Renagel

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
IB/0120/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.4.b - Change in the batch size (including batch	04/08/2023		SmPC, Annex II, Labelling and PL	

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

	size ranges) of the finished product - Downscaling down to 10-fold B.II.a.3.z - Changes in the composition (excipients) of the finished product - Other variation B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP - Including batch control/testing B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.a.1.a - Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking - Changes in imprints, bossing or other markings B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
IAIN/0121	A.1 - Administrative change - Change in the name and/or address of the MAH	23/05/2023		SmPC, Labelling and PL	

PSUSA/2697/202110	Periodic Safety Update EU Single assessment - sevelamer	10/06/2022	n/a		PRAC Recommendation - maintenance
IA/0119	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	13/04/2022	n/a		
N/0117	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/11/2021		PL	
IA/0116/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	07/09/2021	n/a		
N/0115	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/10/2020	14/01/2021	PL	
WS/1775	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	17/04/2020	n/a		Removal of identified or potential risks from the list of safety concerns as these risks are fully characterized and are followed up via routine pharmacovigilance.

	by new additional data to be submitted by the MAH where significant assessment is required 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				
IG/1106	A.7 - Administrative change - Deletion of manufacturing sites	15/01/2020	14/01/2021	SmPC, Labelling and PL	
PSUSA/2697/ 201810	Periodic Safety Update EU Single assessment - sevelamer	27/06/2019	23/08/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2697/201810.
IG/1003	A.1 - Administrative change - Change in the name and/or address of the MAH	20/12/2018	23/08/2019	SmPC, Labelling and PL	
PSUSA/2697/ 201710	Periodic Safety Update EU Single assessment - sevelamer	14/06/2018	n/a		PRAC Recommendation - maintenance
WS/1383	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.f.1.e - Stability of FP - Change to an approved stability protocol	07/06/2018	n/a		

N/0108	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/12/2017	23/08/2019	Labelling and PL	
PSUSA/2697/ 201610	Periodic Safety Update EU Single assessment - sevelamer	09/06/2017	n/a		PRAC Recommendation - maintenance
PSUSA/2697/ 201510	Periodic Safety Update EU Single assessment - sevelamer	23/06/2016	31/08/2016	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2697/201510.
WS/0867	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.5 of the SmPC regarding drug-drug interaction between sevelamer and proton pump inhibitors. The Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to implement editorial changes in section 4.8 of the SmPC of Renvela and Sevelamer carbonate Zentiva in order to harmonize the wording for all Sevelamer compounds. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/02/2016	31/08/2016	SmPC and PL	Changes in gastric acidity with acid suppressants may potentially alter the efficacy of sevelamer HCL. During post-marketing experience, very rare cases of increased phosphate levels have been reported in patients taking proton pump inhibitors co-administered with sevelamer hydrochloride.
WS/0803	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.11.b - Introduction of, or change(s) to, the	19/11/2015	n/a		

	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				
WS/0770	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	01/10/2015	31/08/2016	SmPC and PL	
PSUSA/2697/ 201410	Periodic Safety Update EU Single assessment - sevelamer	11/06/2015	n/a		PRAC Recommendation - maintenance
PSUV/0101	Periodic Safety Update	18/12/2014	17/02/2015	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUV/0101.
R/0100	Renewal of the marketing authorisation.	25/09/2014	19/11/2014	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, including all variations introduced since the marketing authorisation was granted, the Rapporteur considers that the risk-benefit balance of Renagel, in treatment of hyperphosphataemia in adult patients receiving haemodialysis or peritoneal dialysis, remains favourable and therefore recommends the renewal of the marketing authorisation for unlimited period.
IG/0418	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV	11/04/2014	n/a		

	(including contact details) and/or changes in the PSMF location				
N/0098	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/02/2014	19/11/2014	PL	
IA/0097/G	This was an application for a group of variations. B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	28/10/2013	n/a		
N/0096	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/10/2013	19/11/2014	PL	
IG/0332	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	24/07/2013	n/a		
IG/0283	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/03/2013	n/a		
N/0092	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/08/2012	19/11/2014	PL	
N/0091	Minor change in labelling or package leaflet not	12/04/2012	19/11/2014	PL	

	connected with the SPC (Art. 61.3 Notification)				
WS/0188	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of section 4.4 of the SmPC in order to include precaution information regarding difficulties in swallowing tablets and section 4.6. In order to add information on fertility. In addition, the list of local representatives in the Package Leaflet has been updated. Furthermore, the WSA proposed this opportunity to bring the PI in line with the latest QRD template version 8.0. Minor linguistic corrections have also been made to the Italian Annexes of Renvela. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	17/11/2011	22/12/2011	SmPC, Annex II, Labelling and PL	The MAH was requested to perform a signal review on Renagel/Renvela for difficulties in swallowing/choking/aspiration due to obstruction of the airways or aspiration of tablet remnants in association with treatment with Renagel/Renvela. A total of seven cases were identified. Four of these patients recovered, for 2 the outcomes are unknown, and 1 case was fatal (acute MI). In five cases, patients had to be hospitalized/hospitalization was prolonged and/or patients underwent bronchoscopy/endoscopy. The CHMP subsequently identified 12 cases in EudraVigilance on 17 March 2011. The CHMP requested the MAH to perform a cumulative review of cases of possible complications of swallowing Renagel/Renvela tablets, in particular focusing on the MedDRA PTs dysphagia, choking, aspiration, foreign body aspiration and oral administration complication. Swallowing is complex mechanical event, which can be influenced by a great many factors in Chronic Kidney Disease (CKD) patients. It is known for example that these patients often suffer from dysfunctional salivary glands. Furthermore, since hypertension is a frequent co-morbidity in CKD, water retention in the salivary gland's secretory process is not uncommon. Furthermore, concomitant conditions common in CKD patients (e.g. xerostomia, diabetic autonomic neuropathy, GERD and iron deficiency) can affect swallowing. CKD patients are generally also an older population with age related physiological changes such as laryngeal nerve dysfunction contributing to

					dysphagia and swallowing complications. The MAH performed a number of searches in different media to identify relevant case reports. The MAH's global safety database was queried for adverse events coding to specific Preferred Terms and MedDRA High Level Group Terms. In addition a search of medical literature was performed using Pubmed, OVID, EMBASE, and Biosis to identify any publications discussing choking on or difficulty swallowing and sevelamer. In addition, both the Renagel Integrated Summary of Safety submitted with the Renagel MAA and the Renagel and Renvela post-approval safety studies were reviewed. Finally, The FDA Adverse Event Reporting System (AERS) database was also queried. During this query similar data regarding other drugs currently indicated for treatment of hyperphosphatemia in dialysis patients was also retained. The CHMP conclusion is that the MAH has taken adequate action in regards to these sporadic reports of swallowing difficulties by adding a precaution on the use of tablet in swallowing-impaired patients in the product SPC. There are no clinical nor quality related reason as to why Renvela/Renagel should be more difficult to swallow than other similar products.
IA/0090	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	05/05/2011	n/a		

IA/0089	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	12/11/2010	n/a	Annex II and PL	
II/0087	Update of Summary of Product Characteristics and Package Leaflet	22/04/2010	02/06/2010	SmPC and PL	Following the assessment of Renagel PSUR 10 (covering the period from 01 May 2008 - 30 October 2008), the MAH was requested by the CHMP to update section 4.8 of the Summary of Product Characteristics by adding "diverticulitis" under post-marketing experience. The MAH has hereby submitted a type II variation to update section 4.8 of the SPC accordingly and has also proposed consequential changes to the Package Leaflet. The CHMP considered this type II variation to be acceptable and agreed on amendments to be introduced in the Summary of Product Characteristics and the Package Leaflet.
R/0084	Renewal of the marketing authorisation.	24/09/2009	08/12/2009	SmPC, Labelling and PL	Based on the review of the available information, the CHMP is of the opinion that the quality, the safety and the efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considers that the benefit/risk profile for Renagel continues to be favourable. The CHMP is however of the opinion that one additional five year renewal on the basis of pharmacovigilance grounds is required. The MAH should continue to submit 6 monthly PSURs.
IA/0088	IA_13_a_Change in test proc. for active substance - minor change	26/11/2009	n/a		
IA/0086	IA_13_a_Change in test proc. for active substance - minor change	05/10/2009	n/a		

	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure				
IB/0082	IB_17_a_Change in re-test period of the active substance	27/08/2009	n/a		
IB/0085	IB_33_Minor change in the manufacture of the finished product	29/07/2009	n/a		
II/0078	Amendment to sections 4.4, 4.5 and 4.8 of the SPC following the assessment of PSUR 8, and introduction of rash, pruritus and abdominal pain as adverse events observed during post marketing surveillance. Minor typographical errors in the SPC are also corrected. The PL is amended accordingly. Update of Summary of Product Characteristics and Package Leaflet	25/06/2009	27/07/2009	SmPC and PL	Following a CHMP request during the assessment of PSUR 8, the MAH introduced the following changes to the Summary of Product Characteristics: - Addition of 'diverticulosis' to the list of gastrointestinal disorders requiring careful assessment of risks and benefits in section 4.4. - The statement on section 4.4 about cases of increased TSH levels was moved to section 4.5. - In section 4.8, the sentence 'in very rare cases, intestinal obstruction and ileus/subileus have been observed in patients during treatment with Renagel' was changed to 'during post-approval use of Renagel, cases of pruritus, rash, abdominal pain, intestinal obstruction, ileus/subileus and intestinal perforation have been reported'. Rash, pruritus and abdominal pain are introduced at the MAH's initiative after a revision of the current post marketing data. The Package Leaflet is updated accordingly.
N/0081	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/06/2009	n/a	Labelling and	

				PL	
IA/0083	IA_13_a_Change in test proc. for active substance - minor change	22/06/2009	n/a		
IB/0080	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	29/04/2009	n/a	SmPC	
IA/0079	IA_28_Change in any part of primary packaging material not in contact with finished product	18/02/2009	n/a		
IA/0077	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.) IA_05_Change in the name and/or address of a manufacturer of the finished product	19/12/2008	n/a	Annex II and PL	
IB/0075	IB_10_Minor change in the manufacturing process of the active substance	29/10/2008	n/a		
IB/0070	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	15/08/2008	13/08/2008	SmPC, Labelling and PL	
IA/0073	IA_13_a_Change in test proc. for active substance - minor change IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	09/07/2008	n/a		
IA/0072	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	09/07/2008	n/a		
IA/0071	IA_38_a_Change in test procedure of finished	09/07/2008	n/a		

	product - minor change to approved test procedure				
II/0066	Update of section 4.8 of the Summary of Product Characteristics (SPC) and section 4 of the Package Leaflet (PL). Update of Summary of Product Characteristics and Package Leaflet	24/04/2008	18/06/2008	SmPC and PL	The MAH reviewed the safety data of six studies performed with Renagel and has identified that the adverse events of headache, hypotension, hypertension, pain, pruritis, rash and pharyngitis should be removed from the current list of adverse events. In addition, the Package Leaflet is revised to reflect the outcome of a user testing exercise and to update the details of local representatives.
II/0065	Update of sections 5.1 and 4.8 of the Summary of Product Characteristics to reflect the results of a comparative clinical study in haemodialysis patients. Update of Summary of Product Characteristics	24/04/2008	18/06/2008	SmPC	The MAH conducted a one year duration clinical study, to compare the effects of sevelamer hydrochloride and calcium carbonate on bone turnover and mineralization in haemodialysis patients. The results suggest that sevelamer hydrochloride and calcium carbonate had comparable effects on bone mineralization and bone turnover. Another objective of the study was to assess the safety of sevelamer hydrochloride. Adverse events occurring during the study were consistent with patients' underlying renal disease and with the current sevelamer hydrochloride safety profile.
IA/0069	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	07/04/2008	n/a		
IA/0068	IA_13_a_Change in test proc. for active substance - minor change	19/03/2008	n/a		
II/0056	Update of section 4.1 of the SPC to extend the indication to patients receiving peritoneal dialysis. Consequentially the sections 4.2, 4.4, 4.5, 4.8, and 5.1 of the SPC have been updated. Relevant sections	26/04/2007	01/06/2007	SmPC, Labelling and PL	Please refer to Scientific Discussion: Renagel-H-C-254-II-56

	of the PL have been amended accordingly. In addition the MAH also took the opportunity to update the Product Information in accordance to the latest QRD template. The Package Leaflet was also updated to include the local representatives for the new Member States (Bulgaria and Romania). Extension of Indication				
IA/0064	IA_09_Deletion of manufacturing site	20/03/2007	n/a		
IA/0063	IA_09_Deletion of manufacturing site IA_47_a_Deletion of a pharmaceutical form	20/03/2007	n/a	SmPC, Annex II, Labelling and PL	
IA/0062	IA_28_Change in any part of primary packaging material not in contact with finished product	20/03/2007	20/03/2007	SmPC, Labelling and PL	
IB/0061	IB_37_b_Change in the specification of the finished product - add. of new test parameter	23/02/2007	n/a		
IB/0060	IB_33_Minor change in the manufacture of the finished product	31/01/2007	n/a		
IA/0059	IA_13_a_Change in test proc. for active substance - minor change	14/12/2006	n/a		
IA/0057	IA_37_a_Change in the specification of the finished product - tightening of specification limits	30/08/2006	n/a		
S/0055	Annual re-assessment.	27/04/2006	26/06/2006	Annex II	The benefit/risk profile of Renagel continues to be

					favourable in the approved indication. Since all specific obligations (studies requested at the time of the granting of the Marketing Authorisation) have been fulfilled, the CHMP concluded that there are no remaining grounds for the Marketing Authorisation to remain under exceptional circumstances".
N/0054	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/01/2006	n/a	PL	
N/0052	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/12/2005	n/a	PL	
IA/0053	IA_13_a_Change in test proc. for active substance - minor change	02/12/2005	n/a		
IA/0051	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	03/10/2005	n/a		
IA/0050	IA_13_a_Change in test proc. for active substance - minor change	08/09/2005	n/a		
II/0049	The variation relates to updates of sections 4.4 and 4.5 of the SPC with consequent changes to the PL in order to include information on worsening metabolic acidosis when switching from other phosphate binders where lower bicarbonate levels were observed in sevelamer-treated patients compared to calcium-treated patients, as well as on relevant interactions between sevelamer, cyclosporin A and mycophenolate mofetil following the CHMP's assessment of the 4th and 5th annual re-	27/07/2005	31/08/2005	SmPC and PL	Information was added to section 4.4 (Special warnings and special precautions for use) of the Summary of Product Characteristics (SPC) on that patients with chronic renal failure are predisposed to develop metabolic acidosis. Worsening of acidosis has been reported upon switching from other phosphate binders to sevelamer in a number of studies where lower bicarbonate levels in sevelamer-treated patients compared to patients treated with calcium-based binders were observed. Close monitoring of serum bicarbonate levels is recommended.

	assessments. Further, the contact details of the local representatives for Iceland, Italy and Poland were updated. Update of Summary of Product Characteristics and Package Leaflet				Information was added to section 4.5 (Interactions with other medicinal products and other forms of interaction) on that reduced levels of cyclosporine and mycophenolate mofetil have been reported in transplant patients when coadministered with Renagel without any known clinical consequences (i.e graft rejection). The possibility of an interaction with clinical consequences cannot be excluded and a close monitoring of blood concentrations of mycophenolate-mofetil and cyclosporine should be considered during the use of combination and after its withdrawal.
II/0048	Change(s) to the test method(s) and/or specifications for the active substance	26/05/2005	01/06/2005		
S/0046	Annual re-assessment.	21/04/2005	21/04/2005		The benefit/risk profile of sevelamer remains positive. The Community Marketing Authorisation should remain under exceptional cirucumstances pending the report of a clinical trial.
IB/0047	IB_17_a_Change in re-test period of the active substance	08/03/2005	n/a		
R/0042	Renewal of the marketing authorisation.	18/11/2004	26/01/2005	SmPC, Annex II, Labelling and PL	The benefit/risk profile of Renagel continues to be favourable in the approved indication.
IA/0045	IA_13_a_Change in test proc. for active substance - minor change	10/01/2005	n/a		
II/0044	Quality changes	18/11/2004	24/11/2004		

IA/0043	IA_36_ b_Change in shape or dimensions of the container/closure - other pharm. forms	29/07/2004	n/a		
IB/0040	IB_07_c_Replacement/add. of manufacturing site: All other manufacturing operations ex. batch release IA_08_b_02_Change in BR/QC testing - repl./add. manuf. responsible for BR - incl. BC/testing	29/06/2004	n/a	Annex II and PL	
IA/0041	IA_32_a_Change in batch size of the finished product - up to 10-fold	10/06/2004	n/a		
IA/0039	IA_09_Deletion of manufacturing site	26/05/2004	n/a		
S/0038	Annual re-assessment.	24/03/2004	24/03/2004		The benefit/risk profile of sevelamer remains positive. The Community Marketing Authorisation should remain under exceptional cirucumstances pending the report of a clinical trial.
II/0029	Update of sections 4.2, 4.5 and 5.1 of the SPC and the section 4 of the PL following the 3rd annual reassessment. Update of Summary of Product Characteristics and Package Leaflet	25/09/2003	27/01/2004	SmPC and PL	The section 4.2 of the SPC was updated with information on that the average actual daily dose in the chronic phase of a one-year clinical study was 7 grams of sevelamer.In section 4.5 of the SPC information was added based on interaction studies in healthy volunteers. Renagel had no effect on the bioavailability of digoxin, warfarin, enalapril or metoprolol. However, the bioavailability of ciprofloxacin was decreased by approximately 50% when co-administered with Renagel in a single dose study. Consequently, Renagel should not be taken simultaneously with ciprofloxacin. Renagel may affect the bioavailability of other medicinal products. When administering any medicinal product where a reduction in the bioavailability could have a clinically significant effect on safety or efficacy, the medicinal product should be

					administered at least one hour before or three hours after Renagel, or the physician should consider monitoring blood levels.In section 5.1 of the SPC it was added that sevelamer is free of metal.
IB/0036	IB_14_a_Change in manuf. of active substance without Ph. Eur. certificate - change in manuf. site	03/12/2003	n/a		
IA/0037	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	11/11/2003	n/a		
I/0035	16_Change in the batch size of finished product	20/10/2003	22/10/2003		
I/0033	11b_Change in supplier of an intermediate compound used in manufacture of the active substance	09/10/2003	15/10/2003		
I/0030	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	21/08/2003	25/08/2003		
I/0032	01_Withdrawal of the manufacturing authorisation for a site of manufacture	14/08/2003	19/08/2003		
I/0028	12_Minor change of manufacturing process of the active substance	11/08/2003	19/08/2003		
I/0027	12_Minor change of manufacturing process of the active substance	11/08/2003	19/08/2003		
I/0025	14_Change in specifications of active substance	11/08/2003	19/08/2003		

I/0024	12_Minor change of manufacturing process of the active substance	11/08/2003	19/08/2003		
S/0023	Annual re-assessment.	25/04/2003	14/07/2003	Annex II	The benefit/risk profile of sevelamer remains positive. The Community Marketing Authorisation should remain under exceptional circumstances pending the report of a clinical trial.
I/0026	24_Change in test procedure of active substance	24/06/2003	27/06/2003		
I/0021	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	24/03/2003	22/04/2003	Annex II and PL	
I/0022	16_Change in the batch size of finished product	24/03/2003	31/03/2003		
I/0019	12_Minor change of manufacturing process of the active substance 12a_Change in specification of starting material/intermediate used in manuf. of the active substance	04/03/2003	11/03/2003		
II/0017	Update of sections 4.4 and 4.8 of the SPC and the section 4 of the PL as requested by the CHMP following the assessment of the PSUR 4, as well as update of section 5.1 of the SPC to fulfill a specific obligation. Update of Summary of Product Characteristics and Package Leaflet	21/11/2002	04/03/2003	SmPC and PL	Section 4.4 of the SPC was updated with information on that in very rare cases, intestinal obstruction and ileus/subileus have been observed in patients during treatment and that constipation may be a preceding symptom. Thus, patients who are constipated should be monitored carefully while being treated with Renagel and treatment should be re-evaluated in patients who develop severe constipation. In section 4.8 of the SPC it was added that in very rare cases, intestinal obstruction and ileus/subileus have been

					observed in patients during treatment.In section 5.1 of the SPC it was added that the effects on phosphate and calcium were proven to be maintained throughout a study with one year follow-up.
I/0018	24_Change in test procedure of active substance 25_Change in test procedures of the medicinal product	04/10/2002	15/10/2002		
I/0014	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	19/09/2002	14/10/2002		
N/0016	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/08/2002	07/10/2002	PL	
S/0013	Annual re-assessment.	25/04/2002	26/07/2002		
I/0015	01_Change following modification(s) of the manufacturing authorisation(s)	10/07/2002	11/07/2002		
I/0012	08_Change in the qualitative composition of immediate packaging material	10/12/2001	19/02/2002	SmPC	
I/0011	03_Change in the name and/or address of the marketing authorisation holder	10/12/2001	19/02/2002	SmPC, Labelling and PL	
S/0007	Annual re-assessment.	31/05/2001	06/02/2002	Annex II	
I/0010	15_Minor changes in manufacture of the medicinal product 16_Change in the batch size of finished product	10/12/2001	n/a		

	01_Change following modification(s) of the manufacturing authorisation(s)				
I/0009	15_Minor changes in manufacture of the medicinal product	28/09/2001	23/10/2001		
I/0008	30_Change in pack size for a medicinal product	22/06/2001	15/10/2001	SmPC, Labelling and PL	
II/0006	Update of Summary of Product Characteristics and Package Leaflet	26/04/2001	09/08/2001	SmPC and PL	
X/0004	X-3-iv_Change or addition of a new pharmaceutical form	14/12/2000	23/04/2001	SmPC, Annex II, Labelling and PL	
X/0003	X-3-iv_Change or addition of a new pharmaceutical form	14/12/2000	23/04/2001	SmPC, Annex II, Labelling and PL	
I/0005	26_Changes to comply with supplements to pharmacopoeias	02/03/2001	11/03/2001		
II/0002	Update of or change(s) to the pharmaceutical documentation	21/09/2000	29/11/2000		
I/0001	01_Change in the name of a manufacturer of the medicinal product	28/04/2000	12/05/2000		