Vectibix

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/0105	Update of section 4.8 of the SmPC in order to update the information regarding the incidence of infusion-related reactions to reflect the total number of subjects. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial and administrative changes	13/03/2025		SmPC, Annex II and PL	SmPC new text Across monotherapy and combination mCRC clinical studies (n = 2 224), infusion-related reactions (occurring within 24 hours of any infusion), which may include signs and symptoms such as chills, fever or dyspnoea, were reported in approximately 1% of Vectibix-treated patients, of which

[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).

	to the PI and to bring it in line with the latest QRD template version 10.4, and 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				0.3% were severe (grade 3 and 4). For more information, please refer to the Summary of Product Characteristics.
IG/1743	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)	28/06/2024		Annex II	
PSUSA/2283/ 202209	Periodic Safety Update EU Single assessment - panitumumab	14/04/2023	n/a		PRAC Recommendation - maintenance
IB/0101	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	29/11/2022	n/a		
II/0099	B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	01/09/2022	n/a		
IA/0100	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	05/07/2022	14/10/2022	SmPC	
PSUSA/2283/ 202109	Periodic Safety Update EU Single assessment - panitumumab	05/05/2022	n/a		PRAC Recommendation - maintenance

II/0097	Update of section 4.4 and 4.8 of the SmPC in order to add the risk of corneal perforation to the risks of keratitis and ulcerative keratitis and to add corneal perforation (including keratorhexis, which also includes lowest level term corneal rupture) to the list of the adverse reactions, respectively following a safety evaluation. The package leaflet has been updated accordingly. In addition, the applicant took the opportunity to remove frequency information due to variations in case frequency in section 4.8 of the SmPC and section 4 of the PL. Furthermore, the PI is being brought in line with the latest QRD template (version 10.2) and minor editorial changes was made in the PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/10/2021	14/10/2022	SmPC and PL	
PSUSA/2283/ 202009	Periodic Safety Update EU Single assessment - panitumumab	20/05/2021	16/07/2021	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2283/202009.
PSUSA/2283/ 201909	Periodic Safety Update EU Single assessment - panitumumab	17/04/2020	n/a		PRAC Recommendation - maintenance
R/0094	Renewal of the marketing authorisation.	25/07/2019	23/09/2019	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Vectibix in the approved indication remains favourable and therefore recommended the renewal of the marketing

					authorisation with unlimited validity.
II/0093	Submission of RMP version 24 for panitumumab to align the important identified and potential risks and missing information in line with the EMA Guideline on Good Pharmacovigilance Practices Module V (Revision 2). As a consequence Section D in Annex II of the Product Information has been updated to reflect removal of the additional risk minimisation measures. The MAH is taking the opportunity to make corrections to the section 4.2 and 4.4 of the SmPC in order to include the table on dose modification previously located in section 4.4. Section 4.4 of the SmPC and package leaflet are also updated to implement the latest excipient guidelines recommendation wording on sodium Content. In addition, minor corrections are introduced on section 4.8 of the SmPC and to the list of representatives in the package leaflet 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	11/07/2019	23/09/2019	SmPC, Annex II, Labelling and PL	
PSUSA/2283/ 201809	Periodic Safety Update EU Single assessment - panitumumab	11/04/2019	n/a		PRAC Recommendation - maintenance
IB/0091/G	This was an application for a group of variations.	04/01/2019	n/a		

	A.7 - Administrative change - Deletion of manufacturing sites 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				
IG/0946	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	04/06/2018	18/12/2018	PL	
PSUSA/2283/ 201709	Periodic Safety Update EU Single assessment - panitumumab	12/04/2018	n/a		PRAC Recommendation - maintenance
II/0086	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/01/2018	18/12/2018	SmPC and PL	Section 4.4 and section 4.8 of the SmPC and relevant sections of the PL have been updated to reflect a re-analysis of the safety information. No additional risks were added to the Special warnings and precautions for use Section 4.4 and no adverse drug reactions were added or deleted from Section 4.8 of the Vectibix SmPC, changes mainly affect the overall incidence, severity, and seriousness of some of the currently labelled adverse drug reactions from pooling all indications into one table or a renaming of some of the terms.
IG/0853	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	10/11/2017	30/01/2018	Annex II and PL	

PSUSA/2283/ 201609	Periodic Safety Update EU Single assessment - panitumumab	05/05/2017	n/a		PRAC Recommendation - maintenance
II/0084	B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS	21/04/2017	n/a		
IAIN/0085	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	10/03/2017	30/01/2018	Annex II and PL	
II/0080	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	23/02/2017	30/01/2018	Annex II	The MAH has submitted data to fulfil the Annex II obligation "To submit results of biomarker analyses from the Vectibix clinical programme including Study 20080763 (according to Supplementary Statistical Analysis Plan dated 20 September 2013), Study 20070820 and Study 20060447. Analyses are subject to assay development, qualification, validation (where appropriate), sample availability, and appropriate informed consent". No relevant biomarker could be identified in addition to RAS from the results of these analyses and the results do not impact the current benefit-risk balance of Vectibix.
IA/0082	B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	28/11/2016	n/a		
II/0079	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	10/11/2016	27/02/2017	SmPC and PL	

	data				
IB/0081/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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	09/11/2016	n/a		
II/0076/G	This was an application for a group of variations. Update of section 6.6 of the SmPC to improve the descriptions of product appearance within the vial, a specification that the medicinal product should be withdrawn from vials via a 21-guage or smaller hypodermic needle, and further emphasis that Vectibix vials are intended for single-use only. In addition, the MAH is taking the opportunity to delete the 10 mL pack size (EU/1/07/423/002). B.II.e.5.b - Change in pack size of the finished product - Deletion of a pack size(s) C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	15/09/2016	27/02/2017	SmPC, Labelling and PL	
IA/0078	A.7 - Administrative change - Deletion of manufacturing sites	07/09/2016	n/a		

IB/0077	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	01/08/2016	n/a		
PSUSA/2283/ 201509	Periodic Safety Update EU Single assessment - panitumumab	14/04/2016	n/a		PRAC Recommendation - maintenance
IB/0075	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	31/03/2016	27/02/2017	Annex II	
II/0073	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	28/01/2016	n/a		
II/0072/G	This was an application for a group of variations. B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.a.4.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant effect on the overall quality of the AS 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.e - Change in the specification parameters and/or limits of an AS, starting	19/11/2015	n/a		

	material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol B.II.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 B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product B.II.d.3 - Variations related to the introduction of real-time release or parametric release in the manufacture of the finished product B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation				

II/0071	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	19/11/2015	n/a		
IA/0070	A.7 - Administrative change - Deletion of manufacturing sites	29/04/2015	13/04/2016	Annex II	
IB/0069	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	20/04/2015	n/a		
PSUSA/2283/ 201409	Periodic Safety Update EU Single assessment - panitumumab	10/04/2015	n/a		PRAC Recommendation - maintenance
II/0065	Extension of Indication to include use in the first-line setting in combination with FOLFIRI in the treatment of adult patients with wild-type RAS metastatic colorectal cancer (mCRC) for Vectibix; as a consequence, sections 4.1 and 5.1 of the SmPC have been updated. In addition, the MAH took the opportunity to introduce minor editorial updates throughout the PI. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	26/02/2015	31/03/2015	SmPC	Refer to scientific discussion Vectibix-H-C-741-II-65
WS/0660	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	26/03/2015	n/a		

	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				
IB/0068	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	05/03/2015	n/a		
R/0064	Renewal of the marketing authorisation.	20/11/2014	15/01/2015	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 Vectibix.
II/0063	Update of section 4.8 of the SmPC to add the new ADRs 'urinary tract infection', 'dry lips', 'hyperhidrosis' and 'dermatitis', and update of the efficacy data in section 5.1 of the SmPC based on the results from the wild-type RAS tumour analysis of study 20050181. Further, some of the Kirsten rat sarcoma-2 viral oncogene (KRAS) (exon 2) data has been deleted from Section 5.1 of the SmPC to ensure that concise and appropriate information is provided to physicians. The Package Leaflet has been updated	18/12/2014	31/03/2015	SmPC and PL	Study 20050181 was a phase III, randomized, open-label, well-controlled study designed to compare the efficacy of panitumumab in combination with FOLFIRI to the efficacy of FOLFIRI alone as second-line treatment for mCRC. The second-line indication was based on this study, the primary analysis of which was conducted by KRAS exon 2 status. A predefined retrospective subset analysis of 586 patients of the 597 patients with wild-type KRAS (exon 2) mCRC was performed, where tumour samples from these patients were tested for additional RAS and BRAF mutations. The

	accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				RAS/BRAF ascertainment was 85% (1014 of 1186 randomized patients). The incidence of these additional RAS mutations (KRAS exons 3, 4 and NRAS exons 2, 3, 4) in the wild-type KRAS (exon 2) population was approximately 19%. The incidence of BRAF exon 15 mutation in the wild-type KRAS (exon 2) population was approximately 8%. Among patients with wild-type RAS mCRC, PFS, OS, and ORR were improved for subjects receiving panitumumab plus chemotherapy (FOLFOX or FOLFIRI) compared with those receiving chemotherapy alone. Patients with additional RAS mutations beyond KRAS exon 2 were unlikely to benefit from the addition of panitumumab to FOLFIRI and a detrimental effect was seen with the addition of panitumumab to FOLFOX in these patients. BRAF mutations in exon 15 were found to be prognostic of worse outcome. BRAF mutations were not predictive of the outcome for panitumumab treatment in combination with FOLFOX or FOLFIRI. In summary, the results of Study 20050181 confirmed previous results showing that the benefit of panitumumab is confined to wild-type RAS tumours, as already reflected in the current indication for Vectibix.
PSUV/0062	Periodic Safety Update	06/11/2014	n/a		PRAC Recommendation - maintenance
N/0061	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/05/2014	05/12/2014	PL	
IB/0060	B.II.g.4.b - Changes to an approved change management protocol - Minor changes that do not change the strategy defined in the protocol	12/05/2014	n/a		

PSUV/0057	Periodic Safety Update	08/05/2014	n/a		PRAC Recommendation - maintenance
II/0059/G	This was an application for a group of variations. Changes of manufacturing sites responsible for quality control testing of the finished product. B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method A.7 - Administrative change - Deletion of manufacturing sites	25/04/2014	n/a		
II/0056	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	25/04/2014	05/12/2014	SmPC and PL	
R/0054	Renewal of the marketing authorisation.	19/12/2013	21/02/2014	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 and therefore recommends the renewal of the conditional MA for Vectibix, subject to the Specific Obligations and Conditions as laid down in Annex II

					to the Opinion.
IA/0058	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	14/01/2014	n/a		
II/0052	Changes to the manufacturing process of the active substance. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	18/12/2013	n/a		
IAIN/0055/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	24/10/2013	n/a		
II/0051	Post-approval change management protocol for a finished product manufacturing site. B.II.g.2 - Design Space - Introduction of a post approval change management protocol related to the finished product	19/09/2013	n/a		
IAIN/0053	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV	02/09/2013	n/a		

	(including contact details) and/or changes in the PSMF location				
II/0050	Restriction of the indication for the treatment of colorectal cancer to patients with wild-type RAS tumours for Vectibix, further to the CHMP request to update the PI in line with new biomarker data As a consequence, sections 4.1 and 5.1 of the SmPC are updated. In addition, sections 4.2, 4.3, 4.4 and 4.5 of the SmPC are updated in order to amend the safety information regarding use of Vectibix in patients with mutant RAS tumours. The Package Leafle is updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives and to add the details of the Croatian local representative in the Package Leaflet. Furthermore, the PI is being brought in line with the latest QRD template version 9.0. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	27/06/2013	25/07/2013	SmPC, Annex II, Labelling and PL	Please refer to Scientific Discussion 'Vectibix-H-C-741-II-0050-Assessment Report-Variation'.
II/0047	Additional manufacturing site for the finished product B.II.g.2 - Design Space - Introduction of a post approval change management protocol related to the finished product	21/03/2013	n/a		
IAIN/0049	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/03/2013	n/a		

IB/0048/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.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 B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	06/03/2013	n/a		
R/0043	Renewal of the marketing authorisation.	15/11/2012	14/01/2013	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 and therefore recommends the renewal of the conditional MA for Vectibix, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
IA/0046	B.I.b.2.a - Change in test procedure for AS or	22/11/2012	n/a		

	starting material/reagent/intermediate - Minor changes to an approved test procedure				
IB/0044	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	14/11/2012	n/a		
II/0039/G	This was an application for a group of variations. Additional site for the manufacture of the active substance and control of the active substance and finished product B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product 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.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	19/07/2012	23/08/2012	Annex II	

IAIN/0042	B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing	15/08/2012	25/10/2012	Annex II and PL	
II/0038	Update of section 4.6 of the SmPC in order to modify the warning on avoidance of pregnancy and breast-feeding following Vectibix treatment. The Package Leaflet is updated in accordance. In addition, minor changes to section 4.6 of the SmPC and to corresponding information in the PL are made. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	24/05/2012	27/06/2012	SmPC and PL	Based on the pharmacokinetic properties of panitumumab, pregnancy and breastfeeding should be avoided during the course of treatment with Vectibix and for two months following the last dose. Women who are or become pregnant or women who breast-feed while on treatment with Vectibix should (be encouraged to) enroll in Amgen's Pregnancy and Lactation Surveillance Programme, respectively.
II/0037	Update of sections 4.4 and 4.8 of the SmPC in order to amend the warning on dermatological reactions to include necrotising fasciitis as possible complication of such reactions following relevant cases reported in PSUR7. The description of skin and subcutaneous tissue adverse events in section 4.8 of the SmPC is also amended to include this information. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor changes to section 4.8 of the SmPC and to the Package Leaflet and to update the list of local representatives in the Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	24/05/2012	27/06/2012	SmPC and PL	Life threatening and fatal infectious complications including necrotising fasciitis and sepsis have been reported in patients treated with Vectibix subsequent to the development of severe dermatological reactions. Treatment with Vectibix should be withheld or discontinued in the event of dermatologic toxicity with severe or life threatening inflammatory or infectious complications.

IAIN/0041/G	This was an application for a group of variations. 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.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	16/05/2012	n/a		
IAIN/0040	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	20/04/2012	n/a		
R/0034	Renewal of the marketing authorisation.	15/12/2011	17/02/2012	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 Vectibix, subject to the Specific Obligations and Conditions as laid down in Annex II to the Opinion.
IB/0036	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	27/01/2012	n/a		
II/0032	Update of sections 4.4 and 4.8 of the SmPC to reinforce the warning regarding pulmonary complications following newly identified Interstitial	15/12/2011	20/01/2012	SmPC and PL	Cases of interstitial lung disease (ILD) were reported in a Japanese post-marketing study of Vectibix. Although the diagnosis of ILD and the causal relationship with Vectibix

	Lung Disease (ILD) cases from a post-marketing Japanese study and to add ILD as an ADR with unknown frequency. The warnings on pulmonary complications, electrolyte disturbances and acute renal failure in case of severe diarrhoea in section 4.4 of the SmPC were further updated as requested by CHMP following the review of PSUR 6. The PL was amended accordingly. The MAH also took the opportunity to include skin necrosis in the ADRs table in section 4.8 of the SmPC, as it was already mentioned in SmPC and PL, but it had been reported in the post-marketing setting with an unknown frequency. Minor editorial changes were further made to the SmPC and PL and the list of local representatives in the PL was also updated. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				treament were not determined, the existing warning on pulmonary complications was amended to mention the newly identified, sometimes fatal cases and to advise for reconsideration of Vectibix treatment in patients with a history of interstitial pneumonitis or pulmonary fibrosis. Moreover, the existing warning on electrolyte disturbances was amended to strengthen the recommendation on repletion of electrolytes in such type of disturbance and the warning on diarrhoea was updated to recommend that patients with severe diarrhoea should seek medical attention urgently.
II/0027	Changes to the manufacturing process of the active substance B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol	19/01/2012	19/01/2012		
II/0017	Extension of Indication To extend the metastatic colorectal cancer indication to include the use of panitumumab in combination with FOLFOX in first line treatment and with FOLFIRI	22/09/2011	10/11/2011	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Vectibix-H-C-741-II-0017-Assessment Report-Variation'

	in second line treatment after failure of first-line fluoropyrimidine-based chemotherapy (excluding irinotecan), in patients with wild-type KRAS (Kirsten rat sarcoma) tumours based on safety and efficacy results from two pivotal phase 3 clinical studies (20050203 and 20050181) and other supportive clinical studies. Further amendments to the product information were made, in particular a contraindication against use of panitumumab in combination with FOLFOX in patients with mutant KRAS tumour status and special warnings that KRAS mutation status must always be determined prior to administration of panitumumab. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IA/0035	B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	05/10/2011	n/a		
IA/0033	C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV	12/08/2011	n/a		
IA/0031/G	This was an application for a group of variations. C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the	28/06/2011	n/a		

	back-up procedure of the QPPV 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				
IA/0030/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 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	31/05/2011	n/a	Annex II	
II/0025	Update of sections 4.4 and 4.8 of the SmPC with the addition of keratitis/ulcerative keratitis requested in follow up to the assessment of PSUR 5. The PL was amended accordingly. The MAH took the opportunity to implement one QRD SmPC change and to make editorial changes to the PL. Finally, the version number of the DDPS was deleted from Annex II. 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	14/04/2011	23/05/2011	SmPC, Annex II and PL	Four cases of keratitis, three of which accompanied by corneal ulceration, were reported with panitumumab in the post-marketing setting. Cases of keratitis were reported in panitumumab clinical trials with a frequency of 0.2% to 0.7%. (Ulcerative) keratitis is a known adverse event of EGFR inhibition. As a result, the Product Information was updated to include keratitis and ulcerative keratitis in the list of adverse drug reactions observed during treatment with Vectibix. Patients who develop ocular toxicities while receiving Vectibix should be monitored for evidence of keratitis or ulcerative keratitis and therapy should be interrupted or discontinued if patients present with ulcerative keratitis, while continuation should be carefully

	MAH				considered with keratitis in the absence of corneal ulceration. Vectibix should be used cautiously in patients with a history of keratitis, ulcerative keratitis or severe dry eye. Use of contact lenses has also been associated with keratitis and ulceration of the cornea.
IB/0028/G	This was an application for a group of variations. B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	02/05/2011	n/a		
II/0024/G	This was an application for a group of variations. To add a site for the manufacture of the finshed product and control of the active substance B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for biological/immunological medicinal products. 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	14/04/2011	20/04/2011		

IB/0026	B.II.e.z - Change in container closure system of the Finished Product - Other variation	14/04/2011	n/a		
IB/0022	Change to the manufacture of the active substance. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	26/01/2011	n/a		
IB/0021	Changes to the control of the cell banks. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	26/01/2011	n/a		
R/0018	Renewal of the marketing authorisation.	27/09/2010	13/12/2010	SmPC, Annex II, Labelling and PL	
IA/0020/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - 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 B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete	11/11/2010	n/a		

	parameter) A.7 - Administrative change - Deletion of manufacturing sites				
IA/0023/G	This was an application for a group of variations. C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database 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	09/11/2010	n/a	Annex II	
IA/0019/G	This was an application for a group of variations. 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.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 C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH	25/08/2010	n/a	Annex II	
II/0016	Update of sections 4.3, 4.4 and 4.8 of the SmPC and sections 2 and 4 of the PL with information on two post-marketing reports of fatal infusion reactions. In	18/03/2010	29/04/2010	SmPC, Labelling and	Following two post-marketing reports of fatal infusion reactions, the wording of the contraindication in case of hypersensitivity was amended so that the use of Vectibix is

	addition, section 4.8 of the SmPC and section 4 of the PL were updated regarding Adverse Drug Reactions as requested by the CHMP following PSUR assessments. Furthermore, the MAH took the opportunity to update the List of Local Representatives in the PL. The Product Information has also been updated in line with the latest QRD template. Update of Summary of Product Characteristics, Labelling and Package Leaflet			PL	contraindicated in patients with a history of severe or life-threatening hypersensitivity reaction. Moreover, the warnings on infusion-related and other hypersensitivity reactions were updated with information on the two reports of fatal infusion reactions and also regarding the management of such reactions. Updated information on the reports was also included in SmPC section 4.8 and the table of ADRs was amended to include specific clinical manifestations of infusion-related and other hypersensitivity reactions including (but not limited to) angioedema and anaphylactic reaction. The table was also updated with the inclusion of ADRs the addition of which had previously been requested by the CHMP following assessment of PSURs. An introductory paragraph on the most common ADRs reported in monotherapy trials in mCRC was added and the information on the differences of the types and frequencies of ADRs between the overall population and the population of patients with wild-type KRAS in monotherapy mCRC trials was updated. The information on skin and subcutaneous tissue disorders in SmPC section 4.8 was expanded primarily to reflect the types and frequencies of the severe ones and information on severe ADRs regarding Vectibix in combination with other anti-cancer agents and/or monotherapy was included in this section. Section 2 and 4 of the PL were updated in accordance with the SmPC changes.
R/0012	Renewal of the marketing authorisation.	17/12/2009	15/03/2010	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 this medicinal product continues to be adequately and sufficiently demonstrated to support a

					Conditional Marketing Authorisation and considered that the benefit risk profile of Vectibix has not substantially changed since time of Conditional Marketing Authorisation. It is therefore concluded that a renewal can be granted for one year. However, an urgent safety variation is needed to update the product information, especially with respect to fatal infusion-related reactions; the MAH should commit to submit this variation by the end of January 2010.
II/0015	Changes to the manufacturing process and control of the drug substance Change(s) to the manufacturing process for the active substance	21/01/2010	03/02/2010		
II/0014	Change to the manufacturing process of the drug substance. Change(s) to the manufacturing process for the active substance	22/10/2009	03/11/2009		
II/0013	Changes in the control of the drug substance Change(s) to the test method(s) and/or specifications for the active substance	24/09/2009	05/10/2009		
II/0011	Change to the control of the drug substance and drug product Change(s) to the test method(s) and/or specifications for the active substance	25/06/2009	01/07/2009		

II/0010	Update of the SPC sections 4.4 and 4.8 and corresponding changes to the Package Leaflet with respect to a review of safety information related to dermatitis acneiform, infusion reactions, renal failure and gastrointestinal disorders and update of SPC sections 4.4 and 5.1 to reflect further analysis related to the PACCE (20040249) clinical investigation, as requested by the CHMP following the assessment of SOB 04. A minor editorial change has also been introduced in the Labelling. Update of Summary of Product Characteristics, Labelling and Package Leaflet	19/02/2009	07/04/2009	SmPC, Labelling and PL	Information of infusion related and delayed hypersensitivity reactions was included in the SPC and Package Leaflet. In clinical studies, infusion-related reactions (occurring within 24 hours of any infusion) were reported in 3% of Vectibix treated patients, of which <1% were severe (NCI-CTC grade 3-4). Severe infusion reactions included anaphylactic reactions, bronchospasm, and hypotension. The infusion should be stopped and Vectibix should be permanently discontinued if a severe infusion reaction occurs. Delayed hypersensitivity reactions have been reported, including a fatal case of angioedema that occurred more than 24 hours after the infusion. Permanently discontinue Vectibix if a severe hypersensitivity reaction occurs. An additional analysis of efficacy data from a a randomized, open-label, multicentre study on the efficacy of bevacizumab and oxaliplatin- or irinotecan-containing chemotherapeutic regimens with and without Vectibix in the first-line treatment of metastatic colorectal cancer by KRAS status was provided and included in the SPC. This analysis did not identify a subset of subjects who benefited from panitumumab in combination with oxaliplatin- or irinotecan based chemotherapy and bevacizumab. The overall findings of this retrospective analysis of efficacy and safety data by KRAS status do not alter the conclusions of the main study, namely, that panitumumab treatment combined with chemotherapy and bevacizumab is associated with an unfavourable benefit-to-risk profile irrespective of tumor KRAS mutational status. Therefore administration of Vectibix in combination with bevacizumab

					containing chemotherapy combinations should be avoided.
R/0009	Renewal of the marketing authorisation.	18/12/2008	19/03/2009		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 this medicinal product continues to be adequately and sufficiently demonstrated to support a Conditional Marketing Authorisation and considered that the benefit risk profile of Vectibix has not substantially changed since time of Conditional Marketing Authorisation. Although the uncertainties associated with the Conditional Marketing Authorisation remain, important data are expected within the next reporting period and CHMP can support the Renewal.
II/0008	Update of the SPC in section 4.4 (Special Warnings and precautions for use) related to the information on hypomagnesaemia and other electrolyte disturbances. In addition, section 6.3 (Shelf life) is updated to modify the recommendation related to the permitted storage of Vectibix after dilution for clarity purposes. The package leaflet has been revised accordingly. Update of Summary of Product Characteristics and Package Leaflet	20/11/2008	22/12/2008	SmPC and PL	The information on hypomagnesaemia and other electrolytes has been updated in section 4.4 of the Summary of Product Characteristics as follows: Progressively decreasing serum magnesium levels leading to severe (grade 4) hypomagnesaemia have been observed in some patients. Patients should be periodically monitored for hypomagnesaemia and accompanying hypocalcaemia prior to initiating Vectibix treatment, and periodically thereafter for up to 8 weeks after the completion of treatment. Magnesium repletion is recommended, as appropriate. Other electrolyte disturbances, including hypokalaemia, have also been observed. Repletion of these electrolytes is also recommended, as appropriate. The storage conditions have been clarified in section 6.3 of the SmPC, to ensure that product quality is protected, as it is more appropriate to limit storage post dilution to the 2-8º C storage temperature for no longer than 24 hours.

					The package leaflet has been updated accordingly.
II/0007	Changes to the manufacturing process and control of the drug substance and drug product. Change(s) to the manufacturing process for the active substance	20/11/2008	28/11/2008		
II/0006	The Marketing Authorisation Holder applied to update the Detailed Description Pharmacovigilance Systems (DDPS) (Version 3.0). Consequently, Annex II has been updated using standard text including the new version numbers of these documents. Update of DDPS (Pharmacovigilance)	25/09/2008	24/10/2008	Annex II	As a result of updating the summary of pharmacovigilance systems submitted to the MHRA in May 2008, the MAH DDPS has been updated to Version 3.0. There have been no significant changes made to Amgen's pharmacovigilance systems. The changes made to version 3.0 are administrative and provide further clarity around the pharmacovigilance systems in place.
II/0004	Update of section 4.8 of the SPC to include pulmonary embolism as an adverse reaction. The Package Leaflet has been updated accordingly. Further minor editorial corrections to the Labelling following specimen review have also been made. Update of Summary of Product Characteristics, Labelling and Package Leaflet	26/06/2008	08/08/2008	SmPC, Labelling and PL	Section 4.8 of the SPC was updated to include "pulmonary embolism" - frequency: common. In the Package Leaflet section 4, "Pulmonary embolism (blood clots in the lung)" has been added. Further minor editorial corrections to the Labelling following specimen review have also been made.
II/0002	To introduce an additional site for the manufacture of the finished product and release and stability testing of the active substance and finished product. To revise a specification and test method for active substance and finished product. Change(s) to the manufacturing process for the	24/07/2008	29/07/2008		

	finished product				
II/0003	Change(s) to the test method(s) and/or specifications for the finished product	26/06/2008	15/07/2008		
IB/0005	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	18/06/2008	n/a	SmPC	
II/0001	Quality changes	24/04/2008	30/04/2008		