Vidaza

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
II/0057	Update of section 4.2 of the SmPC in order to include a statement advising health care professionals not to interchange azacitidine formulations (injectable versus oral), and update section 4.6 of the SmPC to revise the recommended duration of contraception use for women and men. The Package Leaflet is	28/04/2022		SmPC and PL	Due to differences in the exposure, the dose and schedule recommendations for oral azacitidine are different from those for injectable azacytidine and should not be used interchangeably. Women of childbearing potential have to use effective contraception for at least 6 months after treatment. Men

[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).

	updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				are advised not to father a child while receiving treatment and must use effective contraception during and for at least 3 months after treatment. For more information, please refer to the Summary of Product Characteristics.
PSUSA/274/202105	Periodic Safety Update EU Single assessment - azacitidine	27/01/2022	28/03/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/274/202105.
IAIN/0056	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	18/11/2021	28/03/2022	Annex II and PL	
IAIN/0054	C.I.11.a - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of wording agreed by the competent authority	14/07/2021	n/a		
T/0053	Transfer of Marketing Authorisation	12/05/2021	28/06/2021	SmPC, Labelling and PL	
IB/0052	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	23/02/2021	28/06/2021	SmPC	
IG/1265	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor	18/11/2020	n/a		

	changes to an approved test procedure				
WS/1934	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	06/11/2020	28/06/2021	SmPC	
IB/0049/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.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products 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	06/05/2020	n/a		
IB/0048	B.II.d.1.g - Change in the specification parameters and/or limits of the finished product - Addition or	27/05/2019	n/a		

	replacement (excluding biological or immunological product) of a specification parameter wit its corresponding test method as a result of a safety or quality issue				
PSUSA/274/201805	Periodic Safety Update EU Single assessment - azacitidine	31/01/2019	02/04/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/274/201805.
IA/0047	A.7 - Administrative change - Deletion of manufacturing sites	11/03/2019	08/04/2020	Annex II and PL	
IAIN/0046	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	12/10/2018	02/04/2019	Annex II and PL	
IB/0043	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	11/09/2018	n/a		
IA/0044	A.7 - Administrative change - Deletion of manufacturing sites	17/08/2018	n/a		
T/0042	Transfer of Marketing Authorisation	22/06/2018	30/07/2018	SmPC, Labelling and PL	
IB/0041	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/05/2017	12/04/2018	SmPC and PL	

IB/0040	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	20/03/2017	12/04/2018	SmPC, Annex II, Labelling and PL	
IB/0039/G	This was an application for a group of variations. B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.g - Change in the specification parameters and/or limits of the finished product - Addition or replacement (excluding biological or immunological product) of a specification parameter wit its corresponding test method as a result of a safety or quality issue	10/01/2017	n/a		
IA/0038/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	25/10/2016	n/a		
IA/0037	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)	09/06/2016	n/a		

IB/0036	C.I.6.z - Change(s) to therapeutic indication(s) - Other variation	08/06/2016	29/06/2016	SmPC	
PSUSA/274/201505	Periodic Safety Update EU Single assessment - azacitidine	28/01/2016	30/03/2016	SmPC and PL	Please refer to Vidaza PSUSA/00000274/201505 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
II/0030	Extension of Indication to add treatment of adult patients aged 65 years or older who are not eligible for HSCT with AML with >30% marrow blasts according to the WHO classification, based on the pivotal phase III study AZA- AML-001. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet. A revised RMP version 12.0 was agreed during the procedure. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	24/09/2015	28/10/2015	SmPC and PL	For further information please refer to the published Assessment Report: Vidaza H-978-II-30-AR.
IA/0035	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	21/10/2015	n/a		
IA/0034/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of	21/08/2015	n/a		

	manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites				
IG/0590	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	22/07/2015	n/a		
IA/0031	A.7 - Administrative change - Deletion of manufacturing sites	15/04/2015	n/a		
PSUV/0029	Periodic Safety Update	18/12/2014	17/02/2015	SmPC and PL	Please refer to Vidaza PSUV-29 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
II/0028	Update of sections 4.2, 4.4 and 5.2 of the SmPC, upon request by the CHMP following the assessment of Study AZA PH US 2007 PK 006 (FU2 006.1), with new information regarding the pharmacokinetics of azacitidine as well as pharmacokinetics presented per renal function status. Further, the MAH took the opportunity to implement editorial changes in the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/09/2014	27/10/2014	SmPC	Following subcutaneous administration of a single 75 mg/m2 dose, azacitidine was rapidly absorbed with peak plasma concentrations of 750 ± 403 ng/mL occurring at 0.5 h after dosing (the first sampling point). The absolute bioavailability of azacitidine after subcutaneous relative to intravenous administration (single 75 mg/m2 doses) was approximately 89% based on area under the curve (AUC). Area under the curve and maximum plasma concentration (Cmax) of subcutaneous admiminstration of azacitidine were approximately proportional within the 25 to 100 mg/m2 dose range. Renal impairment has no major effect on the pharmacokinetic exposure of azacitidine after single and multiple subcutaneous administrations. Following subcutaneous administration of a single 75 mg/m2 dose, mean exposure values (AUC and Cmax) from subjects with

					mild, moderate and severe renal impairment were increased by 11-21%, 15-27%, and 41-66%, respectively, compared to normal renal function subjects. However, exposure was within the same general range of exposures observed for subjects with normal renal function. Azacitidine can be administered to patients with renal impairment without initial dose adjustment provided these patients are monitored for toxicity since azacitidine and/or its metabolites are primarily excreted by the kidney. Thus, azacitidine can be administered to patients with renal impairment without initial dose adjustment. Although no clinically relevant differences in the frequency of adverse reactions were noted between subjects with normal renal function compared to those with renal impairment, patients with renal impairment should be closely monitored for toxicity since azacitidine and/or its metabolites are primarily excreted by the kidney.
IA/0027	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	21/05/2014	n/a		
R/0024	Renewal of the marketing authorisation.	19/09/2013	13/11/2013	SmPC, Annex II, Labelling and PL	Considering the cumulative experience with Vidaza, it can be concluded that the benefit-risk balance remains positive. Despite the recognition of several new ADRs in the post-marketing setting, the safety profile can be considered acceptable for the claimed indication. It is recommended that the renewal be granted with unlimited validity.
IB/0026/G	This was an application for a group of variations.	16/08/2013	n/a		

	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.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test				
IA/0025/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	03/07/2013	n/a		
IA/0023/G	This was an application for a group of variations. B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier A.7 - Administrative change - Deletion of	05/02/2013	n/a		

	manufacturing sites				
IA/0022	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 currently approved batch size	13/12/2012	n/a		
IB/0021	A.7 - Administrative change - Deletion of manufacturing sites	16/07/2012	n/a		
IA/0020/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place A.4 - Administrative change - Change in the name	14/06/2012	08/10/2012	Annex II and PL	

	and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS 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) A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites				
A20/0017	Pursuant to Article 20 of Regulation (EC) No 726/2004, the European Commission requested on 17 November 2011, the opinion of the CHMP on measures necessary to ensure the quality and the safe use of the above mentioned medicinal product further to the inspection findings at the Ben Venue Laboratories (BVL) manufacturing site located in Bedford, Ohio (USA).	16/02/2012	25/05/2012		Please refer to the assessment report: EMEA/H/C/978/A-20/0017
IG/0168/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV	24/05/2012	n/a		

	C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.f - Changes to an existing pharmacovigilance system as described in the DDPS - Deletion of topics covered by written procedure(s) describing pharmacovigilance activities 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				
II/0018	Update of section 4.8 of the SmPC to include a new adverse drug reaction of "cellulitis" with a frequency of "common" following the request of CHMP further to the assessment of PSUR 10. The Package Leaflet has been updated in accordance. The MAH also took the opportunity to make minor editorial changes to section 4.2 and to update section 5.3 to include an additional foetal abnormality observed in rats that was omitted from the SmPC in the original MAA. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article	15/03/2012	20/04/2012	SmPC and PL	The reporting rate of cellulitis in the latest PSUR 010 and in the cumulative reporting rate for Vidaza was found to be 0.046%. In total, 47 adverse drug reactions of cellulitis were reported, with 37 events reported as serious and 10 events as non-serious. While there were 8 cases with fatal outcome, cellulitis was reported along with other infections and myelosuppression and other confounding factors such as diabetes mellitus, skin disorders and various malignacies. Based on the data submitted, the CHMP assessed that a causal relationship between azacitidine and cellulitis was probable. Following the CHMP assessment of the PSUR, the MAH proposed to update the SmPC to include "cellulitis" as a new adverse drug reaction in section

	45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				4.8 of the SmPC and update the package leaflet accordingly. The MAH also took the opportunity to update section 5.3 to include an additional foetal abnormality observed in rats that was omitted from the SmPC in the original MAA.
II/0011	At the request of the CHMP following the assessment of the 4th PSUR, the MAH proposed the update of sections 4.4 and 4.8 of the SmPC in order to add a warning on laboratory tests to be performed prior to therapy and to include "injection site necrosis" and "tumour lysis syndrome" as rare adverse drug reactions. The Package Leaflet was proposed to be updated accordingly. In addition, the MAH took the opportunity to implement a clarification of the wording in section 5.2 of the SPC. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH	17/11/2011	22/12/2011	SmPC and PL	As requested by the CHMP, following the assessment of 4th EU periodic safety update report, the MAH applied to include injection site necrosis and tumour lysis syndrome as rare adverse reactions in section 4.8 of the SmPC and section 4 of package leaflet and to include a warning in section 4.4. of the SmPC tests to perform laboratory tests regarding liver and renal function prior to treatment with Vidaza. Furthermore, a statement in section 5.2 (Metabolism) of the SmPC was modified for additional clarity to the prescriber.
IA/0015	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	11/11/2011	n/a		
IG/0100/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance	23/08/2011	n/a		

	system as described in the DDPS - Change in the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.f - Changes to an existing pharmacovigilance system as described in the DDPS - Deletion of topics covered by written procedure(s) describing pharmacovigilance activities 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				
IB/0014/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are	23/08/2011	n/a		

	aseptically manufactured) excluding biological/ immunological medicinal products B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place				
II/0009	Update of section 4.8 of the SmPC to include Interstitial Lung Disease as requested by the CHMP following the assessment of the last PSUR and additional editorial amendments. The package leaflet was updated accordingly. The wording in Section 5.2 of the SmPC was amended to improve clarity. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH	23/06/2011	10/08/2011	SmPC and PL	The Marketing Authorisation Holder (MAH) submitted a periodic safety update report (PSUR) covering the period of 19 May 2010 to 18 November 2010 on 10 January 2011. One of the findings from this PSUR identified interstitial lung disease as a safety signal and as consequence was being added to the Vidaza company core data sheet (CCDS). In light of the new safety signal, the MAH was requested to submit a variation to update section 4.8 of the SmPC to include Interstitial Lung Disease as an adverse reaction. As a result, the package leaflet was also updated to reflect the additional key symptoms associated with interstitial lung disease.

					Furthermore, the wording in Section 5.2 of the Vidaza SmPC was amended to improve clarity.
IB/0013	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	25/07/2011	n/a	SmPC and Labelling	The MAH applied to implement the CHMP conclusions regarding Vidaza Follow up Measure 005. In addition, the MAH took the opportunity to introduce two minor lingusitc changes to the Slovenian and Swedish Vial "inner" label text.
IA/0012/G	This was an application for a group of variations. C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.f - Changes to an existing pharmacovigilance system as described in the DDPS - Deletion of topics covered by written procedure(s) describing pharmacovigilance activities C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site	21/06/2011	n/a		

	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				
II/0007	Update of the SmPC to include information on the risk of fatal infections in section 4.8 following the assessment of PSUR 3/PSU 014. The package leaflet has been updated accordingly. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/04/2011	14/06/2011	SmPC and PL	Further to the assessment of the third periodic safety update report covering the period of 19 November 2009 through 18 May 2010 (PSUR 3/PSU 0014) the MAH has updated the Summary of Product Characteristics (SmPC) in order to include information on the risk of fatal infections such as neutropenic sepsis and pneumonia in section 4.8. In addition the package leaflet has been updated accordingly.
II/0005	Update of the SmPC to include a precaution not to use filters after the product is reconstituted in sections 4.2 and 6.6, to update the recommendations to patients with hepatic and renal impairment in section 4.4 and to include information on hepatic and renal adverse reactions in section 4.8. All changes were requested following the assessment of PSUR 2/PSU013. The Package leaflet has been updated accordingly. In addition, minor editorial corrections have been included in Section 5.2. Furthermore, changes were made to the SmPC, Annex II and Package Leaflet to bring them in line with the current QRD template and to improve internal consistency. C.I.3.b - Implementation of change(s) requested	14/04/2011	14/06/2011	SmPC, Annex II and PL	Further to the assessment of the second periodic safety update report covering the period of 19 May 2009 to 18 November 2009 (PSUR 2/PSU 0013) the MAH has updated the Summary of Product Characteristics (SmPC) in order to include a precaution not to use filters after the product is reconstituted in sections 4.2 and 6.6, to update the recommendations to patients with hepatic and renal impairment in section 4.4 and to include information on hepatic and renal adverse reactions in section 4.8, some of which can be life-threatening.

	following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				
IA/0010/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.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing	08/06/2011	n/a	SmPC, Annex II, Labelling and PL	
IB/0008/G	This was an application for a group of variations. B.II.f.1.b.3 - Stability of FP - Extension of the shelf life of the finished product - After dilution or reconstitution (supported by real time data) B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	03/05/2011	n/a	SmPC, Labelling and PL	
IB/0006/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.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	15/11/2010	n/a		

	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition				
IA/0004/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD 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	09/07/2010	n/a	Annex II	
IB/0003	C.I.3.a - Implementation of change(s) requested	01/07/2010	n/a	SmPC	To include the study results on the interaction of azacitidine

	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				with CYP2B6 and CYP2C8 in section 5.2 of the SmPC following the assessment of FUM 004.
II/0001	Update of the Detailed Description of the Pharmacovigilance System (DDPS) to version 6.0, in light of a reorganisation within Celgene's Drug Safety Department concerning the risk management activities. Consequently, Annex II has been updated with the new version number of the agreed DDPS. The MAH has also taken the opportunity to correct a translation error that occurred in the Portuguese Package Leaflet. Update of DDPS (Pharmacovigilance)	24/09/2009	20/10/2009	Annex II	Update of the Detailed Description of the Pharmacovigilance System (DDPS) to version 6.0, in light of a reorganisation within Celgene's Drug Safety Department concerning the risk management activities. Consequently, Annex II has been updated with the new version number of the agreed DDPS. A translation error in the Portuguese Package Leaflet was corrected.
IA/0002	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	13/05/2009	n/a		