Holoclar

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
IB/0067	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	08/10/2024	n/a		
PSUSA/10352 /202402	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial	03/10/2024	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).

	cells containing stem cells				
IAIN/0066	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	28/06/2024	n/a		
IB/0064	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	23/05/2024	n/a		
PSUSA/10352 /202308	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	07/03/2024	n/a		PRAC Recommendation - maintenance
IA/0063	B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	22/02/2024	n/a		
R/0058	Renewal of the marketing authorisation.	14/12/2023	22/02/2024	SmPC, Annex II and PL	The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated. Furthermore, the CHMP considered that, as all Specific Obligations have been fulfilled, there are no remaining grounds for the marketing authorisations to remain conditional and therefore

					recommends the granting of the MA no longer subject to Specific Obligations for Holoclar. Changes to the Product Information have been introduced, including the following: In 4.4. Special warnings and precautions for use: […] Autologous use Holoclar is intended solely for autologous use and must not, under any circumstances, be administered to other patients. Holoclar must not be administered if the information on the product labels and lot number do not match the patient's identity. […] Transmission of an infectious agent Holoclar could contain potentially infected biological material. Although Holoclar is tested for sterility and mycoplasma, a risk of transmission of infectious agents exists. Healthcare professionals administering Holoclar must, therefore, monitor patients for signs and symptoms of infections after treatment and treat appropriately, if needed. Although the risk is considered to be very low and routinely controlled in the manufacturing. […] Precautions for use A thorough evaluation of the patient should be done taking into consideration not only the clinical need of the candidate, but also the biological and pathophysiologic alterations in the wound bed environment, to define the timing of any procedure and allow the proper engraftment and growth of the stem cells of the living tissue that constitute Holoclar. Concomitant surgeries should be

					excluded and anticipated or deferred to Holoclar implantation. Concomitant eyelids malposition, conjunctival scarring with fornix shortening, corneal anaesthesia and/or conjunctival anaesthesia or severe hypoaesthesia, pterygium and severe dry eye are potential complicating factors. When possible, Concomitant eye problems should be corrected prior to Holoclar implantation. At any of the steps of the treatment with Holoclar, topical lidocaine or anaesthetics containing adrenaline must be avoided. In 4.5. Interaction with other medicinal products and other forms of interaction: The concomitant use of topical lidocaine or anaesthetics containing adrenaline must be avoided as they reduce the colony forming efficiency. Please see the Product Information for all details.
IAIN/0062	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	29/11/2023	n/a		
T/0060	Transfer of Marketing Authorisation	25/09/2023	18/10/2023	SmPC, Labelling and PL	
PSUSA/10352 /202302	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	28/09/2023	n/a		PRAC Recommendation - maintenance

IAIN/0059/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.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	22/09/2023	18/10/2023	Annex II and PL	
IAIN/0057	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	22/06/2023	n/a		
IA/0054	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)	20/04/2023	n/a		
IAIN/0055	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	17/04/2023	n/a		
IB/0053	B.I.b.z - Change in control of the AS - Other variation	30/03/2023	n/a		

PSUSA/10352 /202208	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	16/03/2023	n/a		PRAC Recommendation - maintenance
IAIN/0052	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	08/03/2023	n/a		
IAIN/0051	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	20/02/2023	n/a		
IA/0050	B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	06/02/2023	n/a		
R/0048	Renewal of the marketing authorisation.	10/11/2022	13/01/2023		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Holoclar, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
PSUSA/10352 /202202	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	29/09/2022	n/a		PRAC Recommendation - maintenance

IB/0045	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	29/07/2022	n/a		
IAIN/0047	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	15/07/2022	n/a		
IAIN/0046	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	23/06/2022	n/a		
IB/0044	B.I.z - Quality change - Active substance - Other variation	01/06/2022	n/a		
IA/0042/G	This was an application for a group of variations. B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	25/04/2022	n/a		

IAIN/0041/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	19/04/2022	n/a		
PSUSA/10352 /202108	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	10/03/2022	n/a		PRAC Recommendation - maintenance
R/0039	Renewal of the marketing authorisation.	14/10/2021	09/12/2021		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this

					medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Holoclar, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
PSUSA/10352 /202102	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	30/09/2021	n/a		PRAC Recommendation - maintenance
IB/0038	B.I.b.z - Change in control of the AS - Other variation	16/09/2021	n/a		
IB/0036	B.II.c.z - Change in control of excipients in the Finished Product - Other variation	04/05/2021	n/a		
PSUSA/10352 /202008	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	11/03/2021	n/a		PRAC Recommendation - maintenance
IB/0035	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	15/01/2021	n/a		
IB/0034	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	15/01/2021	n/a		
R/0032	Renewal of the marketing authorisation.	15/10/2020	07/01/2021	SmPC, Annex II, Labelling and PL	The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this

					medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Holoclar, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
PSUSA/10352 /202002	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	01/10/2020	n/a		PRAC Recommendation - maintenance
T/0031	Transfer of Marketing Authorisation	18/05/2020	12/06/2020	SmPC, Annex II, Labelling and PL	
IB/0029	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	30/03/2020	n/a		
PSUSA/10352 /201908	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	12/03/2020	n/a		PRAC Recommendation - maintenance
R/0026	Renewal of the marketing authorisation.	14/11/2019	21/02/2020	SmPC and Annex II	
IA/0027	B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	04/10/2019	n/a		
PSUSA/10352 /201902	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	05/09/2019	n/a		PRAC Recommendation - maintenance

IB/0023	B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB	28/03/2019	n/a		
PSUSA/10352 /201808	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	14/03/2019	n/a		PRAC Recommendation - maintenance
N/0024	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/02/2019	21/02/2020	PL	
R/0021	Renewal of the marketing authorisation.	15/11/2018	15/01/2019	SmPC	The CHMP having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Holoclar, subject to the Specific Obligations and Conditions as laid down in Annex II to the opinion.
PSUSA/10352 /201802	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	06/09/2018	n/a		PRAC Recommendation - maintenance
IB/0019	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	18/05/2018	n/a		

IB/0018/G	This was an application for a group of variations. B.I.z - Quality change - Active substance - Other variation B.I.z - Quality change - Active substance - Other variation	18/05/2018	n/a		
PSUSA/10352 /201708	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	08/03/2018	n/a		PRAC Recommendation - maintenance
IB/0017	B.I.z - Quality change - Active substance - Other variation	04/01/2018	n/a		
R/0015	Renewal of the marketing authorisation.	12/10/2017	11/12/2017		The CAT, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Holoclar, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
PSUSA/10352 /201702	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	28/09/2017	n/a		PRAC Recommendation - maintenance
IA/0014/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	28/07/2017	n/a		

	material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) 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.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material				
II/0012/G	This was an application for a group of variations. 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 B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other	22/06/2017	11/12/2017	SmPC and PL	

	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				
PSUSA/10352 /201608	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	09/03/2017	n/a		PRAC Recommendation - maintenance
IB/0011	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	07/02/2017	n/a		
R/0008	Renewal of the marketing authorisation.	13/10/2016	08/12/2016		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligation and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Holoclar, subject to the Specific Obligation and Conditions as laid down in Annex II to the Opinion.
N/0010	Update of the labelling to include the unique identifier 2D barcode as per QRD template v.10 and update of the package leaflet with the revised	03/11/2016	11/12/2017	Labelling and PL	

	contact details of the local representative for France. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
PSUSA/10352 /201602	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	02/09/2016	n/a		PRAC Recommendation - maintenance
IA/0007/G	This was an application for a group of variations. 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 B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	23/06/2016	n/a		
IB/0006	B.II.c.2.z - Change in test procedure for an excipient - Other variation	10/06/2016	n/a		
IA/0005/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.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability -	27/05/2016	n/a		

	New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer				
PSUSA/10352 /201508	Periodic Safety Update EU Single assessment - ex vivo expanded autologous human corneal epithelial cells containing stem cells	17/03/2016	n/a		PRAC Recommendation - maintenance
IB/0003	B.II.z - Quality change - Finished product - Other variation	18/12/2015	n/a		
R/0001	Renewal of the marketing authorisation.	22/10/2015	10/12/2015		The CHMP, having reviewed the available information on the status of the fulfilment of Specific Obligations and having confirmed the positive benefit risk balance, is of the opinion that the quality, safety and efficacy of this medicinal product continue to be adequately and sufficiently demonstrated and therefore recommends the renewal of the conditional MA for Holoclar, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.