning this interaction in section 4.4. The Package leaflet has been updated accordingly. To update 4.8 of the SmPC to add "Rash exfoliative" as a new undesirable effect. Furthermore minor editorial correction to DE, HR, NO and PL text were introduced. These changes have been previously approved for the reference medicinal	16/04/2014	06/05/2015	SmPC and PL	

	product Plavix in WS/476 and WS/477 respectively 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				
IB/0023	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	20/01/2014	14/05/2014	SmPC	
IB/0020/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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	19/12/2013	n/a		

	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/0021/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	28/10/2013	14/05/2014	SmPC	
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	09/10/2013	14/05/2014	SmPC, Annex II, Labelling and PL	

	product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH				
IB/0016	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	07/09/2012	n/a		
IB/0015/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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.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	07/03/2012	n/a		
IB/0014	B.II.a.3.z - Changes in the composition (excipients) of the finished product - Other variation	02/03/2012	12/09/2012	SmPC and PL	
IB/0011	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)	11/05/2011	n/a	SmPC	
IB/0010	C.I.2.a - Change in the SPC, Labelling or PL of a	15/04/2011	n/a	SmPC, Annex	To update SPC and PIL, sections 4.2 "Posology and method

	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			II and PL	of administration", 4.4 "Special warnings and precautions for use", 4.5 "Interaction with other medicinal products and other forms of interaction" and 5.2 "Pharmacokinetic properties" of clopidogrel/acetyisalicylic acid (ASA) SPC to include new information on the variability of response to clopidogrel due to either genetic variations of the CYP2C19 enzyme or concomitant use of drugs that inhibit the CYP2C19 enzyme such as proton pump inhibitor (PPI). In addition, section 4.8 has been amended with minor details on the CURE study. Additional changes have been added to the SPC and Package Leaflet in order to bring it in line with the revised QRD template (version 7.3). Minor corrections were also made in List of local representatives for Estonia, Latvia, Poland, Greece, Cyprus, United Kingdom and Lithuania.
IA/0012	A.7 - Administrative change - Deletion of manufacturing sites	14/04/2011	n/a		
IB/0009	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	16/07/2010	n/a	SmPC and PL	
IB/0007/G	This was an application for a group of variations. 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.1.z - Change in the manufacturer of AS or of a	11/05/2010	n/a		

	starting material/reagent/intermediate for AS - Other variation				
IA/0008	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	21/04/2010	n/a		
N/0006	The Marketing Authorisation Holder (MAH) took this opportunity to update the contact details for the local representatives in Greece and Austria. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/03/2010	n/a	PL	
II/0001	addition of alternative manufcture for an intermediate and change in manufacturer process of intermediate Change(s) to the manufacturing process for the active substance	17/12/2009	08/01/2010		
IB/0005	IB_18_Replacement of an excipient with a comparable excipient	23/12/2009	n/a	SmPC and PL	
IB/0004	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	13/11/2009	13/11/2009	SmPC, Labelling and PL	
IA/0003	IA_41_a_01_Change in pack size - change in no. of units within range of appr. pack size	10/11/2009	10/11/2009	SmPC, Labelling and	

				PL	
IA/0002	Addition of a manufacturing site for secondary packaging IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	20/10/2009	n/a		