Vyndaqel

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/0092/G	This was an application for a group of variations. 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)	23/04/2024		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).

	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing				
S/0090	11th annual re-assessment	14/12/2023	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 marketing authorisation of Vyndaqel should be maintained.
PSUSA/2842/ 202305	Periodic Safety Update EU Single assessment - tafamidis	30/11/2023	n/a		PRAC Recommendation - maintenance
II/0087	Update of section 4.8 of the SmPC in order to remove the adverse reaction 'vaginal infection' based on a search of cumulative post-marketing cases. The Package Leaflet is updated accordingly. In addition, the MAH takes the opportunity to update the company logo on the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	31/08/2023		SmPC and PL	For more information, please refer to the Summary of Product Characteristics.
IB/0088	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing	27/07/2023	n/a		

	authorisation, including the RMP - Other variation				
IAIN/0086/G	This was an application for a group of variations. 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.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	18/04/2023	n/a		
PSUSA/2842/ 202205	Periodic Safety Update EU Single assessment - tafamidis	15/12/2022	15/02/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2842/202205.
II/0081	Update of section 5.1 of the SmPC in order to update information based on final results from study B3461029 listed as a Specific Obligation in the Annex II of the Product Information. This is a non-interventional PASS sub-study evaluating effects of tafamidis on disease progression in patients with non-Val30Met mutations and symptomatic neuropathy. Consequently, following the fulfilment of the SOB of this Marketing Authorisation under Exceptional Circumstances, the Specific Obligation has been updated in Annex II. The RMP version 9.7 is updated accordingly and agreed. In addition, the MAH took the opportunity to update	15/12/2022	15/02/2023	SmPC, Annex II and PL	For more information, please refer to the Summary of Product Characteristics.

	the list of local representatives in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IAIN/0085/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	10/11/2022	15/02/2023	Annex II and PL	
IA/0084	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	18/10/2022	n/a		
IAIN/0082/G	This was an application for a group of variations.	17/05/2022	n/a		

	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 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.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 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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure A.7 - Administrative change - Deletion of manufacturing sites				
S/0076	10th annual re-assessment.	24/03/2022	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 Vyndaqel should be maintained.
IA/0079	B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer	17/02/2022	n/a		
IA/0078	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	31/01/2022	n/a		
IAIN/0077/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.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms	06/12/2021	09/11/2022	SmPC, Labelling and PL	
PSUSA/2842/ 202105	Periodic Safety Update EU Single assessment - tafamidis	02/12/2021	n/a		PRAC Recommendation - maintenance
IAIN/0075	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	20/09/2021	n/a		

IA/0074	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	02/09/2021	n/a		
IAIN/0072	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	17/06/2021	11/10/2021	Annex II and PL	
IA/0071	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	11/05/2021	n/a		
II/0067	Update of section 4.5 of the SmPC in order to add drug-drug interaction information with Rosuvastatin, a breast cancer resistant protein (BCRP), based on final results from Study B3461075. This is a Phase 1 interventional clinical drug-drug interaction study to estimate the effect of a multiple oral administration of Tafamidis on Rosuvastatin in pharmacokinetics (PK) in healthy participants. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/04/2021	11/10/2021	SmPC	In a clinical study in healthy participants, the exposure of the breast cancer resistant protein substrate rosuvastatin increased approximately 2-fold following multiple doses of 61 mg tafamidis daily dosing. The new information was reflected in the Product Information. For more information, please refer to the Summary of Product Characteristics.
S/0065	9th annual re-assessment	25/03/2021	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 Vyndaqel should be maintained.
IA/0070	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	12/03/2021	n/a		
IA/0069	A.7 - Administrative change - Deletion of manufacturing sites	11/02/2021	11/10/2021	Annex II and PL	
PSUSA/2842/ 202005	Periodic Safety Update EU Single assessment - tafamidis	14/01/2021	n/a		PRAC Recommendation - maintenance
IB/0068	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	11/01/2021	n/a		
IAIN/0066	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	08/12/2020	n/a		
IA/0064	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	20/11/2020	n/a		
IB/0063	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	18/11/2020	n/a		
IB/0062	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/10/2020	11/10/2021	SmPC and PL	

IA/0061/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer	14/09/2020	n/a		
IB/0057	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	03/07/2020	n/a		
IB/0059	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	15/06/2020	n/a		
IA/0058/G	This was an application for a group of variations. B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	29/05/2020	n/a		

S/0055	8th annual re-assessment	30/04/2020	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 of Vyndaqel should be maintained.
IA/0056/G	This was an application for a group of variations. 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.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.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	27/03/2020	n/a		
X/0049/G	This was an application for a group of variations. Annex I_2.(c) Change or addition of a new strength/potency C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data Annex I_1.(a) Replacement of a chemical AS by diff. salt/ester complex/derivative, with the same therapeutic moiety	12/12/2019	17/02/2020	SmPC, Annex II, Labelling and PL	

IB/0053/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.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	20/12/2019	n/a		
PSUSA/2842/ 201905	Periodic Safety Update EU Single assessment - tafamidis	28/11/2019	n/a		PRAC Recommendation - maintenance
N/0054	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/11/2019	17/02/2020	PL	
IB/0050/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.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms 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)	31/07/2019	22/11/2019	SmPC, Labelling and PL	
S/0047	7th annual re-assessment	26/04/2019	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

					of Vyndaqel should be maintained.
IAIN/0048/G	This was an application for a group of variations. 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.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	20/12/2018	22/11/2019	Annex II and PL	
PSUSA/2842/ 201805	Periodic Safety Update EU Single assessment - tafamidis	29/11/2018	n/a		PRAC Recommendation - maintenance
T/0045	Transfer of Marketing Authorisation	11/07/2018	03/08/2018	SmPC, Labelling and PL	
S/0044	6th annual re-assessment	31/05/2018	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 Vyndaqel should be maintained.
II/0041/G	This was an application for a group of variations. B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant	18/01/2018	n/a		

	update to the relevant AS section in the dossier B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS				
PSUSA/2842/ 201705	Periodic Safety Update EU Single assessment - tafamidis	30/11/2017	n/a		PRAC Recommendation - maintenance
II/0043	Update of section 5.3 of the SmPC to include 'fertility and early embryonic development' in the list of non-clinical studies. In addition, the MAH took the opportunity to implement minor revisions to sections 2 and 4.6 of the SmPC, to correct a typographical error in Annex IIE and to align the PI with the latest QRD template version 10.0. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/10/2017	03/08/2018	SmPC, Annex II, Labelling and PL	
IB/0040	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	05/05/2017	n/a		
IA/0039	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	30/03/2017	n/a		

S/0036	5th Annual Re-assessment	23/03/2017	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 Vyndaqel is maintained.
IA/0038	A.7 - Administrative change - Deletion of manufacturing sites	01/03/2017	n/a		
IA/0037	B.II.a.3.b.1 - Changes in the composition (excipients) of the finished product - Other excipients - Any minor adjustment of the quantitative composition of the finished product with respect to excipients	31/01/2017	n/a		
PSUSA/2842/ 201605	Periodic Safety Update EU Single assessment - tafamidis	01/12/2016	n/a		PRAC Recommendation - maintenance
N/0035	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/09/2016	03/08/2018	PL	
R/0032	Renewal of the marketing authorisation.	26/05/2016	22/07/2016	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Vyndaqel in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IA/0033	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	18/05/2016	n/a		

S/0031	4th Annual Re-assessment	25/02/2016	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 the medicinal product, concluded that Marketing Authorisation of Vyndaqel should be maintained.
IA/0030	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	10/12/2015	n/a		
PSUSA/2842/ 201505	Periodic Safety Update EU Single assessment - tafamidis	03/12/2015	n/a		PRAC Recommendation - maintenance
IA/0029/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 A.7 - Administrative change - Deletion of manufacturing sites	30/10/2015	n/a		
II/0027/G	This was an application for a group of variations. B.II.a.1.a - Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking - Changes in imprints, bossing or other markings B.II.a.2.a - Change in the shape or dimensions of the pharmaceutical form - Immediate release tablets, capsules, suppositories and pessaries	17/09/2015	22/07/2016	SmPC, Labelling and PL	

	B.II.a.3.a.1 - Changes in the composition (excipients) of the finished product - Changes in components of the flavouring or colouring system - Addition , deletion or replacement B.II.a.3.b.5 - Changes in the composition (excipients) of the finished product - Other excipients - Change that is supported by a bioequivalence study 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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits 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.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of				

	specification limits B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.d.2.f - Change in test procedure for the finished product - To reflect compliance with the Ph. Eur. and remove reference to the outdated internal test method and test method number B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.e.7.a - Change in supplier of packaging				

	components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product B.II.h.z - Adventitious Agents Safety - Other variation B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer				
N/0026	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/06/2015	22/07/2016	PL	
IB/0025/G	This was an application for a group of variations. B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits	26/05/2015	n/a		
S/0022	Annual re-assessment.	26/02/2015	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 Vyndaquel should be maintained.
II/0021	Update of section 5.1 of the SmPC in order to include information from a recently completed thorough QT study. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/02/2015	13/05/2015	SmPC	The following addition to section 5.1 of the SmPC has been approved in this variation: "A supra-therapeutic, single, 400 mg oral dose of tafamidis solution in mostly healthy male volunteers demonstrated no significant QTc interval prolongation effect, but a trend towards a shortening of QT interval of unknown clinical relevance."
IB/0024	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	15/01/2015	13/05/2015	SmPC, Labelling and PL	
IA/0023	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	19/12/2014	n/a		
PSUV/0018	Periodic Safety Update	04/12/2014	n/a		PRAC Recommendation - maintenance
IA/0020	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	26/09/2014	n/a		
II/0013	Update of section 4.5 of the SmPC to include new data from completed in vitro studies concerning drug interactions.	25/09/2014	13/05/2015	SmPC	In vitro studies with tafamidis suggest that it is unlikely tafamidis will cause drug interactions at clinically relevant concentrations with substrates of UDP glucuronosyltransferase (UGT), P-gp transporters, or

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				organic-transporting polypeptide transporters (OATP1B1 and 1B3). However, in vitro tafamidis inhibits the efflux transporter BCRP (breast cancer resistant protein) with IC50=1.16 µM and may cause drug-drug interactions at clinically relevant concentrations with substrates of this transporter (e.g. methotrexate, rosuvastatin, imatinib). Likewise, tafamidis inhibits the uptake transporters OAT1 and OAT3 (organic anion transporters) with IC50=2.9 µM and IC50=2.36 µM, respectively, and may cause drug-drug interactions at clinically relevant concentrations with substrates of these transporters (e.g. non-steroidal anti-inflammatory drugs, bumetanide, furosemide, lamivudine, methotrexate, oseltamivir, tenofovir, ganciclovir, adefovir, cidofovir, zidovudine, zalcitabine).
IAIN/0019	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	01/09/2014	13/05/2015	Annex II and PL	
PSUV/0015	Periodic Safety Update	13/06/2014	n/a		PRAC Recommendation - maintenance
IB/0017	B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale	22/05/2014	13/05/2015	SmPC	
S/0012	2nd Annual Re-assessment	22/05/2014	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 of Vyndaqel should be maintained.
IB/0016	B.II.e.2.b - Change in the specification parameters	02/05/2014	n/a		

	and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method				
II/0014	Update of section 4.9 of the SmPC based on the recently completed Study B3461040 using higher doses of tafamadis and inclusion of new adverse reactions (hordeolum, photosensitivity and presyncope). Furthermore, the MAH took the opportunity to implement editorial changes with this variation. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/03/2014	06/05/2014	SmPC, Labelling and PL	Following completion of a clinical pharmacology study (B3461040) the Product Information was updated to include new information on overdose. Section 4.9 of the SmPC No cases of acute overdose have been reported. In clinical trials of healthy volunteers, the highest dose of tafamidis given was 120480 mg in a single dose and 60 mg once daily for two weeks. Four treatment-related adverse events were reported at these doses levels in healthy volunteers: headache (mild), somnolence (mild), myalgia (moderate), and insomnia (mild). The reported treatment-related adverse events were mild to moderate and included: headache, somnolence, myalgia, insomnia, hordeolum, photosensitivity reaction, and presyncope.
IB/0011/G	This was an application for a group of variations. 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 B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting	15/01/2014	n/a		

	material/intermediate/reagent - Other variation				
IB/0010	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	20/08/2013	06/05/2014	SmPC, Labelling and PL	
S/0006	1st Annual Re-assessment	25/07/2013	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 Vyndaqel should be maintained.
IA/0009	B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place	25/04/2013	n/a		
II/0007	Update of section 4.8 of the SmPC in order to upgrade the adverse drug reaction frequencies of "vaginal infection" and "upper abdominal pain" from "common" to "very common". The Package Leaflet was updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI was brought in line with the latest QRD template version 8.3. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	25/04/2013	06/05/2014	SmPC, Annex II, Labelling and PL	The CHMP considered that the frequencies of adverse drug reactions using data from the placebo-controlled study for tafamidis were more relevant than using the pooled safety data including uncontrolled studies. Based on this consideration, the frequencies of vaginal infection and upper abdominal pain were re-classified from common (≥1/100 to <1/10) to very common (≥1/10).

IG/0235/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.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV	06/12/2012	n/a		C.I.z - To replace the Detailed Description of the Pharmacovigilance System (DDPS) with the Pharmacovigilance System Master File (PSMF).
IA/0004/G	This was an application for a group of variations. 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.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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	03/10/2012	n/a		
T/0001	Transfer of Marketing Authorisation	23/05/2012	28/06/2012	SmPC, Labelling and PL	Transfer of Marketing Authorisation from Pfizer Specialty UK Ltd. to Pfizer Ltd.
IG/0169/G	This was an application for a group of variations. C.I.9.e - Changes to an existing pharmacovigilance	08/06/2012	n/a		

	system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				