Cystagon

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/0074/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP -	10/12/2024		SmPC, Annex II, Labelling 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).

	Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing				
IA/0073/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 material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) 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	19/11/2024	n/a		
IA/0072	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)	04/11/2024	n/a		
IB/0071	B.II.e.4.z - Change in shape or dimensions of the container or closure (immediate packaging) - Other variation	24/07/2024		PL	
IB/0070	B.II.e.1.z - Change in immediate packaging of the finished product - Other variation	17/04/2024		SmPC, Labelling and PL	
IA/0068	A.7 - Administrative change - Deletion of manufacturing sites	16/06/2023	n/a		

IA/0067	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	05/09/2022	n/a		
IAIN/0066	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	21/10/2021	14/10/2022	SmPC and PL	
IB/0065/G	This was an application for a group of variations. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	16/07/2021	n/a		
PSUSA/10573 /202010	Periodic Safety Update EU Single assessment - mercaptamine (treatment of nephropathic cystinosis)	10/06/2021	n/a		PRAC Recommendation - maintenance
IB/0064/G	This was an application for a group of variations. 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.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site	10/05/2021	n/a		

	B.II.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms				
II/0062	B.I.a.1.b - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a manufacturer of the AS supported by an ASMF	25/03/2021	n/a		
IA/0061	B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State	20/10/2020	n/a		
IA/0060	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	31/01/2020	n/a		
IA/0059	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	19/12/2019	n/a		
IB/0058/G	This was an application for a group of variations. B.I.c.1.a - Change in immediate packaging of the AS	13/12/2019	n/a		

	- Qualitative and/or quantitative composition B.I.d.1.a.1 - Stability of AS - Change in the re-test period/storage period - Reduction B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS				
IG/1085/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 A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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)	16/05/2019	17/04/2020	SmPC, Annex II, Labelling and PL	
N/0056	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/03/2019	17/04/2020	PL	
IA/0055	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	04/01/2019	n/a		
N/0053	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/07/2018	17/04/2020	Labelling and PL	

IA/0054/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.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.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.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 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 -	11/07/2018	n/a		

	Updated certificate from an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)				
IB/0052/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.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation 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.4.z - Change to in-process tests or limits applied during the manufacture of the AS - 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.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition 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	23/05/2018	n/a		

	data				
IA/0051/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.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	23/01/2018	n/a		
IG/0773/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.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	14/02/2017	11/01/2018	Annex II and PL	
IB/0049	B.II.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation	20/09/2016	n/a		
PSUSA/1987/ 201510	Periodic Safety Update EU Single assessment - mercaptamine	09/06/2016	n/a		PRAC Recommendation - maintenance
IG/0686	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	12/05/2016	n/a		

IG/0535	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	06/03/2015	n/a		
IG/0393	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	20/12/2013	n/a		
IG/0392	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	19/12/2013	05/12/2014	Annex II and PL	
PSUV/0043	Periodic Safety Update	27/06/2013	12/09/2013		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUV/0043.
N/0042	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/08/2012	12/09/2013	PL	
N/0041	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/04/2012	12/09/2013	PL	
IA/0040	A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	14/04/2011	n/a		
IB/0039	B.I.b.2.e - Change in test procedure for AS or	08/04/2010	n/a		

	starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
IA/0037	IA_01_Change in the name and/or address of the marketing authorisation holder IA_05_Change in the name and/or address of a manufacturer of the finished product	02/10/2007	n/a	SmPC, Annex II, Labelling and PL	
IA/0036	IA_39_Change/addition of imprints, bossing or other markings	05/09/2007	n/a	SmPC and PL	
R/0034	Renewal of the marketing authorisation.	26/04/2007	21/06/2007	SmPC, Annex II, Labelling and PL	
S/0028	Annual re-assessment.	22/02/2007	17/04/2007	Annex II and PL	
IA/0035	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	16/03/2007	n/a		
IA/0033	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	12/01/2007	n/a		
IA/0032	IA_32_a_Change in batch size of the finished product - up to 10-fold	10/01/2007	n/a		
IA/0030	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	05/12/2006	n/a		

S/0027	Annual re-assessment.	15/09/2005	15/09/2005		
II/0026	Following a CHMP request, the Marketing Authorisation Holder applied for an update of section 4.2 (Posology and method of administration), section 4.4 (Special warnings and special precautions for use) and section 4.8 (Undesirable effects) of the Summary of Product Characteristics (SPC) to include safety information regarding three suspected adverse drug reactions involving skin lesions in children. The Package Leaflet (PL) has been amended accordingly. Update of Summary of Product Characteristics and Package Leaflet	26/05/2005	07/07/2005	SmPC and PL	In December 2004, the MAH (Marketing Authorisation Holder) informed the EMEA and the Rapporteur about three cases of serious skin reactions over the elbows resembling Ehlers-Danlos Syndrome (EDS) in patients treated with Cystagon. All of them were observed in Ireland and one was fatal. The MAH issued a letter in order to inform the concerned specialised physicians about this finding, and requesting information on new cases. As a result, an additional case from Italy was reported (in this fourth case, the child was treated with a formulation of cysteamine chlorhydrate, not Cystagon, when the adverse reaction appeared). Following the evaluation of the available information of these cases, the CHMP requested the MAH to submit a type II variation to reflect the new information. Sections 4.2, 4.4 and 4.8 of the Summary of Product Characteristics (SPC), and relevant sections of the Package Leaflet (PL) were amended in order to include information regarding these events.
S/0025	Annual re-assessment.	16/09/2004	30/09/2004		
S/0023	Annual re-assessment.	25/09/2003	09/01/2004	SmPC, Annex II, Labelling and PL	The CHMP having reviewed the evidence of compliance with the specific obligations submitted by the MAH and having re-assessed the benefit/risk profile of the medicinal product recommended that no amendment of Annexes I and III to Commission Decision is necessary. The CHMP agreed to revise the specific obligations set out in Annex II.C to the Commission Decision. On the basis of the data submitted

					since the Marketing Authorisation, the benefit/risk for Cystagon remained positive. The CHMP therefore recommended the updating of the Community Marketing Authorisation for Cystagon and that the authorisation should remain under exceptional circumstances.
IA/0024	IA_09_Deletion of manufacturing site	19/12/2003	n/a	Annex II and PL	
II/0022	Annual reassessment Update of Summary of Product Characteristics and Package Leaflet	25/04/2003	15/07/2003	SmPC and PL	Following the assessment of the 7th PSUR during the Marketing Authorisation Renewal the CHMP requested the MAH to submit a variation to update section 4.8 of the SPC in order to include nephritic syndrome and to amend this section to be in line with SPC guideline. The following terms were also added to section 4.8 of the SPC: rash, hallucinations, and convulsions. Section 4 of the Package Leaflet was updated accordingly. The sentence regarding the restriction of prescription to specialist was moved from section 4.1 to 4.2 in line with SPC guideline.
R/0021	Renewal of the marketing authorisation.	27/06/2002	10/10/2002	SmPC, Annex II, Labelling and PL	
S/0020	Annual re-assessment.	18/10/2001	28/01/2002		
II/0018	Update of Summary of Product Characteristics	25/01/2001	03/05/2001	SmPC	
I/0019	26_Changes to comply with supplements to pharmacopoeias	23/03/2001	06/04/2001		
S/0017	Annual re-assessment.	21/09/2000	29/01/2001	Annex II	

I/0014	01_Change following modification(s) of the manufacturing authorisation(s)	21/09/2000	29/11/2000	Annex II and PL	
I/0016	08_Change in the qualitative composition of immediate packaging material	21/09/2000	12/10/2000		
I/0015	32_Change of imprints/bossing/marking on tablets/printing on capsules, incl. addition/change of inks	21/09/2000	12/10/2000		
I/0013	15a_Change in IPCs applied during the manufacture of the product	14/07/2000	02/08/2000		
S/0011	Annual re-assessment.	21/10/1999	16/03/2000	Annex II	
II/0010	Update of Summary of Product Characteristics and Package Leaflet	18/11/1999	16/03/2000	SmPC, Labelling and PL	
I/0012	14_Change in specifications of active substance	10/02/2000	01/03/2000		
I/0006	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	23/04/1999	01/07/1999	PL	
I/0009	24_Change in test procedure of active substance	09/06/1999	18/06/1999		
I/0008	14_Change in specifications of active substance	09/06/1999	18/06/1999		
I/0007	08_Change in the qualitative composition of immediate packaging material	09/06/1999	18/06/1999		
S/0005	Annual re-assessment.	17/12/1998	19/04/1999	Annex II	

I/0004	17_Change in specification of the medicinal product	04/03/1998	n/a		
N/0003	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/01/1998	03/03/1998	Labelling and PL	
I/0002	24_Change in test procedure of active substance	05/12/1997	n/a		
I/0001	17_Change in specification of the medicinal product	05/12/1997	n/a		