Zepatier

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
N/0041	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	03/05/2024		Labelling and PL	
IA/0042	A.7 - Administrative change - Deletion of manufacturing sites	29/04/2024	n/a		

[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/0040	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	07/09/2023	n/a		
IB/0039	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	14/04/2023	n/a		
IAIN/0038	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	21/11/2022	24/10/2023	Annex II and PL	
IA/0037	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	27/09/2022	n/a		
PSUSA/10519 /202201	Periodic Safety Update EU Single assessment - elbasvir / grazoprevir	01/09/2022	n/a		PRAC Recommendation - maintenance
II/0033	Submission of the final report from study B20-146 listed as a category 3 study in the RMP. This is a non-imposed joint post-authorisation safety study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (HCC De Novo PASS). C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission	07/07/2022	n/a		

	of studies to the competent authority				
SW/0036	Post Authorisation Safety Study results - EMEA/H/C/PSR/J/0038 – Variation	24/03/2022	02/06/2022	SmPC, Annex II and PL	The observational study and the systematic review/ meta-analysis did not show an increased risk of hepatocellular carcinoma recurrence in patients treated with direct-acting antivirals. The DAA-PASS study commitment is considered fulfilled and the respective products should be removed from the list of medicines under additional monitoring.
II/0034	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	05/05/2022	n/a		
II/0029	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	16/09/2021	22/10/2021	SmPC and PL	
PSUSA/10519 /202101	Periodic Safety Update EU Single assessment - elbasvir / grazoprevir	02/09/2021	n/a		PRAC Recommendation - maintenance
IB/0032	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	20/08/2021	22/10/2021	Annex II	
R/0026	Renewal of the marketing authorisation.	25/02/2021	06/05/2021		
IA/0031	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	25/03/2021	n/a		

IA/0028	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)	11/02/2021	n/a		
IB/0027	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)	25/11/2020	29/01/2021	SmPC	
PSUSA/10519 /202001	Periodic Safety Update EU Single assessment - elbasvir / grazoprevir	03/09/2020	n/a		PRAC Recommendation - maintenance
IB/0025	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	28/05/2020	29/01/2021	SmPC, Annex II, Labelling and PL	
IB/0023	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	31/01/2020	29/01/2021	SmPC and PL	
IB/0022	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	09/10/2019	n/a		
PSUSA/10519 /201901	Periodic Safety Update EU Single assessment - elbasvir / grazoprevir	05/09/2019	n/a		PRAC Recommendation - maintenance
IAIN/0021	C.I.11.a - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of wording agreed by the competent authority	21/06/2019	13/01/2020	Annex II and PL	

IA/0019	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)	19/03/2019	n/a		
PSUSA/10519 /201807	Periodic Safety Update EU Single assessment - elbasvir / grazoprevir	14/02/2019	n/a		PRAC Recommendation - maintenance
IAIN/0018/G	This was an application for a group of variations. A.6 - Administrative change - Change in ATC Code/ATC Vet Code C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/01/2019	13/01/2020	SmPC and PL	
IB/0016	B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	11/09/2018	n/a		
PSUSA/10519 /201801	Periodic Safety Update EU Single assessment - elbasvir / grazoprevir	12/07/2018	n/a		PRAC Recommendation - maintenance
T/0015	Transfer of Marketing Authorisation	23/05/2018	15/06/2018	SmPC, Labelling and PL	
PSUSA/10519 /201707	Periodic Safety Update EU Single assessment - elbasvir / grazoprevir	08/02/2018	n/a		PRAC Recommendation - maintenance
IA/0012	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	13/10/2017	n/a		

PSUSA/10519 /201701	Periodic Safety Update EU Single assessment - elbasvir / grazoprevir	01/09/2017	n/a		PRAC Recommendation - maintenance
IB/0010	C.I.1.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a Union referral procedure - The product is not covered by the defined scope of the procedure but the change(s) implements the outcome of the procedure and no new additional data is required to be submitted by the MAH	05/07/2017	30/11/2017	SmPC, Annex II and PL	
IB/0011/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.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	21/06/2017	n/a		
II/0007	B.II.b.1.d - Replacement or addition of a manufacturing site for the FP - Site which requires an initial or product specific inspection	01/06/2017	n/a		
IA/0009	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	20/04/2017	n/a		

II/0005	Update of section 4.5 of the SmPC in order to update information regarding drug-drug interaction (DDI) of elbasvir/grazoprevir when co-administrated with sunitinib (tyrosine kinase inhibitor). The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to include some editorial changes. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	06/04/2017	30/11/2017	SmPC, Labelling and PL	Co-administration of ZEPATIER with sunitinib may increase sunitinib concentrations leading to an increased risk of sunitinib-associated adverse events. Use with caution; dose adjustment of sunitinib may be required.
II/0006	Update of section 5.2 of the SmPC in order to update the information on absolute bioavailability of elbasvir and grazoprevir following recent Company Core Data Sheet (CCDS) safety information update. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/03/2017	30/11/2017	SmPC	For elbasvir, the absolute bioavailability is estimated to be 32%. For grazoprevir, the absolute bioavailability after a 200 mg single dose ranged from 15 – 27% and after multiple 200 mg doses ranged from 20 – 40%.
IAIN/0004	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	16/12/2016	30/11/2017	SmPC and PL	
IB/0003	B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	16/11/2016	n/a		
IA/0001/G	This was an application for a group of variations. B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold	07/10/2016	n/a		

	compared to the originally approved batch size 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				
IB/0002	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	06/10/2016	n/a		