Diacomit

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/2789/ 202211	Periodic Safety Update EU Single assessment - stiripentol	08/06/2023	n/a		PRAC Recommendation - maintenance
N/0044	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	25/04/2023		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).

IA/0042	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	02/11/2022	n/a		
PSUSA/2789/202111	Periodic Safety Update EU Single assessment - stiripentol	10/06/2022	n/a		PRAC Recommendation - maintenance
IB/0040/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 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	02/12/2021	n/a		
IB/0039/G	This was an application for a group of variations.	30/08/2021	n/a		

	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation 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				
PSUSA/2789/202011	Periodic Safety Update EU Single assessment - stiripentol	10/06/2021	n/a		PRAC Recommendation - maintenance
X/0032	Annex I_2.(c) Change or addition of a new strength/potency	25/03/2021	19/05/2021	SmPC, Labelling and PL	
IB/0036/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 B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement	28/09/2020	n/a		

	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				
IB/0035/G	This was an application for a group of variations. B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient	15/07/2020	n/a		

	- Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure 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)				
PSUSA/2789/201911	Periodic Safety Update EU Single assessment - stiripentol	11/06/2020	n/a		PRAC Recommendation - maintenance
IB/0030/G	This was an application for a group of variations. B.II.a.1.a - Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking - Changes in imprints, bossing or other markings B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-	16/03/2020	09/03/2021	SmPC, Annex II, Labelling and PL	

	sterile medicinal products B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.II.e.6.a - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that affects the product information				
IA/0034/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer	26/02/2020	n/a		

	B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer				
IA/0033/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability -	26/02/2020	n/a		

	Updated certificate from an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)				
IB/0027/G	This was an application for a group of variations. B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.i - Change in the specification parameters and/or limits of the finished product - Ph. Eur. 2.9.40 uniformity of dosage units is introduced to replace the currently registered method, either Ph. Eur. 2.9.5 or Ph. Eur. 2.9.6 B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	08/01/2020	n/a		
IB/0028/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	06/01/2020	n/a		

	variation				
IA/0029/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits 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.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	20/12/2019	n/a		
IB/0026/G	This was an application for a group of variations. B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.i - Change in the specification parameters and/or limits of the finished product - Ph. Eur. 2.9.40 uniformity of dosage units is introduced to replace the currently registered method, either Ph. Eur. 2.9.5 or Ph. Eur. 2.9.6 B.II.d.1.d - Change in the specification parameters	22/11/2019	n/a		

	and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter 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.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
IB/0024/G	This was an application for a group of variations. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	09/09/2019	n/a		
PSUSA/2789/ 201811	Periodic Safety Update EU Single assessment - stiripentol	16/05/2019	n/a		PRAC Recommendation - maintenance
IA/0023	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	03/04/2019	n/a		

	manufacturer of a novel excipient				
R/0021	Renewal of the marketing authorisation.	26/07/2018	20/09/2018	SmPC, Annex II, Labelling and PL	
PSUSA/2789/201711	Periodic Safety Update EU Single assessment - stiripentol	17/05/2018	n/a		PRAC Recommendation - maintenance
PSUSA/2789/201611	Periodic Safety Update EU Single assessment - stiripentol	09/06/2017	n/a		PRAC Recommendation - maintenance
PSUSA/2789/201511	Periodic Safety Update EU Single assessment - stiripentol	09/06/2016	n/a		PRAC Recommendation - maintenance
PSUSA/2789/201411	Periodic Safety Update EU Single assessment - stiripentol	11/06/2015	n/a		PRAC Recommendation - maintenance
II/0016	Update of section 4.2 of the SmPC in order to adjust the dosage by age and to reduce dosing increments for higher doses. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/05/2014	23/06/2014	SmPC, Annex II and PL	In this variation the company updated dosage and dose adjustment to take into account the patient's age and reflect the need for the dose increase to happen gradually.
PSUV/0015	Periodic Safety Update	13/06/2014	n/a		PRAC Recommendation - maintenance
R/0014	Renewal of the marketing authorisation.	24/10/2013	08/01/2014	SmPC, Annex II and PL	The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and

					sufficiently demonstrated. Furthermore, the CHMP considered that, as all Specific Obligations have been fulfilled, there are no remaining grounds for the Marketing Authorisations to remain conditional and therefore recommends the granting of the MA no longer subject to Specific Obligations for Diacomit. The Product information has also been updated to reflect that long-term data has not been collected in a sufficient number of adults to confirm maintenance of effect in this population, although treatment should be continued for as long as efficacy is observed.
R/0012	Renewal of the marketing authorisation.	20/09/2012	22/11/2012		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Diacomit, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
IB/0013	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	17/08/2012	22/11/2012	SmPC and PL	Following up on the outcome of the fifth Diacomit Annual Renewal in 2011 the Rapporteur's final assessment report, dated 18th April 2012, concluded on the review of the data submitted for the cumulative review that the term thrombocytopaenia is added to section 4.8 of the Diacomit SmPC. The MAH is requested to confirm that the 'especially when combined with sodium valproate, usually resolves spontaneously when sodium valproate is reduced or stopped.' will be removed at the time of variation submission. Further it is requested that the MAH specify

					that thrombocytopenia data are derived from both clinical trials and post-marketing experience." The package leaflet has been updated accordingly in Section 4 and also to update the local representatives in three countries.
R/0011	Renewal of the marketing authorisation.	17/11/2011	13/01/2012		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Diacomit, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
IB/0010/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.2.z - Changes in the manufacturing process of the 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 B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting	24/02/2011	n/a		

	material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation				
R/0008	Renewal of the marketing authorisation.	23/09/2010	13/12/2010	Annex II	
II/0009	Addition of relevant pharmacokinetic data in section 5.2 of the SmPC as requested by the CHMP further to the assessment of a pharmacokinetic study in children with Dravet's syndrome (FUM 001). C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/09/2010	05/11/2010	SmPC, Annex II and PL	
II/0007	Update of section 4.8 of the SPC to include abnormal liver function tests, as requested by the CHMP further to the assessment of the 3rd Annual Renewal. Update of Summary of Product Characteristics	21/01/2010	11/03/2010	SmPC and Annex II	The SPC has been updated to reflect that raised levels of liver enzymes can be observed rarely.
R/0006	Renewal of the marketing authorisation.	24/09/2009	26/11/2009	Annex II	The CHMP reviewed the available information on the status of the Specific Obligations for Diacomit. The CHMP confirmed that the quality, safety and efficacy of this medicinal product continue to be adequately demonstrated, and that the benefit/risk balance remains positive. The CHMP recommended that the Marketing Authorisation

					remains 'conditional' until the outstanding Specific Obligation is fulfilled, with the Marketing Authorisation renewed annually. PSURs should be submitted yearly.
IA/0005	IA_32_a_Change in batch size of the finished product - up to 10-fold	03/04/2009	n/a		
II/0004	Update of sections 4.2 and 5.2 of the Summary of Product Characteristics and section 3 of the Package Leaflet (PL) to reflect the non-bioequivalence between the 500 mg capsule and sachet formulation. In addition, details of the local representatives in Denmark, Finland, Norway and Sweden have been added in the PL. Update of Summary of Product Characteristics and Package Leaflet	18/12/2008	28/01/2009	SmPC and PL	Following the assessment of the Specific Obligation 004 (a bioavailability study in 24 subjects to determine the relative bioavailability of the stiripentol sachet versus stiripentol capsule by 2007) the CHMP requested the MAH to submit this type II variation to update sections 4.2 and 5.2 of the SPC and relevant section of PL to reflect the non-bioequivalence between the 500 mg capsule and sachet formulation. The CHMP accepted the submitted bioequivalence study as adequately investigating the bioavailability of the two formulations and although the two formulations are not bioequivalent, the committee concluded that this was adequately addressed with suitable warnings in the SPC and PL.
R/0003	Renewal of the marketing authorisation.	25/09/2008	20/11/2008	Annex II	The CHMP reviewed the available information on the status of the Specific Obligations for Diacomit. The Committee confirmed that the quality, safety and efficacy of this medicinal product continue to be adequately demonstrated, and that its benefit risk balance remains positive. The Committee recommended that the Marketing Authorisation remained 'conditional' until the outstanding specific obligations are fulfilled. The list of Specific obligations has been revised according to the conclusions of the CHMP discussion, to delete

					reference to the following Specific Obligation, "A bioavailability study in 24 subjects to determine the relative bioavailability of the stiripentol sachet versus stiripentol capsule by 2007 (STP 166)", which was considered fulfilled by the CHMP. In addition, both the study title and the deadline for submission of data relevant to the other outstanding SO have been amended.
R/0002	Renewal of the marketing authorisation.	18/10/2007	14/12/2007	SmPC, Annex II, Labelling and PL	The CHMP reviewed the available information on the status of the fulfilment of the Specific Obligations by the MAH. The Committee confirmed that the quality, safety and efficacy of this medicinal product continues to be adequately and sufficiently demonstrated, and that its benefit risk balance remains positive. The Committee recommended that the Marketing Authorisation remains 'conditional' until the remaining specific obligations are fulfilled.
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/06/2007	n/a	PL	