Brinavess

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
T/0044	Transfer of Marketing Authorisation	29/11/2024	19/12/2024	SmPC, Labelling and PL	
IAIN/0043	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	18/10/2023	01/10/2024	Annex II 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).

IB/0042	B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test	14/09/2023	n/a		
PSUSA/3109/ 202208	Periodic Safety Update EU Single assessment - vernakalant hydrochloride	14/04/2023	n/a		PRAC Recommendation - maintenance
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/03/2022	01/10/2024	PL	
IA/0039	A.7 - Administrative change - Deletion of manufacturing sites	07/07/2020	n/a		
R/0037	Renewal of the marketing authorisation.	26/03/2020	02/06/2020		Based on the review of data on quality, safety and efficacy, including all variations introduced since the marketing authorisation was granted, the benefit-risk balance of Brinavess in its approved indication(s) (please refer to the Summary of Product Characteristics) remains favourable and therefore the renewal of the marketing authorisation is recommended, subject to the conditions as detailed in Annex II. The renewal is recommended to be granted with unlimited validity.
PSUSA/3109/ 201908	Periodic Safety Update EU Single assessment - vernakalant hydrochloride	17/04/2020	n/a		PRAC Recommendation - maintenance
II/0035	Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information following updates to the Company Core Safety Datasheet (CCDS) based on the results of an integrated safety analysis performed on data of existing clinical studies. The	31/10/2019	02/06/2020	SmPC, Annex II, Labelling and PL	Sections 4.4 and 4.8 of the Summary of Product characteristics (SmPC) is being updated following updates to the Company Core Safety Datasheet (CCDS) based on the results of an integrated safety analysis performed on data of existing clinical studies with a stronger emphasis on

	Package Leaflet was updated accordingly. Update of the RMP to version 7.0 to incorporate the results from the new safety analysis and from the non-interventional PASS SPECTRUM study, listed as a category 3 study in the RMP (PASS Protocol 6621-049). Update of sections 4.2, 4.4, 4.6, 4.7, 4.8, 5.1, 5.2, 5.3, 6.4 of the SmPC, Annex II, Labelling and Package Leaflet to include editorial changes, to correct typographical errors and to bring the PI in line with the latest QRD template version 10 and well as to update statements related to the excipients in the SmPC and Package Leaflet in line with the EC Guideline (SANTE-2017-11668). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				treatment-related ADRs and an incidence rate above one percent. The warnings regarding hypotension, congestive heart failure, atrial flutter and valvular heart disease were modified in section 4.4 of the SmPC and adverse events "headache", "chest discomfort" and "ECQ QT prolonged" were removed from section 4.8 of the SmPC. These changes were considered consistent with the pooled trial data in the updated summary of clinical safety. The PL has been updated accordingly.
II/0034	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	19/09/2019	02/06/2020	SmPC, Annex II and PL	
IB/0036/G	This was an application for a group of variations. B.I.c.z - Container closure system of the AS - Other variation B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of	10/09/2019	n/a		

	a Member State - Excipient/AS starting material				
N/0033	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/12/2018	02/06/2020	Labelling	
IA/0032	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	10/12/2018	n/a		
T/0031	Transfer of Marketing Authorisation	13/07/2018	08/08/2018	SmPC, Labelling and PL	
IA/0030	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)	18/05/2018	n/a		
PSUSA/3109/ 201708	Periodic Safety Update EU Single assessment - vernakalant hydrochloride	12/04/2018	n/a		PRAC Recommendation - maintenance
IB/0029/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.e - Stability of FP - Change to an approved stability protocol	09/01/2018	08/08/2018	SmPC	
N/0027	Minor change in labelling or package leaflet not	07/06/2017	08/08/2018	Labelling	

	connected with the SPC (Art. 61.3 Notification)				
PSUSA/3109/201608	Periodic Safety Update EU Single assessment - vernakalant hydrochloride	09/03/2017	n/a		PRAC Recommendation - maintenance
N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/09/2016	08/08/2018	PL	
PSUSA/3109/201508	Periodic Safety Update EU Single assessment - vernakalant hydrochloride	17/03/2016	n/a		PRAC Recommendation - maintenance
R/0023	Renewal of the marketing authorisation.	21/05/2015	28/07/2015	SmPC	Based on the review of the available information the CHMP is of the opinion that the quality, the safety and the efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considers that the benefit/risk profile of Brinavess continues to be favourable. The CHMP was of the opinion that an additional five-year renewal on the basis of pharmacovigilance grounds was required.
PSUSA/3109/201408	Periodic Safety Update EU Single assessment - vernakalant hydrochloride	26/03/2015	27/05/2015	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/3109/201408.
IB/0021	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	01/12/2014	n/a		
IAIN/0020	A.1 - Administrative change - Change in the name and/or address of the MAH	03/10/2014	28/11/2014	SmPC, Labelling and PL	

PSUV/0019	Periodic Safety Update	10/04/2014	n/a		PRAC Recommendation - maintenance
IB/0018	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)	15/11/2013	28/11/2014	SmPC	
IAIN/0017/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.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	13/11/2013	28/11/2014	Annex II and PL	
IAIN/0016	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	27/08/2013	n/a		
T/0013	Transfer of Marketing Authorisation	24/05/2013	21/06/2013	SmPC, Labelling and PL	
II/0012	Update of section 4.8 of the SmPC following the results of the ACT V study. The Package Leaflet was updated accordingly. In addition the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore the PI is being brought in line with the QRD template version 8.3.	25/04/2013	21/06/2013	SmPC, Annex II, Labelling and PL	Section 4.8 of the SmPC was updated in order to provide additional information regarding the nature and frequency of adverse events (AEs) related to treatment with vernakalant IV based on the safety results from the ACT V clinical trial.

	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				
IA/0011/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	26/10/2012	n/a		
II/0009	The MAH proposed the update of Section 4.2 of the SmPC, Annex II, IIIA and IIIB in order to include the information about the pre-infusion checklist as a new risk minimisation tool as a follow up to the CHMP's assessment of a case of fatal hypotension. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH	19/07/2012	23/08/2012	Annex II and Labelling	A case of fatal hypotension related to the use of vernakalant hydrochloride (VH) was provided regarding a patient with type 2 diabetes mellitus, hypertension, polymyalgia and a history of coronary artery disease. The available information was considered by the CHMP as insufficient to determine whether the patient was eligible for treatment. Therefore, the causality assessment remains inconclusive. Nevertheless the risk minimization tools will be enhanced and the Pre-Infusion check list will be included as part of the package at the time of administration.
IG/0182	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/08/2012	n/a		
IA/0008	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	24/05/2012	n/a		

II/0007	Update of sections 4.2 and 4.4 of the SmPC in order to update the safety information related to the administration of vernakalant hydrochloride following the recommendations from the assessment of PSUR 005. As a consequence, the description of the educational material was updated. The Package Leaflet was updated in accordance. In addition, the MAH took the opportunity to propose small editorial changes in Sections 4.3, 4.4, 4.8 of the SmPC and in the Package Leaflet. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH	16/02/2012	26/03/2012	SmPC and PL	Following the assessment of the last PSUR and in view of the case reports of hypotension and bradycardia that have been assessed it was proposed to update sections 4.2 and 4.4 of the SmPC to provide further guidance to the healthcare providers regarding the way patients should be monitored during and after administration of Brinavess. With current variation the information was introduced that patient should be frequently monitored for the duration of the infusion of Brinavess and for at least 15 minutes after the completion of the infusion for signs and symptoms of a sudden decrease in blood pressure or heart rate.
IA/0006/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.7 - Administrative change - Deletion of manufacturing sites	20/12/2011	n/a		
N/0005	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/12/2011	26/03/2012	PL	

IG/0112	C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	11/10/2011	n/a		
II/0002	C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH	17/02/2011	14/04/2011	SmPC, Annex II and PL	Since vernakalant was licensed in September 2010, a serious adverse event of severe hypotension and subsequent cardiogenic shock has been reported in a patient receiving i.v. vernakalant in an ongoing clinical study (ACT V). Shortly after the infusion was completed, the patient developed hypotension with cardiac arrest and pulseless electrical activity. A complicated and prolonged resuscitation involving electrical defibrillation and the use of DC cardioversion and amiodarone followed. The patient developed multi-organ failure and passed away 28 days after the initial event. Following the assessment of the information related to this serious case the CHMP recommended modification of the SmPC. Close monitoring of vital signs and continuous monitoring of cardiac rhythm during administration of vernakalant, and up to 2 hours after the start of infusion until clinical and ECG parameters have stabilised, is recommended. Blood pressure should also be monitored, both during vernakalant infusion and at least 15 minutes after the infusion is completed. Patients must not be given any i.v. anti-arrhythmic drugs (class I or class III) within 4 hours prior to, during or up to 4 hours after vernakalant administration. PL and the educational materials were updated to reflect the changes to the SmPC.
IG/0027/G	This was an application for a group of variations. C.I.9.g - Changes to an existing pharmacovigilance	10/11/2010	n/a	Annex II	

	system as described in the DDPS - Change of the site undertaking pharmacovigilance activities C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
N/0001	The Marketing Authorisation Holder took the opportunity to update Annex III A following a mock-up review and also update details for a local representative in Annex IIIB. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/09/2010	n/a	Labelling and PL	