Pravafenix

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
II/0037	Extension of indication to include treatment of mixed hyperlipidaemia in adult patients while on a treatment with pravastatin 40 mg monotherapy or on another moderate-intensity statin regimen for PRAVAFENIX, based on final results from the non-interventional PASS: POSE (Pravafenix Observational	19/09/2024	21/10/2024	SmPC and PL	Please refer to Scientific Discussion 'Pravafenix-H-C-001243-II-0037'

[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).

	Study in Europe); this is a European, observational, three-year cohort comparative study on the safety of the fixed dose combination pravastatin 40 mg/fenofibrate 160 mg (Pravafenix) versus statin alone in real clinical practice. As a consequence, sections 4.1 and 4.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.3 of the RMP has also been submitted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
PSUSA/1363/ 202304	Periodic Safety Update EU Single assessment - fenofibrate / pravastatin	14/12/2023	22/02/2024	SmPC and PL	Please refer to Scientific Conclusions for PSUSA/00001363/202304
IA/0038	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	14/12/2023	n/a		
N/0036	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/11/2023	22/02/2024	PL	
II/0034	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	31/08/2023	n/a		
IAIN/0033	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/04/2023	22/02/2024	SmPC and PL	

PSUSA/1363/ 202104	Periodic Safety Update EU Single assessment - fenofibrate / pravastatin	02/12/2021	n/a		PRAC Recommendation - maintenance
II/0030	Update of section 4.5 of the SmPC in order to add drug-drug interaction information with glitazones resulting in HDL cholesterol decrease, as already mentioned in the Product Information of other products containing fenofibrate 160 mg; update of section 2 and 4.4 of the SmPC to correct the warning on lactose and to implement the wording on sodium, in line with the latest revision of the Excipients guideline. The Package Leaflet and the Labelling are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.2. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/01/2021	10/03/2021	SmPC, Labelling and PL	
IA/0031/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	18/11/2020	n/a		

IA/0029/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	17/06/2020	n/a		
II/0028/G	This was an application for a group of variations. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH	19/03/2020	10/03/2021	SmPC, Annex II, Labelling and PL	
PSUSA/1363/201904	Periodic Safety Update EU Single assessment - fenofibrate / pravastatin	31/10/2019	n/a		PRAC Recommendation - maintenance

IA/0026	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	12/11/2018	n/a		
PSUSA/1363/ 201804	Periodic Safety Update EU Single assessment - fenofibrate / pravastatin	31/10/2018	n/a		PRAC Recommendation - maintenance
PSUSA/1363/ 201704	Periodic Safety Update EU Single assessment - fenofibrate / pravastatin	26/10/2017	n/a		PRAC Recommendation - maintenance
PSUSA/1363/ 201604	Periodic Safety Update EU Single assessment - fenofibrate / pravastatin	27/10/2016	n/a		PRAC Recommendation - maintenance
IA/0022	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	16/06/2016	n/a		
IA/0021	B.III.1.a.z - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - European Pharmacopoeial Certificate of Suitability to the relevant Ph. Eur. Monograph - Other variation	14/06/2016	n/a		
R/0020	Renewal of the marketing authorisation.	19/11/2015	14/01/2016	SmPC, Annex II, Labelling and PL	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 Pravafenix continues to be favourable. The CHMP is of the opinion that the renewal can be granted with unlimited validity.

PSUSA/1363/201504	Periodic Safety Update EU Single assessment - fenofibrate / pravastatin	06/11/2015	n/a		PRAC Recommendation - maintenance
IA/0019	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	17/07/2015	n/a		
PSUSA/1363/201410	Periodic Safety Update EU Single assessment - fenofibrate / pravastatin	07/05/2015	n/a		PRAC Recommendation - maintenance
IB/0015	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/04/2015	14/01/2016	SmPC, Annex II, Labelling and PL	
IA/0017	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	17/04/2015	n/a		
IA/0016	B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	17/04/2015	n/a		
PSUV/0012	Periodic Safety Update	06/11/2014	n/a		PRAC Recommendation - maintenance
IAIN/0013	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	28/10/2014	n/a		

PSUV/0009	Periodic Safety Update	08/05/2014	n/a		PRAC Recommendation - maintenance
N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/04/2014	14/01/2016	PL	
N/0010	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/01/2014	11/02/2014	PL	
II/0005	Update of sections 4.4 and 4.5 of the SmPC in line with the CHMP's request in the assessment of Periodic Safety update Report PSUR 01, in order to include safety data related to drug interaction between pravastatin and fusidic acid leading to an increased risk of rhabdomyolysis; and of section 4.8 of the SmPC to include the adverse reactions "skin rash" and "peripheral polyneuropathy". The Package Leaflet was updated accordingly. 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	21/02/2013	11/02/2014	SmPC and PL	Based on the review of the first periodic safety update report (PSUR), the CHMP recommended an update of section 4.4, 4.5 and 4.8 of the SmPC in order to include safety data related to drug interaction between pravastatin and fusidic acid leading to an increased risk of rhabdomyolysis, and inclusion of the adverse reaction "skin rash" and "peripheral polyneuropathy". The Package Leaflet was updated accordingly.
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/01/2013	11/02/2014	PL	
IB/0008	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)	21/12/2012	11/02/2014	SmPC	

II/0003	This type II variation concerns the update of section 4.4 and 4.8 of the SmPC to include a specific wording regarding the risk of new onset of diabetes. The amendment follows the publication of a meta-analysis which reported that therapy with HMG-CoA reductase inhibitors (statins) overall was associated with a slightly increased risk for the development of new onset diabetes and its assessment by the Pharmacovigilance Working Party (CMDh/PhVWP/042/2012, January 2012, Rev1 March 2012). The Package Leaflet is updated accordingly. The requested variation proposed amendments to the SmPC and 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	19/07/2012	30/08/2012	SmPC and PL	Based on the publication of a meta-analysis that HMGCoA reductase inhibitors (statins) may increase the risk of new onset diabetes (NOD) in patients already at risk of developing the disease was raised recently. The Pharmacovigilance Working Party (PhVWP) conducted a review of this risk based on all available data and concluded that, despite a clear positive risk-benefit balance as to the reduction of major cardiovascular events, HMG-CoA reductase inhibitors may increase the risk of NOD. However this risk appears to be predominantly in patients already at increased risk of developing diabetes, i.e. patients with raised fasting blood glucose at baseline, a history of hypertension, raised triglycerides and raised body mass index at baseline. An association of statin therapy with diabetes mellitus has been agreed and included as a class effect in all statins. Since Pravafenix contains pravastatin, the wording agreed by the PhVWP (Doc.Ref.: CMDh/PhVWP/042/2012, January 2012, Rev1 March 2012) and relevant for pravastatin is implemented for in the Product information of Pravafenix.
IA/0006	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 currently approved batch size	17/08/2012	n/a		
IB/0004	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	20/07/2012	29/10/2012	SmPC, Labelling and PL	

IA/0002	B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	16/02/2012	n/a		