Epidyolex

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
IAIN/0032	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	26/09/2024		SmPC and PL	
R/0031	Renewal of the marketing authorisation.	30/05/2024	26/07/2024	SmPC, 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).

II/0028/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/03/2024	n/a		
PSUSA/10798 /202306	Periodic Safety Update EU Single assessment - cannabidiol (for centrally authorised products only)	11/01/2024	n/a		PRAC Recommendation - maintenance
IA/0030/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 B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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	11/12/2023	n/a		
II/0029	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	23/11/2023	n/a		

II/0025/G	This was an application for a group of variations. B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.d.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product A.7 - Administrative change - Deletion of manufacturing sites	01/06/2023	n/a		
T/0026	Transfer of Marketing Authorisation	15/05/2023	31/05/2023	SmPC, Labelling and PL	
II/0020	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	26/04/2023	05/04/2024	SmPC and PL	
IB/0024/G	This was an application for a group of variations. 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 B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place	21/02/2023	n/a		

	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.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition B.I.b.z - Change in control of the AS - Other variation B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold				
IB/0023	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	02/02/2023	31/05/2023	SmPC, Labelling and PL	Product information updated to add a new pack-size of 3 x 100 ml bottles for Epidyolex 100 mg/ml oral solution (EU/1/19/1389/002).
PSUSA/10798 /202206	Periodic Safety Update EU Single assessment - cannabidiol (for centrally authorised products only)	12/01/2023	n/a		PRAC Recommendation - maintenance
N/0021	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/09/2022	31/05/2023	PL	
IB/0019	B.z - Quality Change - Other variation	19/04/2022	n/a		
IB/0018/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters	21/02/2022	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method 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 B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits 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 originally approved batch size B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				

II/0016	Update of section 5.3 of the SmPC to reflect the conclusions of the study GWTX1504, 104 week oral (gavage) administration carcinogenicity study in mouse. For more information, please refer to the Summary of Product Characteristics. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/01/2022	29/06/2022	SmPC	Update of section 5.3 of the SmPC to reflect the conclusions of the study GWTX1504, 104 week oral (gavage) administration carcinogenicity study in mouse.
II/0015	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	27/01/2022	29/06/2022	SmPC	Update of sections 4.5 and 5.2 of the SmPC to add drug-drug interaction information with everolimus and P-gp substrates following the assessment the study GWCP19195, a phase I open-label pharmacokinetic drug-drug interaction trial to investigate the effect of cannabidiol on the pharmacokinetics of everolimus in healthy subject. In addition, the MAH took the opportunity to introduce editorial updates in section 5.1 and section 4.9 and to update the local representative contact details of France in the Package Leaflet.
PSUSA/10798 /202106	Periodic Safety Update EU Single assessment - cannabidiol (for centrally authorised products only)	13/01/2022	n/a		PRAC Recommendation - maintenance
II/0014/G	This was an application for a group of variations. B.II.d.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product	14/10/2021	n/a		

	B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter				
PSUSA/10798 /202012	Periodic Safety Update EU Single assessment - cannabidiol (for centrally authorised products only)	08/07/2021	n/a		PRAC Recommendation - maintenance
II/0007	Update of sections 4.2 and 6.6 of the SmPC in order to add information regarding enteral administration using nasogastric and gastrostomy tubes. The Package Leaflet is updated accordingly. In addition, the marketing authorisation holder has taken the opportunity to update the list of local representatives in the PL and implement minor editorial changes. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	24/06/2021	29/06/2022	SmPC and PL	
II/0005	Extension of Indication for use as adjunctive therapy of seizures associated with tuberous sclerosis complex (TSC) for patients 2 years of age and older. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. The updated RMP version 2.0 is agreed. The MAH also took the opportunity to correct typographic errors and implement editorial updates as well as implement the updated ethanol statement in compliance with the EC Guideline on Excipient. In addition, the list of local representatives in the PL has been revised to amend contact details for the	25/02/2021	16/04/2021	SmPC and PL	Please refer to Scientific Discussion 'Product Name-H-C-Product Number-II-0005'

	representative(s) of Sweden. The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IA/0012/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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)	17/02/2021	16/04/2021	Annex II and PL	
IB/0011/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	05/02/2021	n/a		

IB/0010	B.II.f.1.b.2 - Stability of FP - Extension of the shelf life of the finished product - After first opening (supported by real time data)	01/02/2021	16/04/2021	SmPC, Labelling and PL	
PSUSA/10798 /202006	Periodic Safety Update EU Single assessment - cannabidiol (for centrally authorised products only)	14/01/2021	n/a		PRAC Recommendation - maintenance
II/0008/G	This was an application for a group of variations. Update of section 4.5 of the SmPC to reflect the data of the rifampicin drug-drug interaction study GWEP17074. Update of section 4.5 of the SmPC to reflect the data of the CYP1A2 substrate (caffeine) drug-drug interaction study GWCP18056. Update of section 4.5 and 5.2 of the SmPC to propose an additional statement regarding the stiripentol interaction based on the pharmacological study GWEP1447 (provided in eCTD sequence 018, P46 006). Update of section 5.2 of the SmPC to reflect the data of the pharmacokinetic study GWEP17076, exploring the impact of meal, milk and alcohol on cannabidiol exposure. In addition, the MAH took the opportunity to correct the MAH address in the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	23/07/2020	09/12/2020	SmPC	Following the drug-drug interaction study GWEP17074 with rifampicin (CYP3A4 Inducer), section 4.5 of the SmPC has been updated to reflect the decrease plasma concentrations of cannabidiol and 7-hydroxy-cannabidiol by approximately 30 and 60% respectively and potential impact on effectiveness. Following the pharmacokinetic study GWEP17076, section 5.2 of the SmPC has been updated to reflect the effect of low-fat/low-calorie meal, bovine milk and alcohol on cannabidiol exposure. Following the drug-drug interaction study GWCP18056 with caffeine (CYP1A2 Substrate), section 4.5 of the SmPC has been updated to reflect the observed increased in caffeine exposure and recommend the monitoring of patients. Following the drug-drug interaction study GWEP1447 with stiripentol and valproate, the statement in section 4.5 of the SmPC has been adjusted to reflect the data. For more information, please refer to the Summary of Product Characteristics

	data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10798 /201912	Periodic Safety Update EU Single assessment - cannabidiol (for centrally authorised products only)	09/07/2020	n/a		PRAC Recommendation - maintenance
IA/0006	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	11/05/2020	n/a		
IB/0003/G	This was an application for a group of variations. B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site 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.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	25/03/2020	n/a		
IAIN/0002/G	This was an application for a group of variations. B.II.b.2.c.2 - Change to importer, batch release	16/12/2019	09/12/2020	SmPC, Annex II and PL	

	arrangements and quality control testing of the FP - Including batch control/testing 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				
IAIN/0001/G	This was an application for a group of variations. 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 B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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 originally approved batch size 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 originally approved batch size	27/11/2019	n/a		