Spedra

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
R/0029	Renewal of the marketing authorisation.	22/02/2018	23/04/2018	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 Spedra in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10066 /201706	Periodic Safety Update EU Single assessment - avanafil	11/01/2018	n/a		PRAC Recommendation - maintenance

[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).

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II/0027/G	This was an application for a group of variations. 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	09/11/2017	23/04/2018	SmPC and PL	In clinical trial TA-401 performed in healthy volunteers and adult males with mild erectile dysfunction, the daily administration of avanafil 100 mg oral doses over a period of 26 weeks was not associated with any untoward effects on sperm concentration, count, motility, or morphology. In study TA-402, no remarkable findings in visual acuity, pupillometry, colour vision discrimination, and intraocular pressure were observed in subjects treated with Spedra. The information already included in section 4.4 of the SmPC regarding non-arteritic anterior ischaemic optic neuropathy (NAION) and the advice to the patients that suddenly loss the vision to consult a physician is considered sufficient
N/0026	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/03/2017	23/04/2018	PL	
PSUSA/10066 /201606	Periodic Safety Update EU Single assessment - avanafil	12/01/2017	n/a		PRAC Recommendation - maintenance
IB/0025	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	09/11/2016	n/a		
IB/0023	B.I.a.3.d - Change in batch size (including batch size ranges) of AS or intermediate - More than 10-fold increase compared to the originally approved batch size	16/06/2016	n/a		
IB/0022	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	07/04/2016	n/a		

IB/0021	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)	10/03/2016	05/12/2016	SmPC	
IA/0020	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	29/02/2016	n/a		
II/0019	Update of section 4.5 of the SmPC with information on inhibition of drug transporters, thus addressing the recommendation at the conclusion of the assessment of REC 003.2. Minor corrections are made in section 4.5 of the SmPC and the contact details of the Bulgarian local representative in the Package Leaflet are also updated. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/02/2016	05/12/2016	SmPC and PL	Based on in vitro data, at clinically relevant concentrations avanafil could be an inhibitor of BCRP. At clinically relevant concentrations avanafil is not an inhibitor of OATP1B1, OATP1B3, OCT1, OCT2, OAT1, OAT3 and BSEP.
PSUSA/10066 /201506	Periodic Safety Update EU Single assessment - avanafil	14/01/2016	n/a		PRAC Recommendation - maintenance
IB/0018	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	16/12/2015	05/12/2016	SmPC, Labelling and PL	
II/0012	B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	19/11/2015	n/a		

	Introduction of a manufacturer of the AS supported by an ASMF				
PSUSA/10066 /201412	Periodic Safety Update EU Single assessment - avanafil	23/07/2015	18/09/2015	SmPC and PL	Please refer to Spedra-PSUSA/00010066/201412 EPAR: Scirntific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IB/0016/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.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.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing 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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	08/05/2015	18/09/2015	Annex II and PL	

	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.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.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation				
IA/0014	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	06/03/2015	18/09/2015	SmPC	
IA/0013	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	04/02/2015	n/a		
II/0007	Update of sections 4.2 and 5.1 of the SmPC further to the results of clinical study TA-501 conducted to examine the onset of the therapeutic effects of avanafil after dosing in men with mild to severe erectile dysfunction. The Package leaflet is updated accordingly. In addition, the MAH takes the opportunity to delete the warning on arrhythmia included in the Package Leaflet to bring it in line with the SmPC and to make minor editorial changes.	18/12/2014	22/01/2015	SmPC and PL	Study TA-501 investigated the onset of action of avanafil at two doses (100 and 200 mg) in terms of per-subject proportion of sexual attempts resulting in satisfactory completion of sexual intercourse. Avanafil demonstrated statistically significant improvement in the primary efficacy variable (average per subject proportion of successful responses by time after dose administration, to the Sexual Encounter Profile 3 - SEP3) as compared with placebo, resulting in successful intercourse in 24.71% of the attempts for the 100 mg dose and

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				28.18% for the 200 mg dose at approximately 15 minutes after dosing compared to 13.78% for placebo. Consequently, the posology of avanafil in section 4.2 of the SmPC is amended to for the recommended dose of 100 mg to be taken as needed approximately 15-30 minutes before sexual activity (see section 5.1 of the SmPC).
PSUV/0010	Periodic Safety Update	09/01/2015	n/a		PRAC Recommendation - maintenance
IB/0011	B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	04/11/2014	n/a		
IB/0008/G	This was an application for a group of variations. B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF 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.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.b.1.d - Change in the specification parameters and/or limits of an AS, starting	18/09/2014	n/a		

	material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) 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 material/intermediate/reagent - Other variation 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 material/intermediate/reagent - Other variation B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS				
IA/0009	B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products	09/09/2014	n/a		
PSUV/0005	Periodic Safety Update	10/07/2014	n/a		PRAC Recommendation - maintenance
IB/0006	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	25/04/2014	n/a		
IB/0003	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	24/02/2014	n/a		

IAIN/0004/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.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 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	03/02/2014	22/01/2015	Annex II and PL	
IB/0002	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)	13/01/2014	22/01/2015	SmPC	
T/0001	Transfer of Marketing Authorisation from VIVUS BV to Menarini International Operations Luxembourg S.A. Transfer of Marketing Authorisation	06/09/2013	02/10/2013	SmPC, Labelling and PL	Transfer of Marketing Authorisation from VIVUS BV to Menarini International Operations Luxembourg S.A.