Cancidas

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
N/0084	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/04/2024		PL	
N/0082	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/10/2023		Labelling	

[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).

IA/0081	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	11/07/2023	n/a		
N/0080	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/12/2022		PL	
II/0078	Submission of an updated RMP version 4.2 in order to remove safety concerns and align it with the EU GVP Module V (Revision 2). C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	29/09/2022	n/a		
PSUSA/576/202112	Periodic Safety Update EU Single assessment - caspofungin	01/09/2022	n/a		PRAC Recommendation - maintenance
IA/0079/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) 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	14/06/2022	n/a		

	intermediate used in the manufacture of the AS or manufacturer of a novel excipient				
WS/2193	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	02/06/2022	n/a		
N/0074	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/09/2021		PL	
IAIN/0073	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	15/02/2021	02/08/2021	Annex II and PL	
IB/0072	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	10/08/2020	02/08/2021	SmPC, Annex II, Labelling and PL	
PSUSA/576/201812	Periodic Safety Update EU Single assessment - caspofungin	11/07/2019	n/a		PRAC Recommendation - maintenance
IB/0070	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	25/02/2019	05/12/2019	SmPC and PL	
IB/0068	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/12/2018	05/12/2019	SmPC and PL	

IA/0069	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	10/12/2018	n/a		
T/0067	Transfer of Marketing Authorisation	17/07/2018	08/08/2018	SmPC, Labelling and PL	
IB/0066	B.II.c.3.z - Change in source of an excipient or reagent with TSE risk - Other variation	12/06/2018	n/a		
IB/0065	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	04/06/2018	n/a		
PSUSA/576/201612	Periodic Safety Update EU Single assessment - caspofungin	01/09/2017	n/a		PRAC Recommendation - maintenance
N/0063	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/02/2017	24/04/2017	Labelling	
IA/0062	A.7 - Administrative change - Deletion of manufacturing sites	05/01/2017	n/a		
II/0061	Update of sections 4.4, 4.8 of the SmPC in order to add a warning on serious cutaneous reactions and to include the new ADRs "toxic epidermal necrolysis" and "Stevens-Johnson Syndrome" with the frequency 'not known' based on the post-marketing experience. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local	23/06/2016	24/04/2017	SmPC, Annex II, Labelling and PL	In this variation the Product information has been updated to include a warning that cases of Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported after post-marketing use of caspofungin. Caution should apply in patients with history of allergic skin reaction.

	representatives in the Package Leaflet and to bring the PI in line with the QRD template version 9.1. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0060	Update of section 5.1 of the SmPC in order to add guidance on the use of anidulafungin and/or micafungin breakpoints as an alternative susceptibility testing for caspofungin. In addition, the Marketing authorisation holder (MAH) took the opportunity to update 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	26/05/2016	24/04/2017	SmPC and PL	The MAH updated the PI with information from revised EUCAST Antifungal Clinical Breakpoint Tables (v. 7.0) in order to harmonise information on Clinical breakpoints for the echinocandins and Candida and to provide guidance to clinicians. EUCAST breakpoints have not yet been established for caspofungin, due to significant inter laboratory variation in MIC ranges for caspofungin. In lieu of breakpoints, Candida isolates that are susceptible to anidulafungin as well as micafungin should be considered susceptible to caspofungin. Similarly, C. parapsilosis isolates intermediate to anidulafungin and micafungin can be regarded intermediate to caspofungin.
PSUSA/576/201412	Periodic Safety Update EU Single assessment - caspofungin	09/07/2015	n/a		PRAC Recommendation - maintenance
II/0058	Update of section 4.8 of the SmPC in order to add clinical ADR term, "gamma-glutamyltransferase increased" in the "Paediatric patients" section as the cumulative review of postmarketing reports of GGT increased includes reports from paediatric and adult patients. The requested variation leads to amendments to the Summary of Product Characteristics.	26/03/2015	10/06/2015	SmPC	

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0056	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	16/09/2014	10/06/2015	SmPC	
IA/0057	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	19/08/2014	n/a		
IB/0055	To align the Product Information to the latest QRD update version 9.0. In addition, following the EMA request the Labelling and the Package Leaflet has been made compliant with regards to the used terms for the active substance. Accordingly, from the Labelling and the Package Leaflet, the words "(as acetate)" have been removed after the active substance. Finally the contact details for the local representative for Portugal in the Package Leaflet have been updated. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	04/06/2014	10/06/2015	SmPC, Annex II, Labelling and PL	
IG/0366	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	08/11/2013	n/a		

	PSMF location				
N/0053	Inclusion of additional local representative of the marketing authorisation holder for the new member state Croatia. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/07/2013	23/04/2014	PL	
II/0052	Changes to the manufacturing process of the finished product. B.II.b.3.b - Change in the manufacturing process of the finished product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product	30/05/2013	30/05/2013		
II/0051	Update of section 4.4 of the SmPC in order to add a warning regarding hypersensitivity and anaphylaxis events as listed in section 4.8 and to provide guidance to healthcare professionals if these events occur. Section 4.8 was updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the PL. Furthermore, Annex II is being brought in line with the latest QRD template version. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	25/04/2013	23/04/2014	SmPC, Annex II and PL	No new safety data were provided in this variation application, however the CHMP agrees that, in order to improve and provide guidance to healthcare professionals caring for patients who may experience a hypersensitivity or anaphylactic reaction as listed in section 4.8, the section 4.4 of the Cancidas SmPC should be updated to include a warning. During the assessment of the procedure, a fatal case of complete heart block after caspofungin treatment was reviewed. It has been reported in a neutropenic patient with aspergillosis. The report is confounded by the prior use of daunorubin and cytarabine. The possibility remains that the complete atrioventricular block may have been caused by systemic aspergillosis, although pericardial and

					myocardial aspergillosis are rare manifestations of systemic aspergillosis which can result in arrhythmias and death. Another explanation could be that histamine released by caspofungin caused the AV block in the patient. Other reports of atrioventricular block were found in the safety database, however they occurred several days to weeks after caspofungin treatment initiation and were confounded by concomitant medication or concurrent conditions. Following the review of these atrioventricular cases, the CHMP agrees with the MAH that currently no changes to the safety data are warranted and the benefit-risk of Cancidas is unchanged. However the CHMP considered that the MAH should monitor this adverse event and provide the relevant safety data within the next PSUR.
IA/0050	A.7 - Administrative change - Deletion of manufacturing sites	26/10/2012	n/a		
IG/0182	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/08/2012	n/a		
IB/0048	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/07/2012	29/11/2012	SmPC, Annex II, Labelling and PL	
IB/0047	C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH	14/05/2012	29/10/2013	SmPC and PL	
N/0044	Update of details of the local representatives for	16/01/2012	29/10/2013	PL	

	Hungary, Portugal, Spain, France, Ireland, Iceland and the United Kingdom in the PL. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
IA/0046/G	This was an application for a group of variations. 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.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	07/12/2011	n/a		
IG/0112	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	11/10/2011	n/a		
R/0043	Renewal of the marketing authorisation.	23/06/2011	07/09/2011	SmPC, Annex II, Labelling and PL	Based on the CHMP review of the available information and on the basis of a re-evaluation of the benefit risk balance, the CHMP is of the opinion that the quality, safety and efficacy of Cancidas continues to be adequately and sufficiently demonstrated and therefore considered that the benefit risk profile of Cancidas continues to be favourable. Considering the safety profile of Cancidas, the CHMP agrees that that the Cancidas should continue to be closely monitored. The remaining safety concerns for Cancidas are in particular hepatitis and pancreatitis. Consequently, the

					MAH should continue to provide PSURs to the CHMP every 2 years, unless otherwise specified. The CHMP is of the opinion that the renewal can be granted with unlimited validity.
II/0042	Following spontaneous report cases received by the MAH, update of section 4.8 Undesirable effects to add the adverse event 'angio-oedema'. The PL was amended accordingly. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	21/10/2010	26/11/2010	SmPC and PL	The MAH's post-marketing adverse effect database from 14.12.2000 to 19.05.2010 contains 3 reports of angio-oedema. One of them, occurring half an hour after the initiation of the caspofungin therapy, describes angio-oedema accompanied by respiratory compromise and hypoxemia and a positive dechallenge. The CHMP agreed that the healthcare providers should be informed of this adverse event and endorsed the addition of 'angio-oedema' to the undesirable effects section of the SmPC. The PL was updated accordingly.
IG/0027/G	This was an application for a group of variations. C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities 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	10/11/2010	n/a	Annex II	
IA/0041/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS	01/07/2010	n/a		

	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)				
II/0039	Addition of an alternative manufcaturer for the finished product. Change(s) to the manufacturing process for the finished product	21/01/2010	11/03/2010	Annex II and PL	
IA/0040	IA_09_Deletion of manufacturing site	02/12/2009	n/a		
II/0038	Update of the Detailed Description of the Pharmacovigilance System (DDPS). Annex II has been updated to reflect the version number of the DDPS. Update of DDPS (Pharmacovigilance)	25/06/2009	23/07/2009	Annex II	The MAH updated its DDPS and submitted therefore this type II variation. The CHMP considers that the Pharmacovigilance System as described by the MAH fulfils the requirements and is considered acceptable.
II/0037	Update of section 4.8 of the SPC to list the increase in liver enzymes and changes in blood cells under the respective SOCs following the assessment of the PSUR covering the period from 14 December 2005 to 13 December 2007. The corresponding changes were made to the Package Leaflet. Update of Summary of Product Characteristics and Package Leaflet	29/05/2009	01/07/2009	SmPC and PL	Following the assessment of the PSUR 10 (14 Dec 2005 to 13 Dec 2007) a Type II variation was submitted to update the SPC section 4.8. The CHMP also requested the MAH to perform a throughout review of all cases with serious and non serious liver ADRs. In addition, the CHMP requested that the SPC be updated to list increase in liver enzymes and changes in blood cells under the respective SOCs (Hepatobiliary disorders and blood lymphatic system disorders). In addition, the classification of Adverse Events between the adult and paediatric sections is aligned. A minor editorial correction in the Package Leaflet is also

					included.
II/0035	Update of sections 4.5, 4.8, 4.9 and 5.1 of the SPC based on pharmacokinetics, safety and efficacy data on caspofungin at three times the authorised daily dose (150 mg) and postmarketing data on higher than approved doses. The Package Leaflet was updated accordingly. Update of Summary of Product Characteristics and Package Leaflet	29/05/2009	01/07/2009	SmPC and PL	Based on new pharmacokinetic, safety and efficacy data the daily dose of caspofungin of 150 mg is being approved. The objective of this variation was to reflect mainly the safety but also the pharmacokinetic and efficacy experience of a higher dosage of caspofungin at three times the authorised daily maintenance dose (i.e. 150 mg daily) tested in patients with invasive candidiasis. Although the submitted data had some limitations and they do not fully permit to recommend the use of this high dose of caspofungin in specific patient populations, it is considered that there may be patients who might benefit from this increased dosage. The relevant sections of the SPC have been updated to reflect the data.
IA/0036	IA_47_a_Deletion of a pharmaceutical form	19/12/2008	n/a	SmPC, Labelling and PL	
II/0033	Extension of the indication to include the paediatric population. Paediatric Art. 8 - Changes to the product information	25/09/2008	26/11/2008	SmPC and PL	Pleases see the Assessment report Cancidas-379-II-33-AR
IA/0034	IA_05_Change in the name and/or address of a manufacturer of the finished product	06/08/2008	n/a		
IA/0032	IA_05_Change in the name and/or address of a manufacturer of the finished product	07/11/2007	n/a		

N/0031	The MAH completed the list of local representatives in the PL to include the two new EU Member States (Bulgaria and Romania) according to the latest EMEA/QRD template. Furthermore the MAH to the this oportunity to update contact details of the local representatives. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/01/2007	n/a	PL	
R/0030	Renewal of the marketing authorisation.	27/07/2006	29/09/2006	SmPC, Annex II, Labelling and PL	
II/0028	Quality changes	23/03/2006	29/03/2006		Change to the manufacturing process for the active substance.
S/0027	Fourth annual reassessment.	26/01/2006	23/03/2006	Annex II	On the basis of the data submitted, the risk/benefit balance in the treatment of invasive candidiasis in adult patients or treatment of invasive aspergillosis in adult patients who are refractory to or intolerant of amphotericin B, lipid formulations of amphotericin B and/or itraconazole (Refractoriness is defined as progression of infection or failure to improve after a minimum of 7 days of prior therapeutic doses of effective antifungal therapy for Cancidas) or empirical therapy for presumed fungal infections (such as Candida or Aspergillus) in febrile, neutropaenic adult patients, remains positive. This annual reassessment report provides the final safety data from 53 patients enrolled in a combination therapy

					study. These safety data remain limited, in particular since most of these patients received caspofungin together with voriconazole (N=30), and only very few patients received either an amphotericin formulation (N=16) or itraconazole (N=7) in combination with caspofungin. As requested by the CHMP, the MAH will address the need for a further comparative study in the Renewal application. The CHMP agreed to revise the specific obligations set out in Annex II.C to the Commission Decision. The CHMP agreed that the Marketing Authorisation should remain under exceptional circumstances.
IA/0029	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	09/03/2006	n/a		
S/0026	Third annual reassessment.	17/02/2005	10/05/2005	Annex II	On the basis of the data submitted, the risk/benefit in the treatment of invasive candidiasis in adult patients or treatment of invasive aspergillosis in adult patients who are refractory to or intolerant of amphotericin B, lipid formulations of amphotericin B and/or itraconazole (Refractoriness is defined as progression of infection or failure to improve after a minimum of 7 days of prior therapeutic doses of effective antifungal therapy for Cancidas) or empirical therapy for presumed fungal infections (such as Candida or Aspergillus) in febrile, neutropaenic adult patients, remains positive. This annual reassessment report includes new safety data

					from 52 patients with invasive aspergillosis enrolled in a combination therapy study . These safety data present the first preliminary results from Cancidas given in combination with other antifungal agents in clinical trials. The final data, including the 12-month follow-up visit, will be submitted to the CHMP by 1Q2007. The CHMP agreed to revise the specific obligations set out in Annex II.C to the Commission Decision. The CHMP agreed that the Marketing Authorisation should remain under exceptional circumstances.
II/0025	Quality changes. Quality changes	21/10/2004	28/10/2004		Quality changes related to the finished product.
II/0020	Further to findings from clinical studies on concomitant use of caspofungin and cyclosporin A. Update of Summary of Product Characteristics and Package Leaflet	16/09/2004	28/10/2004	SmPC, Annex II, Labelling and PL	The SPC was updated in its sections 4.4 "Special warnings and special precautions for use" and 4.5 "Interaction with other medicinal products and others forms of interactions" to include information on the concomitant use of caspofungin with cyclosporin A, following findings from clinical studies on healthy volunteers. The results showed an increase of the AUC of caspofungin by approximately 35% when co-administered with cyclosporine A. Furthermore, despite the fact that no serious hepatic adverse events were noted in a retrospective study of 40 patients treated during marketed use with caspofungin and/or cyclosporin for 1 to 290 days, close monitoring of liver enzymes should be considered if the two medicinal products are used concomitantly.

					The SPC was also updated in its section 4.8 "Undesirable effects" following the assessment of the PSUR covering the period 14.06.2003 - 13.12.2003 to replace "low platelets", "low potassium", and "low sodium" by "thrombocytopenia", "hypokalemia" and "hyponatremia". Finally, the MAH included editorial changes in the section 6.6 "Instructions for use and handling" of the SPC to align Cancidas 70mg to Cancidas 50mg.
IB/0022	IB_07_c_Replacement/add. of manufacturing site: All other manufacturing operations ex. batch release	12/10/2004	n/a		
IB/0023	IB_33_Minor change in the manufacture of the finished product	09/09/2004	n/a		
IA/0021	IA_32_a_Change in batch size of the finished product - up to 10-fold	18/05/2004	n/a		
II/0017	To include "Empirical therapy for presumed fungal infections (such as Candida and Aspergillus) in febrile, neutropaenic adult patients". Extension of Indication	24/03/2004	13/05/2004	SmPC and PL	Please refer to the Scientific discussion:Cancidas-H-379-II-17
S/0018	Second annual re-assessment	26/02/2004	11/05/2004	Annex II	On the basis of the data submitted , the risk/benefit in the treatment of invasive candidiasis in non-neutropaenic adult patients or treatment of invasive aspergillosis in adult patients who are refractory to or intolerant of amphotericin B, lipid formulations of amphotericin B and/or itraconazole (Refractoriness is defined as progression of infection or failure to improve after a minimum of 7 days of prior

					therapeutic doses of effective antifungal therapyfor Cancidas) remains positive. There was however the necessity to update the SPC in the variation II/17, to include information that doses higher than 70 mg daily have not been adequately studied. The CPMP agreed to revise the specific obligations set out in Annex II.C to the Commission Decision. The CPMP agreed that the Marketing Authorisation should remain under exceptional circumstances.
IB/0019	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition)	19/02/2004	n/a		
II/0016	Further to the findings from testing of isolates as part of a microbiological surveillance program. Update of Summary of Product Characteristics	20/11/2003	05/02/2004	SmPC	The section 5.1 "Pharmacodynamic properties" of the SPC has been modified further to an update regarding surveillance monitoring for clinical isolates with reduced susceptibility to caspofungin in compliance with a post-approval commitment.
II/0015	Further to post-marketing surveillance. Update of Summary of Product Characteristics and Package Leaflet	20/11/2003	05/02/2004	SmPC and PL	The section 4.8 "Undesirable effects" of the SPC has been updated as follows: - removal of reference to "one case of" anaphylaxis, since reports of hypersensitivity exhibited features of systemic involvement that could be argued to be consistent with initial symptoms of anaphylaxis. In addition, the references to "dyspnoea, stridor, and worsening of rash", which applied to one specific patient, were deleted since in general, anaphylaxis may have different presentations. - addition of "hypercalcaemia", "hepatic dysfonction", "swelling" and "peripheral oedema" as post-marketing reactions. Together with the addition of hypercalcaemia as a post-marketing reaction, the MAH proposed to delete

					"high calcium" from the adverse events described in the SPC due to a reporting rate of 'only' 0.5%. The section 4 of the PL has been updated accordingly. The section 6.6 "Instructions for use and handling" of the 70mg vial SPC has been updated to include information on how to reconstitute 35mg of 70mg vials for patients with moderate hepatic insufficiency.
I/0014	11_Change in or addition of manufacturer(s) of active substance	04/07/2003	17/07/2003		
S/0012	First annual re-assessment	23/01/2003	19/05/2003	Annex II	On the basis of the data submitted since the Marketing Authorisation and taking into consideration the safety data presented in the 1st PSUR covering the period from 14.06.2001 to 13.12.2001, the overall risk/benefit of Caspofungin MSD has not been changed and remains favourable. The CPMP agreed to revise the specific obligations set out in Annex II.C to the Commission Decision. The CPMP agreed that the Marketing Authorisation should remain under exceptional circumstances.
I/0013	02_Change in the name of the medicinal product (either invented name of common name)	04/03/2003	09/04/2003	SmPC, Labelling and PL	
I/0010	25_Change in test procedures of the medicinal product	10/02/2003	26/02/2003		
I/0009	25_Change in test procedures of the medicinal product	10/02/2003	26/02/2003		

II/0002	To include "Invasive Candidiasis in non-neutropenic patients". Extension of Indication	21/11/2002	17/02/2003	SmPC and PL	Please refer to the Scientific discussion:Cancidas-H-379-II-02
I/0008	31_Change in container shape	08/11/2002	12/11/2002		
I/0006	12_Minor change of manufacturing process of the active substance	08/11/2002	12/11/2002		
I/0005	11_Change in or addition of manufacturer(s) of active substance	08/11/2002	12/11/2002		
I/0007	13_Batch size of active substance	23/09/2002	07/10/2002		
I/0004	16_Change in the batch size of finished product	16/08/2002	29/08/2002		
I/0003	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	02/08/2002	29/08/2002		