EMA/48166/2021

JETREA

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
IA/0053	A.7 - Administrative change - Deletion of manufacturing sites	11/12/2020		Annex II and PL	
IB/0052	C.I.7.a - Deletion of - a pharmaceutical form	06/11/2020		SmPC, Labelling and	

[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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				PL	
T/0051	Transfer of Marketing Authorisation	06/08/2020	15/09/2020	SmPC, Labelling and PL	
II/0050	B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method	16/07/2020	n/a		
PSUSA/10122 /201910	Periodic Safety Update EU Single assessment - ocriplasmin	14/05/2020	n/a		PRAC Recommendation - maintenance
IB/0048	B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol	23/03/2020	n/a		
PSUSA/10122 /201810	Periodic Safety Update EU Single assessment - ocriplasmin	16/05/2019	n/a		PRAC Recommendation - maintenance
II/0042/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	14/02/2019	n/a		

IB/0046/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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	13/02/2019	n/a		
N/0044	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/01/2019	31/07/2019	PL	
IAIN/0043/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	27/09/2018	31/07/2019	SmPC, Annex II, Labelling and PL	
IAIN/0041	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	07/08/2018	n/a		
IB/0040/G	This was an application for a group of variations. B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	30/07/2018	31/07/2019	SmPC, Labelling and PL	

	B.II.f.1.e - Stability of FP - Change to an approved stability protocol				
N/0039	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/05/2018	31/07/2019	PL	
PSUSA/10122 /201710	Periodic Safety Update EU Single assessment - ocriplasmin	17/05/2018	n/a		PRAC Recommendation - maintenance
IB/0037	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	04/01/2018	n/a		
R/0033	Renewal of the marketing authorisation.	12/10/2017	08/12/2017	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of JETREA in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IB/0036	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	28/11/2017	n/a		
PSUSA/10122 /201704	Periodic Safety Update EU Single assessment - ocriplasmin	26/10/2017	n/a		PRAC Recommendation - maintenance
N/0035	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/08/2017	13/10/2017	PL	
PSUSA/10122 /201610	Periodic Safety Update EU Single assessment - ocriplasmin	05/05/2017	n/a		PRAC Recommendation - maintenance

N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/02/2017	13/10/2017	PL	
II/0026	Update of sections 4.4, 4.8 and 5.1 of the SmPC to reflect new long-term safety and efficacy data based on the final CSR for study TG-MV-014 in fulfilment of the post-authorisation measure MEA 002. The SmPC updates also address PRAC recommendations in conclusion to PSUR 6 (EMEA/H/C/PSUSA/00010122/201510). The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in the annexes, to align the annexes with the latest QRD templates (v9.1 and 10) and to update the contact details of the local representative in Spain in the Package Leaflet. An updated RMP version 7b was agreed during the procedure. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	10/11/2016	13/10/2017	SmPC, Annex II and PL	The clinical efficacy and safety of JETREA for the treatment of vitreomacular traction (VMT) was assessed in 3 double-masked studies. For information on the design and main results of study TG-MV-014 please refer to section 5.1 of the Summary of Product Characteristics. Over 1400 patients have been treated with the recommended dose of 0.125 mg of JETREA in interventional clinical studies. All adverse reactions were ocular. The most commonly reported adverse reactions were vitreous floaters, eye pain, photopsia and chromatopsia as well as conjunctival haemorrhage resulting from the injection procedure. The most clinically relevant adverse reactions included blindness transient, retinal tear, retinal detachment, lens subluxation and macular hole progression. For further information, please refer to section 4.8 of the Summary of Product Characteristics. Ophthalmological examinations may be abnormal following the administration of JETREA. These include optical coherence tomography (OCT), ophthalmoscopy (foveal reflex), colour vision test (Roth 28-hue) and full-field ERG. This should be taken into consideration when using these tests for the diagnosis or monitoring of other conditions.
PSUSA/10122 /201604	Periodic Safety Update EU Single assessment - ocriplasmin	27/10/2016	n/a		PRAC Recommendation - maintenance
IB/0030	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	22/08/2016	n/a		

PSUSA/10122 /201510	Periodic Safety Update EU Single assessment - ocriplasmin	13/05/2016	n/a		PRAC Recommendation - maintenance
IB/0028/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.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.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	20/04/2016	n/a		
IB/0027	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	12/04/2016	n/a		
IA/0025	B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol	16/02/2016	n/a		
IB/0023/G	This was an application for a group of variations.	06/01/2016	n/a		

	B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.f.1.e - Stability of FP - Change to an approved stability protocol				
PSUSA/10122 /201504	Periodic Safety Update EU Single assessment - ocriplasmin	06/11/2015	n/a		PRAC Recommendation - maintenance
PSUSA/10122 /201410	Periodic Safety Update EU Single assessment - ocriplasmin	21/05/2015	17/07/2015	SmPC and PL	Please refer to Jetrea PSUSA-10122-201410 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IA/0021	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	02/06/2015	n/a		
X/0013	The Marketing Authorisation Holder (MAH), ThromboGenics NV, submitted to the European Medicines Agency (EMA) an application for a line extension for Jetrea to introduce a formulation with adjusted fill volume for Jetrea 0.375 mg/0.3 mL Annex I_2.(d) Change or addition of a new pharmaceutical form	26/02/2015	24/04/2015	SmPC, Annex II, Labelling and PL	With this application, the (MAH) applied for a new pharmaceutical form and strength, Jetrea 0.375mg/0.3ml solution for injection, which no longer requires dilution prior to injection. The CHMP considered that the quality of Jetrea solution for injection was acceptable when used in accordance with the conditions defined in the product information. There was no new clinical or non-clinical data affecting the benefit-risk profile of Jetrea. However, there was a concern of possible medication errors upon introduction of the new formulation as the previously existing formulation (concentrate of solution for injection) requires dilution prior to injection, while the new formulation does not. Mix-ups between the two formulations could result in dilution errors and administration of inadequate doses. To mitigate this

					risk, the MAH confirmed the intention to remove existing stocks of the concentrate from user sites at the same time when the new formulating is launched. Furthermore, the packaging and labelling of the new formulation were designed in a way to clearly differentiate between the concentrate and the new solution for injection. In addition, the PRAC and the CHMP considered that a DHPC was needed in order to highlight the risk of inadvertent dilution of the new formulation prior to injection, which could lead to under-dosing and delivery of a sub-therapeutic dose. Overall, based on the measures described above, the CHMP was of the opinion that the benefits of Jetrea in the treatment of vitreomacular traction in adult patients, including when associated with macular hole of diameter less than or equal to 400 microns, continued to outweigh its risks and thus concluded that the benefit-risk profile remained favourable.
IB/0020/G	This was an application for a group of variations. B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.f.1.e - Stability of FP - Change to an approved stability protocol	15/04/2015	n/a		
IB/0018	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	27/11/2014	n/a		
PSUV/0014	Periodic Safety Update	06/11/2014	n/a		PRAC Recommendation - maintenance

IB/0016	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	22/10/2014	24/04/2015	SmPC	
IB/0017	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	26/09/2014	n/a		
IB/0015	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	05/08/2014	n/a		
II/0011/G	This was an application for a group of variations. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	24/07/2014	n/a		

	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.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				
IB/0012	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	25/06/2014	n/a		
PSUV/0008	Periodic Safety Update	08/05/2014	n/a		PRAC Recommendation - maintenance
II/0007	B.II.f.1.c - Stability of FP - Change in storage conditions for biological medicinal products, when the stability studies have not been performed in accordance with an approved stability protocol	20/03/2014	30/10/2014	SmPC and PL	
IA/0010	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	25/02/2014	n/a		
N/0009	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/02/2014	30/10/2014	PL	
IB/0006	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	19/12/2013	n/a		

IB/0005	C.I.3.z - 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 - Other variation	21/11/2013	30/10/2014	SmPC, Annex II and PL	
IB/0003/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.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	12/11/2013	n/a		
IAIN/0004/G	This was an application for a group of variations. A.6 - Administrative change - Change in ATC Code/ATC Vet Code 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	11/11/2013	30/10/2014	SmPC, Annex II and PL	
IAIN/0002	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	03/09/2013	n/a		
IAIN/0001	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging	10/06/2013	n/a		

	site				