Clopidogrel Viatris

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
II/0049/G	This was an application for a group of variations. B.II.e.1.b.3 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Deletion of an immediate packaging container without a complete deletion of a strength	16/05/2024		SmPC, Labelling 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).

	or pharmaceutical form B.II.a.3.b.5 - Changes in the composition (excipients) of the finished product - Other excipients - Change that is supported by a bioequivalence study				
IB/0050/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	07/12/2023	18/12/2023	SmPC and PL	
IB/0047/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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.z - Quality change - Active substance - Other variation	01/06/2023	n/a		

IB/0048/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.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	26/05/2023	n/a		
IB/0046	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	03/08/2022	04/08/2023	SmPC and PL	
IB/0045/G	This was an application for a group of variations. 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 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.III.2.a.1 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply	02/06/2022	n/a		

	with the Ph. Eur. or with a national pharmacopoeia of a Member State - AS B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF				
N/0044	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/03/2022	04/08/2023	PL	
IB/0043	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	17/01/2022	03/02/2022	SmPC, Labelling and PL	
T/0042	Transfer of Marketing Authorisation	19/10/2021	09/11/2021	SmPC, Labelling and PL	
IAIN/0041	A.2.a - Administrative change - Change in the (invented) name of the medicinal product for CAPs	06/10/2021	25/10/2021	SmPC, Labelling and PL	
IAIN/0040/G	This was an application for a group of variations. 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	28/07/2021	25/10/2021	SmPC, Annex II, Labelling and PL	

	site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site 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				
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	17/05/2021	01/06/2021	SmPC, Annex II and PL	
T/0037	Transfer of Marketing Authorisation	28/01/2021	12/02/2021	SmPC, Labelling and PL	
IAIN/0038	A.2.a - Administrative change - Change in the (invented) name of the medicinal product for CAPs	13/01/2021	11/02/2021	SmPC, Labelling 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 product - Implementation of change(s) for which NO new additional data is required to be submitted by	04/11/2020	11/02/2021	SmPC and PL	

	the MAH				
IB/0035/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	30/01/2020	04/05/2020	SmPC and PL	
IAIN/0034	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	27/09/2019	04/05/2020	SmPC and PL	
IB/0033/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	23/05/2019	04/05/2020	SmPC and PL	

	new additional data is required to be submitted by the MAH				
IB/0032	B.II.b.4.e - Change in the batch size (including batch size ranges) of the finished product - More than 10-fold increase compared to the originally approved batch size for immediate release (oral) pharmaceutical form	14/05/2019	n/a		
N/0031	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/09/2018	17/04/2019	PL	
IAIN/0030	A.1 - Administrative change - Change in the name and/or address of the MAH	01/06/2018	17/04/2019	SmPC, Labelling and PL	
IB/0029	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	23/04/2018	17/04/2019	SmPC and PL	
IB/0028	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	24/07/2017	n/a		
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	18/05/2017	31/05/2017	SmPC, Labelling and PL	

	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				
N/0026	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/03/2016	04/07/2016	PL	
IB/0025/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	22/01/2016	04/07/2016	SmPC and PL	

	the MAH				
II/0020	B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF	24/09/2015	n/a		
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	08/07/2015	04/07/2016	SmPC and PL	
R/0017	Renewal of the marketing authorisation.	24/07/2014	18/09/2014	SmPC, Labelling and PL	The MAH has not performed any efficacy studies in the period after the initial marketing authorisation or provided any literature review on the efficacy/effectiveness. The MAH refers in the clinical overview to the modifications of the SmPC confirming the efficacy of clopidogrel in the proposed indications. On the basis of the review of the safety information covering the period of this renewal, the CHMP concluded that the safety profile of Apotex remains favourable in the approved indications. In line with the reference medicinal product it is recommended to continue close monitoring of all reports of adverse reactions received from worldwide sources and the occurrence of late stent thrombosis after clopidogrel withdrawal for the next reporting interval and cumulatively follow the literature for potential new emerging information that may alter the efficacy-safety of clopidogrel. The CHMP recommends that the renewal be granted with

					unlimited validity.
PSUSA/820/201311	Periodic Safety Update EU Single assessment - acetylsalicylic acid / clopidogrel, clopidogrel	10/07/2014	n/a		PRAC Recommendation - maintenance
IB/0019/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 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	29/04/2014	18/09/2014	SmPC and PL	

	the MAH				
IB/0016	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	03/01/2014	18/09/2014	SmPC and PL	
IB/0015/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	31/10/2013	18/09/2014	SmPC and PL	
IAIN/0014/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	14/10/2013	18/09/2014	Annex II and PL	

	B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site 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				
IB/0013/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	11/10/2013	18/09/2014	SmPC, Annex II, Labelling and PL	
II/0012	To add an alternative manufacturer of the active substance, clopidogrel besilate. B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is supported by an ASMF	25/04/2013	n/a		

N/0010	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/03/2013	18/09/2014	PL	
IAIN/0011	To replace the Detailed Description of the Pharmacovigilance System (DDPS) with the Pharmacovigilance System Master File (PSMF). C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/02/2013	n/a		
IB/0009/G	This was an application for a group of variations. 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) B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	27/03/2012	15/10/2012	SmPC, Labelling and PL	
IB/0008/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 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	02/08/2011	n/a	SmPC and PL	Update of sections 4.2 "Posology and method of administration" and 5.1 "Phamacodynamic properties" of clopidogrel SPC to include new paediatric information available for clopidogrel. Update of section 4.1 with addition of indication "Prevention of atherothrombotic events". Editorial changes to harmonise the text with the Plavix text as well as a change to the local representatives telephone number in the package leaflet.

IB/0007/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 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 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	17/05/2011	n/a	SmPC, Annex II and PL	To update the Product Information as already approved for the reference product Plavix. - Additional indication (Acute Coronary Syndrome) - Extension of Indication: Extension of the acute coronary syndrome (ACS) indication as follows: "ST segment elevation acute myocardial infarction, in combination with ASA in medically treated patients eligible for thrombolytic therapy". - Update of Summary of Product Characteristics and Package Leaflet to reword the indication as follows: "Non-ST segment elevation acute coronary syndrome (unstable angina or non-Q-wave myocardial infarction), including patients undergoing a stent placement following percutaneous coronary intervention, in combination with acetylsalicylic acid (ASA)." This grouped variation also includes the following change that was already approved for the reference product Plavix: - Amendments were introduced in the Summary of Product Characteristics (SPC) and Package Leaflet to update sections 4.2 "Posology and method 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/acetylsalicylic 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)

					Furthermore, the DDPS version number and date were deleted as a change to Annex IIB as stated in the procedural announcement of October and November 2010.
II/0005	To add an alternative route of synthesis of the active substance (clopidogrel besylate) at the already approved manufacturing site. B.I.a.1.c - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions	18/11/2010	25/11/2010		
IB/0006	C.I.8.b - Introduction of a new Pharmacovigilance system - which has been assessed by the relevant NCA/EMA for another product of the same MAH	28/10/2010	n/a	Annex II	To update the Pharmacovigilance system to version 7.0 of the MAH, Apotex Europe B.V.
IB/0004	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	28/07/2010	n/a	SmPC and PL	
IB/0003/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 B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging	21/05/2010	n/a	Annex II and PL	

	site B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.2.b.2 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the currently approved batch size A.7 - Administrative change - Deletion of manufacturing sites				
IB/0002	IB_02_Change in the name of the medicinal product	20/01/2010	n/a	SmPC, Labelling and PL	
T/0001	Transfer of Marketing Authorisation	25/11/2009	11/12/2009	SmPC, Labelling and PL	The Marketing Authorisation Holder was transferred from Mylan S.A.S. to Apotex Europe BV.