Vedrop

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/0052/G	This was an application for a group of variations. 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 -	10/12/2024		SmPC, Annex II, Labelling 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).

	Not including batch control/testing A.1 - Administrative change - Change in the name and/or address of the MAH				
PSUSA/2981/ 202307	Periodic Safety Update EU Single assessment - tocofersolan	07/03/2024	n/a		PRAC Recommendation - maintenance
II/0047	Submission of an updated RMP version 10.2 in order to remove all important potential risks and missing information from the list of safety concerns, to align with the new RMP format according to Good Pharmacovigilance Practices Module V Revision 2 and to remove one closed post-authorisation safety study of category 2 (Recordati Rare Diseases' Vedrop registry) from the pharmacovigilance plan. 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	07/03/2024	n/a		The Vedrop registry study (final study report was submitted to the European Medicines Agency (EMA) on 20 April 2017 in variation II/0022) collected safety data on a significant proportion of treated patients and did not point to serious adverse consequences of Vedrop treatment. From a risk management perspective, no specific pharmacovigilance activities are foreseen to further characterise the risks of Vedrop. Removal of the safety concerns related to Vedrop from the RMP is justified.
S/0049	14th annual re-assessment	22/02/2024	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation under exceptional circumstances of Vedrop should be maintained.
PSUSA/2981/ 202207	Periodic Safety Update EU Single assessment - tocofersolan	16/03/2023	n/a		PRAC Recommendation - maintenance

S/0044	13th annual re-assessment	23/02/2023	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that the marketing authorisation under exceptional circumstances of Vedrop should be maintained.
IA/0046/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.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition	13/01/2023	n/a		
PSUSA/2981/ 202107	Periodic Safety Update EU Single assessment - tocofersolan	10/03/2022	n/a		PRAC Recommendation - maintenance
S/0041	12nd annual re-assessment	24/02/2022	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Vedrop should be maintained.
IAIN/0043	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging -	20/12/2021	n/a		

	Device with CE marking				
PSUSA/2981/202007	Periodic Safety Update EU Single assessment - tocofersolan	11/03/2021	n/a		PRAC Recommendation - maintenance
S/0039	11th annual re-assessment	28/01/2021	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Vedrop should be maintained under exceptional circumstances.
S/0035	10th annual re-assessment.	27/02/2020	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation under exceptional circumstances of Vedrop should be maintained.
PSUSA/2981/201907	Periodic Safety Update EU Single assessment - tocofersolan	13/02/2020	n/a		PRAC Recommendation - maintenance
IA/0038/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 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.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.c.1.a - Change in immediate packaging of the AS	08/01/2020	n/a		

	- Qualitative and/or quantitative composition				
IA/0037	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	19/11/2019	n/a		
IG/1085/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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)	16/05/2019	12/05/2020	SmPC, Annex II, Labelling and PL	
N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/03/2019	12/05/2020	PL	
S/0031	9th annual re-assessment.	28/02/2019	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation under exceptional circumstances of Vedrop should be maintained.

PSUSA/2981/201807	Periodic Safety Update EU Single assessment - tocofersolan	14/02/2019	n/a		PRAC Recommendation - maintenance
N/0029	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/07/2018	12/05/2020	Labelling and PL	
IA/0028/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 compared to the originally approved batch size 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	04/06/2018	n/a		
S/0027	8th annual re-assessment.	22/02/2018	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that marketing authorisation of Vedrop should be maintained under exceptional circumstances.
PSUSA/2981/201707	Periodic Safety Update EU Single assessment - tocofersolan	08/02/2018	n/a		PRAC Recommendation - maintenance
IB/0025/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	19/10/2017	n/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.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 B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process 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 B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products				
IA/0024	B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products	04/10/2017	05/02/2018	SmPC and PL	
II/0022	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/07/2017	05/02/2018	Annex II	The final study report for Vedrop covered patient data from September 2007 to February 2017 and included data from 508 registry patients and 3.059 patient visits. The studied population represented a significant proportion of patients (18 % of all patients exposed to Vedrop worldwide) in which the efficacy and safety were monitored. These data confirm the benefit-risk balance of Vedrop in the approved

					indication. Consequently, the remaining specific obligation is considered fulfilled and the positive benefit/risk ratio for Vedrop in the approved indication remains unchanged. Due to the rarity of the disease, and despite the additional data gathered through the fulfilment of the specific obligations, the data are still not as comprehensive as a full marketing authorisation would require. The MAH shall therefore continue to provide yearly updates on any new information concerning efficacy and safety of the product in patients with congenital chronic cholestasis or hereditary cholestasis as a condition (specific obligation) to the marketing authorisation under exceptional circumstances.
IA/0023	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	28/06/2017	n/a		
S/0019	7th Annual Re-assessment.	23/03/2017	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligation and the impact of the data submitted by the MAH on the benefit/risk profile of the medicinal product, concluded that the benefit/risk profile of Vedrop remains positive and that the Marketing Authorisation under exceptional circumstances of Vedrop should be maintained.
IG/0773/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	14/02/2017	05/02/2018	Annex II and PL	

	responsible for importation and/or batch release - Not including batch control/testing				
PSUSA/2981/ 201607	Periodic Safety Update EU Single assessment - tocofersolan	09/02/2017	n/a		PRAC Recommendation - maintenance
IAIN/0018	B.II.d.1.h - Change in the specification parameters and/or limits of the finished product - Update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur. for the finished product	15/09/2016	n/a		
IG/0686	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	12/05/2016	n/a		
PSUSA/2981/ 201507	Periodic Safety Update EU Single assessment - tocofersolan	11/02/2016	n/a		PRAC Recommendation - maintenance
S/0015	6th Annual re-assessment	28/01/2016	n/a		The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of Vedrop, concluded that its Marketing Authorisation should be maintained. The Marketing Authorisation should remain under exceptional circumstances.
IG/0535	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	06/03/2015	n/a		
PSUSA/2981/	Periodic Safety Update EU Single assessment -	12/02/2015	n/a		PRAC Recommendation - maintenance

201407	tocofersolan				
S/0012	Annual re-assessment.	22/01/2015	n/a		
II/0011/G	This was an application for a group of variations. This was an application for a group of variations. To replace a manufacturer of active substance supported by an ASMF To replace the excipient sodium propyl parahydroxybenzoate with sodium ethyl parahydroxybenzoate and to increase the amount of excipient sodium methyl parahydroxybenzoate To widen the specification limits for sodium methyl parahydroxybenzoate in the specifications of the finished product To change the expression of specification limits for the monoester of TPGS in the specifications of the finished product To change the expression of specification limits for the diester of TPGS in the specifications of the finished product To change the expression of specification limits for the free PEG in the specifications of the finished product	20/11/2014	06/11/2015	SmPC, Labelling and PL	

	To add a new specification parameter assay of sodium ethyl parahydroxybenzoate to the specifications of the finished product To remove the specification parameter assay of sodium propyl parahydroxybenzoate from the specifications of the finished product To replace the test procedure for assay of potassium sorbate and the test procedure for assay of sodium methyl parahydroxybenzoate with the single test procedure for assay of sodium methyl parahydroxybenzoate, sodium ethyl parahydroxybenzoate and potassium sorbate B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF B.II.a.3.b.2 - Changes in the composition (excipients) of the finished product - Other excipients - Qualitative or quantitative changes in one or more excipients that may have a significant impact on the safety, quality or efficacy of the product B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation				

	B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method 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)				
R/0007	Renewal of the marketing authorisation.	20/02/2014	23/04/2014	SmPC, Labelling and PL	Based on the CHMP review of the available information and on the basis of a re-evaluation of the benefit risk balance, the CHMP is of the opinion that the quality, safety and efficacy of Vedrop continues to be adequately and sufficiently demonstrated and therefore considered that the benefit risk profile of Vedrop continues to be favourable. Following data from the ongoing registry and spontaneous reports in which no patient reported a renal insufficiency that could be related to Vedrop and data from the registry showing no impact on estimated glomerular filtration rate the precautionary statement "Renal function and serum osmolarity should be evaluated and monitored under treatment with Vedrop" was deleted from 4.4 of the SmPC. Furthermore following three cases of abdominal pain including one positive de-challenge reported abdominal pain was added with the frequency unknown in 4.8 of the SmPC.
S/0006	Fourth Annual Re-assessment	23/01/2014	21/03/2014	SmPC, Annex II, Labelling and PL	The CHMP, having reviewed the evidence of compliance with the specific obligations and the impact of the data submitted by the MAH on the benefit/risk profile of the

					medicinal product, concluded that Marketing Authorisation of Vedrop should be maintained.
PSUV/0008	Periodic Safety Update	06/03/2014	n/a		PRAC Recommendation - maintenance
IG/0393	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	20/12/2013	n/a		
IG/0392	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	19/12/2013	21/03/2014	Annex II and PL	
S/0004	Third Annual Re-assessment	21/02/2013	22/04/2013	Annex II	The CHMP, having reviewed the evidence of compliance with the specific obligations submitted by the MAH and having re-assessed the benefit/risk profile of the medicinal product, concluded that the benefit/risk balance for the product remains favourable.
N/0005	Update of the list of local representatives contact details. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/11/2012	22/04/2013	PL	
S/0002	Second annual re-assessment	21/06/2012	30/08/2012		The CHMP, having reviewed the evidence of compliance with the specific obligations submitted by the MAH and having re-assessed the benefit/risk profile of Vedrop, concluded that the benefit/risk balance for Vedrop in its approved indication remains favourable. The CHMP agreed

					that the Marketing Authorisation should remain under exceptional circumstances. For more clarity an editorial change to the indication wording has been implemented.
IG/0111	C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH	27/09/2011	n/a	Annex II	
S/0001	First Annual Re-assessment	18/11/2010	28/02/2011	Annex II	The CHMP, having reviewed the evidence of compliance with the specific obligations submitted by the MAH and having re-assessed the benefit/risk profile of Vedrop, concluded that the benefit/risk balance for Vedrop in its approved indication remains favourable. The CHMP agreed that the Marketing Authorisation should remain under exceptional circumstances.