



## Deltyba

### Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification <sup>1</sup> issued on	Commission Decision Issued <sup>2</sup> / amended on	Product Information affected <sup>3</sup>	Summary
IB/0060	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)	07/09/2022		SmPC	
II/0053	Update of section 4.8 of the SmPC in order to update the list of adverse drug reactions (ADRs table)	01/09/2022		SmPC and PL	The MAH has proposed an update of section 4.8 of the SmPC, based on a statistical and medical judgement of

<sup>1</sup> 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.

<sup>2</sup> 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.

<sup>3</sup> SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).



	<p>following the development of an improved methodology to identify relevant ADRs likely attributable to delamanid. The section 4 of the Package Leaflet is updated accordingly. The RMP version 4.1 has also been submitted.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>				<p>ADRs seen in the two clinical trials 204 (phase 2) and 213 (phase 3) as well from all post-marketing sources. Some ADRs were removed due to insufficient supporting evidence to retain them, in addition there was an update of some of the ADR frequencies, grouping of terms and addition of hypothyroidism with a frequency "common". For more information, please refer to the Summary of Product Characteristics.</p>
IB/0058	B.II.z - Quality change - Finished product - Other variation	18/07/2022	n/a		
IA/0057/G	<p>This was an application for a group of variations.</p> <p>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</p> <p>B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process</p>	07/06/2022	n/a		
R/0052	Renewal of the marketing authorisation.	27/01/2022	22/03/2022	SmPC, Annex II and PL	<p>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 Delyba, subject to the Specific Obligations and Conditions as laid down in Annex II</p>

					to the opinion.
PSUSA/10213 /202104	Periodic Safety Update EU Single assessment - delamanid	16/12/2021	16/02/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s) for PSUSA/10213/202104.
IAIN/0056	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	01/02/2022	n/a		
IA/0055	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	04/01/2022	n/a		
IB/0054/G	This was an application for a group of variations.  B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing 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)	12/11/2021	16/02/2022	SmPC, Annex II and PL	
X/0046/G	This was an application for a group of variations.  Annex I_2.(d) Change or addition of a new pharmaceutical form C.I.6.a - Change(s) to therapeutic indication(s) -	22/07/2021	16/09/2021	SmPC, Annex II, Labelling and PL	

	Addition of a new therapeutic indication or modification of an approved one				
PSUSA/10213 /202010	Periodic Safety Update EU Single assessment - delamanid	10/06/2021	n/a		PRAC Recommendation - maintenance
II/0048	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	29/04/2021	16/09/2021	SmPC and Annex II	
R/0047	Renewal of the marketing authorisation.	25/02/2021	13/04/2021	Annex II	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 Delytba, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion. The due date of SOB 002 in Annex II of the PI has been changed to Q1 2023.
II/0045	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	09/04/2021	16/09/2021	Annex II	
IA/0050	A.7 - Administrative change - Deletion of manufacturing sites	01/03/2021	16/09/2021	Annex II and PL	

II/0040	<p>Extension of indication to include adolescents and children with a body weight of at least 30 kg. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.2 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.1 and the Marketing Authorisation Holder (MAH) took the opportunity to make minor editorial changes.</p> <p>C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one</p>	17/09/2020	27/10/2020	SmPC, Annex II, Labelling and PL	Please refer to Scientific Discussion 'Deltyba-H-C-002552-II-0040'
IAIN/0044	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	25/06/2020	n/a		
PSUSA/10213 /201910	Periodic Safety Update EU Single assessment - delamanid	14/05/2020	n/a		PRAC Recommendation - maintenance
R/0041	Renewal of the marketing authorisation.	27/02/2020	23/04/2020	Annex II	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 Deltyba, subject to the Specific Obligations and Conditions as laid down in Annex II

					to the opinion. No changes to the Product Information (PI) are introduced with this renewal procedure.
IA/0042	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)	03/12/2019	n/a		
II/0037	C.I.13 MIC report as amendment to CSR 242-09-213.  C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	24/10/2019	n/a		
IB/0038	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	05/08/2019	n/a		
PSUSA/10213/201810	Periodic Safety Update EU Single assessment - delamanid	29/05/2019	25/07/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10213/201810.
IA/0039/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 A.7 - Administrative change - Deletion of manufacturing sites	12/06/2019	n/a		

R/0033	Renewal of the marketing authorisation.	31/01/2019	02/04/2019	SmPC, Annex II and PL	<p>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 Delyba, subject to the modified Specific Obligations and Conditions as laid down in Annex II to the opinion.</p> <p>Minor amendments to the product information are introduced, pertaining the correct denotation for tenofovir disoproxil", (245 mg daily) (SmPC section 4.5) and adding of antimalarials with QT-prolonging potential, to be listed in "special considerations – cardiac risk factors" (SmPC section 4.4. and PL).</p>
IAIN/0035/G	<p>This was an application for a group of variations.</p> <p>B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site</p> <p>B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site</p> <p>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</p> <p>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</p>	13/02/2019	n/a		

	control/testing takes place				
PSUSA/10213 /201804	Periodic Safety Update EU Single assessment - delamanid	29/11/2018	n/a		PRAC Recommendation - maintenance
II/0030	<p>Update of the RMP (finally approved version 2.11), as requested by PRAC following the assessment of the Annual renewal to revise the risk re-categorisation justifications and lay language wording, as well as to add clarifications to the described additional pharmacovigilance activities to assess the effectiveness of risk minimisation measures and the set up date of an EU network of laboratories.</p> <p>C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required</p>	06/09/2018	n/a		
IAIN/0031	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	11/06/2018	02/04/2019	Annex II and PL	
PSUSA/10213 /201710	Periodic Safety Update EU Single assessment - delamanid	17/05/2018	n/a		PRAC Recommendation - maintenance



II/0021	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/05/2018	02/04/2019	SmPC, Annex II and PL	
R/0027	Renewal of the marketing authorisation.	22/02/2018	19/04/2018	Annex II	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 Delyba, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
N/0029	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/04/2018	02/04/2019	PL	
PSUSA/10213 /201704	Periodic Safety Update EU Single assessment - delamanid	30/11/2017	n/a		PRAC Recommendation - maintenance
IB/0026	B.II.f.1.e - Stability of FP - Change to an approved stability protocol	09/10/2017	n/a		
IA/0025/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 or pharmaceutical form  B.II.e.5.b - Change in pack size of the finished product - Deletion of a pack size(s)	26/09/2017	19/04/2018	SmPC, Labelling and PL	

II/0020/G	<p>This was an application for a group of variations.</p> <p>B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product</p> <p>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)</p> <p>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)</p> <p>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</p>	14/09/2017	n/a		
IB/0023	B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter	26/07/2017	n/a		
IB/0022	B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure	26/07/2017	n/a		

PSUSA/10213 /201610	Periodic Safety Update EU Single assessment - delamanid	05/05/2017	n/a		PRAC Recommendation - maintenance
N/0019	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/05/2017	19/04/2018	PL	
R/0017	Renewal of the marketing authorisation.	26/01/2017	03/03/2017	Annex II	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 Delyba, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
PSUSA/10213 /201604	Periodic Safety Update EU Single assessment - delamanid	01/12/2016	n/a		PRAC Recommendation - maintenance
II/0014	Update of section 5.1 of the SmPC further to the submission of final clinical study report for trial 242-12-244 "Determination of Delamanid MIC Values and Sub-species Analysis of Mycobacterium tuberculosis Complex Isolates". Moreover the MAH has taken the occasion to implement version 10.0 of the QRD template. The date of the latest renewal has been included as well.  C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	06/10/2016	03/03/2017	SmPC and Labelling	The statement that a clinical breakpoint for delamanid has not been determined has been removed from the SmPC.

IAIN/0016	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	05/10/2016	n/a		
IB/0013/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.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	07/06/2016	n/a		
PSUSA/10213 /201510	Periodic Safety Update EU Single assessment - delamanid	13/05/2016	n/a		PRAC Recommendation - maintenance
R/0010	Renewal of the marketing authorisation.	28/01/2016	11/03/2016		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 Delyba, subject to the Specific Obligations and Conditions as laid down in Annex II of the Marketing Authorisation.
N/0012	Inclusion of the list of the local representatives at the end of the package leaflet.  Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/03/2016	03/03/2017	PL	

PSUSA/10213 /201504	Periodic Safety Update EU Single assessment - delamanid	06/11/2015	n/a		PRAC Recommendation - maintenance
IA/0009	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)	16/09/2015	n/a		
IB/0007/G	<p>This was an application for a group of variations.</p> <p>1) B.I.d.1 a.4 (Type IB) – to increase the retest period of the active substance from 48 months to 60 months when stored below 30°C.</p> <p>2) B.II.f.1 b.1 (Type IB) – to increase the shelf-life of the finished product packaged in glass bottles and aluminum/aluminum foil blisters from 4 years to 5 years (section 6.3 of the SmPC is updated).</p> <p>In addition the MAH took the opportunity to add the date of the latest renewal in the SmPC, to correct a typographical error in the SmPC (for all languages), and to correct a typographical error in the Latvian version of the package leaflet. Moreover, a typographical error has been corrected in Modules 2.3.P.2, 2.3.P.3, 3.2.P.2.3, 3.2.P.3.3, 3.2.P.3.4.</p> <p>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</p> <p>B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale</p>	03/06/2015	11/03/2016	SmPC and PL	

	(supported by real time data)				
II/0006	<p>Submission of final study report for Trial 242-13-246 "A Phase 1 Trial to Assess the Mass Balance and Pharmacokinetics of 14C-OPC-67683 Following Oral Administration in Healthy Subjects"</p> <p>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority</p>	21/05/2015	n/a		
PSUSA/10213 /201410	Periodic Safety Update EU Single assessment - delamanid	07/05/2015	n/a		PRAC Recommendation - maintenance
R/0004	Renewal of the marketing authorisation.	26/02/2015	24/04/2015		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 Delyba, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
IB/0002/G	<p>This was an application for a group of variations.</p> <p>B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes</p> <p>B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale</p>	06/08/2014	24/04/2015	SmPC, Labelling and PL	

	(supported by real time data) B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation				
IAIN/0003	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	17/07/2014	n/a		
IAIN/0001/G	<p>This was an application for a group of variations.</p> <p>A.5.a - To change the name of the site responsible for primary packaging, secondary packaging, import and batch release of the finished product. The address remains unchanged.</p> <p>B.II.b.2.c.1 - To add an alternative site responsible for importation and batch release of the finished product.</p> <p>In addition, the applicant took the opportunity to amend product information and labelling with editorial changes.</p> <p>A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release</p> <p>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</p>	12/06/2014	24/04/2015	Annex II and PL	

	responsible for importation and/or batch release - Not including batch control/testing				
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