EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Clopidogrel DURA

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
PSUSA/00820	Periodic Safety Update EU Single assessment - ACETYLSALICYLIC ACID, CLOPIDOGREL	10/07/2014	n/a		PRAC Recommendation - maintenance
R/0017	Renewal of the marketing authorisation.	20/03/2014	22/05/2014	SmPC, Annex II, Labelling and PL	The safety and efficacy of clopidogrel have been demonstrated by several large clinical studies. No literature review on the efficacy/effectiveness has been submitted by the MAH within this application. Since the clinical efficacy of clopidogrel in the approved indications is well established and evidence of clinical efficacy has been discussed at time of

[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).

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					approval the CHMP finds acceptable the MAH approach of not performing a literature review on the efficacy/effectiveness of clopidogrel. The beneficial effect of Clopidogrel Dura remains in line with that of the originator product (Plavix), and is considered positive.
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 the	23/04/2014		SmPC and PL	

	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	19/12/2013	22/01/2014	SmPC	
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	14/11/2013	22/01/2014	SmPC	
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	16/09/2013	22/01/2014	SmPC, Annex II, Labelling and PL	

	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/0013/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.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	21/05/2013	22/01/2014	SmPC	
IB/0012/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 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	08/03/2013	n/a		
IA/0011/G	This was an application for a group of variations. B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase	18/01/2013	n/a		

	compared to the currently approved batch size A.7 - Administrative change - Deletion of manufacturing sites				
IB/0010	B.II.a.3.z - Changes in the composition (excipients) of the finished product - Other variation	18/01/2013	22/01/2014	SmPC and PL	
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	08/08/2011	n/a	SmPC	
IA/0008	A.7 - Administrative change - Deletion of manufacturing sites	13/04/2011	n/a		
IB/0007	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	11/03/2011	n/a	SmPC, Annex II and PL	To update the Summary of Product Characteristics and Package Leaflet of the concerned product following assessment of the same change for the reference product Plavix further to the adoption by the CHMP of the following conclusions: Amendments should be 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). In addition, the deletion of DDPS number 1.3 and dated 24 April 2008 was introduced in Annex IIB as requested by the EMA with the procedural announcement in October and November 2010.
IB/0006	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	11/08/2010	n/a	SmPC, Labelling and PL	
IB/0004/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 starting material/reagent/intermediate for AS - Other variation	08/06/2010	n/a		
IA/0005	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	03/06/2010	n/a		
IB/0003	IB_18_Replacement of an excipient with a comparable excipient	25/01/2010	n/a	SmPC and PL	
II/0001	addition of alternative manufcture for an intermediate	17/12/2009	06/01/2010		

	and change in manufacturer process of intermediate Change(s) to the manufacturing process for the active substance				