CellCept

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/0170/G	This was an application for a group of variations. C.I.6.a: Extension of indication to include paediatric patients (1 year to 18 years of age) for hepatic and cardiac transplants and to extend the indication for renal transplants for paediatric patients starting from	14/11/2024	13/12/2024	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Cellcept-H-C-000082-II-0170-G'

[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).

	1 year, based on pharmacokinetic data, published literature and the Roche Global Safety Database. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, 5.2, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 1.2 of the RMP has also been approved. Type IB (C.I.z): Update of the precautions to be taken before handling or administering the medicinal product in section 4.2 of the SmPC for the CellCept 500 mg tablets formulation in order to be in line with the other CellCept formulations. The Package Leaflet is updated to cross reference section 2 in section 6 for sodium content, in line with the QRD guidance. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and bring the PI in line with the latest QRD template version 10.3. The group of variations leads to amendments to the Summary of Product Characteristics, Annex II and Package Leaflet. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				
IA/0176/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of	09/10/2024	n/a		

	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				
IA/0175/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	24/04/2024	n/a		
IA/0174/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	09/04/2024	n/a		

PSUSA/10550 /202305	Periodic Safety Update EU Single assessment - mycophenolate mofetil, mycophenolic acid	25/01/2024	25/03/2024	SmPC	Please refer to CellCept, Myclausen, Mycophenolate mofetil Teva, Myfenax EMEA/H/C/PSUSA/00010550/202305 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation
IB/0173/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.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	22/03/2024	n/a		
IB/0172	B.II.a.3.z - Changes in the composition (excipients) of the finished product - Other variation	30/10/2023	n/a		
IB/0169	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	15/03/2023	25/03/2024	SmPC, Labelling and PL	
PSUSA/10550 /202105	Periodic Safety Update EU Single assessment - mycophenolate mofetil, mycophenolic acid	16/12/2021	16/02/2022	PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10550/202105.
IA/0168	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)	26/01/2022	n/a		
IA/0167/G	This was an application for a group of variations.	01/12/2021	n/a		

	B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
II/0165/G	This was an application for a group of variations. C.I.4 (Type II) - Update section 5.1 of the SmPC based on a literature review on mycophenolate mechanism of Action. C.I.4 (Type II) - Update section 5.2 of the SmPC to add new information to the Distribution and Elimination subsections based on a literature review. C.I.4 (Type II) - Update of sections 4.5 and 5.2 of the SmPC to amend the existing information on patients taking oral contraceptives based on study Roche Report N-181041/ BP 15543. C.I.Z (Type IB) - Update section 2 of the Package Leaflet to align the wording of the text with the SmPC section 4.4 and update section 6 of the Package Leaflet to add the quantity of the active substance, mycophenolate based on recommendations from NCA (Ireland) and EMA respectively. The Package Leaflet is updated accordingly. In addition, the Marketing Authorisation Holder (MAH) has taken the opportunity to implement minor editorial changes to the SmPC and Package Leaflet. Furthermore, the PI is being brought in line with the	11/11/2021	16/02/2022	SmPC, Labelling and PL	Following evidence from a literature review on mycophenolate mechanism of Action, section 5.1 of the SmPC has been updated to state that in addition to its inhibition of IMPDH and the resulting deprivation of lymphocytes, MPA also influences cellular checkpoints responsible for metabolic programming of lymphocytes. Section 5.2 of the SmPC has been updated to add information about clearance and half-life based on available evidence from literature including studies in healthy volunteers, non-transplant patients and patients with solid organ transplants. Based on the results from a pharmacokinetic/pharmacodynamic interaction study of mycophenolate mofetil and oral contraceptives in non-transplant patients, sections 4.5 and 5.2 of the SmPC have been revised to more precisely reflect that the pharmacodynamics and pharmacokinetics of oral contraceptives were not affected to a clinically relevant degree when co-administered with CellCept. In addition, sections 4.5, 4.6, 5.1, 5.2 and 5.3 have been updated to bring the PI in line with the EMA SmPC guideline. The PL has been updated accordingly.

	latest QRD template version 10.2. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IA/0164/G	This was an application for a group of variations. 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 B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place	11/05/2021	n/a		
IA/0163	B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer	25/02/2021	n/a		

II/0161	Update of section 4.4 of the SmPC to amend the existing warning on infections due to potential increase severity of COVID-19 in patients treated with Mycophenolic acid (MPA) based on cumulative reviews from available data. Additionally, consideration of dose adjustment has been suggested in case of clinically significant COVID-19. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/02/2021	16/02/2022	SmPC	Update of section 4.4 of the SmPC to amend the existing warning on infections due to potential increase severity of COVID-19 in patients treated with Mycophenolic acid (MPA) based on cumulative reviews from available data. Additionally, consideration of dose adjustment has been suggested in case of clinically significant COVID-19.
PSUSA/10550 /202005	Periodic Safety Update EU Single assessment - mycophenolate mofetil, mycophenolic acid	10/12/2020	18/02/2021	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10550/202005.
IA/0162	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	16/02/2021	n/a		
IA/0160	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)	27/01/2021	n/a		
IB/0159	B.II.z - Quality change - Finished product - Other variation	30/10/2020	18/02/2021	SmPC, Labelling and PL	
IA/0157	B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved	16/06/2020	n/a		

	manufacturer				
IB/0156/G	This was an application for a group of variations. B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product B.II.f.1.e - Stability of FP - Change to an approved stability protocol	02/06/2020	15/09/2020	SmPC, Labelling and PL	
IAIN/0155	B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	12/03/2020	15/09/2020	SmPC, Labelling and PL	
IG/1196/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)	19/02/2020	n/a		

II/0149/G	This was an application for a group of variations. B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold 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	16/01/2020	n/a		
IAIN/0153/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 B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products	20/12/2019	n/a		
IA/0152	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	11/12/2019	n/a		

PSUSA/10550 /201905	Periodic Safety Update EU Single assessment - mycophenolate mofetil, mycophenolic acid	28/11/2019	n/a		PRAC Recommendation - maintenance
IAIN/0151	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	21/11/2019	n/a		
IAIN/0150/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 B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	04/10/2019	15/09/2020	SmPC, Labelling and PL	
II/0146	Update of section 4.8 of the SmPC to update the safety information based on the reassessment of all available evidence from clinical trials, post-marketing experience and literature and to present ADRs in compliance with the SmPC guideline. Update of section 4.4 of the SmPC to include therapeutic dose	19/09/2019	15/09/2020	SmPC, Annex II, Labelling and PL	The SmPC section 4.4 has been updated since TDM should be beneficial for patients co-treated with drugs known to interfere with MPA in improving therapeutic outcome. The SmPC section 4.7 has been updated to include a statement on a moderate influence on the ability to drive based on the ADRs of somnolence, confusion, dizziness,

	monitoring for the addition or removal of an interacting medication based on an expert consensus. Update of section 4.7 of the SmPC to include a statement on the moderate influence on the ability to drive. Update of section 5.2 of the SmPC based on current literature on the pharmacokinetics in geriatric patients. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes throughout the PI and to bring the PI in line with the latest QRD template version 10.1. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				tremor and hypertension which have been reported at a high frequency. The SmPC section 4.8 has been updated to replace all specific infections under the umbrella terms bacterial, fungal and viral infections, to include neoplasm, pseudolymphoma, ecchymosis, venous thrombosis, mouth ulceration, abdominal distension, haematuria, hernia protozoal infections, lymphoma, lymphoproliferative disorder, aplasia pure red cell, bone marrow failure, lymphocele, gingival hyperplasia as ADR and to replace anorexia by decreased appetite, myasthenic syndrome by muscular weakness, gastric ulcer and duodenal ulcer by gastrointestinal ulcer. PTs previously under SOC investigations are now included under the SOC Renal and urinary disorders (PTs of blood creatinine increased and blood urea increased), under the SOC Hepatobiliary disorders (PTs of hepatic enzyme increased, blood lactate dehydrogenase increased and blood alkaline phosphatase increased) and under the SOC Metabolism and nutrition disorders (PT of weight decreased). The SmPC section 5.2 has been updated based on a review of the literature studies on pharmacokinetics indicating the absence of an important effect of age on MPA pharmacokinetics. The PL has been updated accordingly.
IB/0147/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	04/06/2019	n/a		

	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.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.b.1.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.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting 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.1.e - Change in the specification parameters and/or limits of an AS, starting 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.1.e - Change in the specification parameters and/or limits of an AS, starting 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.1.e - Change in the specification parameters and/or limits of an AS, starting 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				
IA/0145	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	31/01/2019	n/a		
PSUSA/10550 /201805	Periodic Safety Update EU Single assessment - mycophenolate mofetil, mycophenolic acid	29/11/2018	n/a		PRAC Recommendation - maintenance
IA/0144	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	13/09/2018	n/a		
N/0143	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/08/2018	15/09/2020	PL	
IG/0944/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new/updated or	14/06/2018	n/a		

	deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)				
IA/0140	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)	19/03/2018	n/a		
T/0139	Transfer of Marketing Authorisation	20/02/2018	12/03/2018	SmPC, Labelling and PL	
PSUSA/10550 /201705	Periodic Safety Update EU Single assessment - mycophenolate mofetil, mycophenolic acid	14/12/2017	05/03/2018	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10550/201705.
IG/0887	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)	29/01/2018	n/a		
II/0137	Update of section 4.4 of the SmPC in order to update the information on concomitant use of tacrolimus with CellCept and to provide recommendations on therapeutic drug monitoring for management of transplant patients, based on reviews of the medical literature and clinical treatment guidelines. In	18/01/2018	12/03/2018	SmPC and PL	The SmPC section 4.4 on interactions has been updated to state that therapeutic drug monitoring of MPA may be appropriate when switching combination therapy (e.g. from ciclosporin to tacrolimus or vice versa) or to ensure adequate immunosuppression in patients with high immunological risk (e.g. risk of rejection, treatment with

	addition, the Marketing authorisation holder (MAH) took the opportunity to correct inconsistencies in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				antibiotics).
II/0136	Update of sections 4.4 and 4.5 of the SmPC of all pharmaceutical forms, in order to update information regarding potential interactions with antibiotics and other drugs interfering with glucuronidation pathway, based on a review of published literature. The package leaflet is updated accordingly. In addition, update of section 6.6 of the SmPC and section 3 of the package leaflet to improve the recommendations regarding safe handling of the powder for oral suspension formulation as well as other minor editorial changes. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/11/2017	05/03/2018	SmPC and PL	Antibiotics eliminating β-glucuronidase-producing bacteria in the intestine (e.g. aminoglycoside, cephalosporin, fluoroquinolone, and penicillin classes of antibiotics) may interfere with the enterohepatic recirculation of phenolic glucuronide of mycophenolic acid (MPAG) /mycophenolic acid (MPA) and should therefore be used with caution due to their potential to reduce systemic MPA exposure and thus reduce the efficacy of CellCept. Drugs inhibiting glucuronidation of MPA may increase MPA exposure and caution is therefore recommended when administering these drugs concomitantly with CellCept, e.g. concomitant administration of CellCept with the antifungal isavuconazole leads to a 35% increase in exposure to MPA.
IA/0134/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 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 A.7 - Administrative change - Deletion of	12/06/2017	n/a		

	manufacturing sites 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				
IB/0133	Addition of 2 new specified degradation products, N-oxyde analog and Z-isomer with a limit of max 0.10%, to the specifications for the finished product, in order to comply with current Pharmacopoeial requirements for Mycophenolate Mofetil capsules. In addition, the applicant also took the opportunity to perform editorial amendments to P.5.2. 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	21/12/2016	n/a		
PSUSA/2099/201605	Periodic Safety Update EU Single assessment - mycophenolate mofetil	01/12/2016	n/a		PRAC Recommendation - maintenance
II/0128/G	This was an application for a group of variations. B.II.a.3.b.6 - Changes in the composition (excipients) of the finished product - Other excipients - Replacement of a single excipient with a comparable excipient with the same functional characteristics and at a similar level 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	15/09/2016	n/a		

	release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes 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 B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold 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 B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method				
N/0132	Update of Annex IIIA to add the 2D barcode unique identifier according to QRD template vs 10. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/08/2016	05/03/2018	Labelling	
IG/0667/G	This was an application for a group of variations.	08/04/2016	n/a		

	B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer B.III.1.b.4 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Deletion of certificates (in case multiple certificates exist per material)				
IA/0129/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.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 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 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 B.II.d.1.d - Change in the specification parameters	29/02/2016	n/a		

	and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.i - Change in the specification parameters and/or limits of the finished product - Ph. Eur. 2.9.40 uniformity of dosage units is introduced to replace the currently registered method, either Ph. Eur. 2.9.5 or Ph. Eur. 2.9.6 B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits				
II/0121	Update of sections 4.3, 4.4 and 4.6 of the SmPC in order to add a contraindication in pregnant women, unless there is no suitable alternative treatment to prevent transplant rejection, and update the safety information related to pregnancy. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the PI in line with the latest QRD template version. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/10/2015	27/11/2015	SmPC and PL	The MAH submit a variation to update of sections 4.3, 4.4 and 4.6 of the SmPC in order to add a contraindication in pregnant women, unless there is no suitable alternative treatment to prevent transplant rejection and update the safety information related to pregnancy. The Package Leaflet is updated accordingly. The Marketing authorisation holder (MAH) took the opportunity to update the PI in line with the latest QRD template version. In addition, Additional risk minimisation measures in a pregnancy prevention program have also been added in Annex II of the opinion.

IB/0126	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	26/10/2015	n/a		
IB/0127	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	23/10/2015	n/a		
IA/0125	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	14/07/2015	n/a		
IG/0573	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	01/07/2015	n/a		
IA/0123	B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	21/05/2015	n/a		
II/0122/G	This was an application for a group of variations. Update of sections 4.4, 4.5 and 5.2 of the SmPC in order to update the safety information related to MPA exposure and switching therapies, potential change in MPA exposure when MMF and telmisartan are used concomitantly and updates of pharmacokinetics/biotransformation data. This	26/03/2015	27/11/2015	SmPC	Following a review of the current information available on MPA exposure, consequent interactions, information of switch of therapy and additional pharmacokinetic data, the Marketing Authorisation Holder (MAH) has updated the Company Core Data Sheet (CDS) and proposes some updates to the SmPC in line with the CDS update as part of this application. Therefore, sections 4.4, 4.5 and 5.2 of the SmPC are being updated in order to amend the safety

	procedure is a grouping variation. The requested group of variations proposed amendments to the Summary of Product Characteristics. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				information related to MPA exposure and switching therapies, potential change in MPA exposure when MMF and telmisartan are used concomitantly and updates of pharmacokinetics/biotransformation data.
II/0119	Update of sections 4.4 and 4.8 of the SmPC following assessment of safety signal (SDA036) in order to add a warning and update safety information on bronchiectasis and hypogammaglobulineamia. The Package Leaflet is updated accordingly. A DHPC has also been endorsed as additional risk minimization measure on communication regarding bronchiectasis and hypogammaglobulineamia. In addition, the MAH has taken the opportunity to correct editorial errors in annex I and IIIB regarding imprints on the capsules and embossing on the tablets. C.I.z - Changes (Safety/Efficacy) of Human and	20/11/2014	19/12/2014	SmPC and PL	Based on cumulative reviews provided on bronchiectasis and hypogammaglobulineamia these two adverse drug reactions have been implemented in the product information for CellCept. A DHPC has also been issued as an additional risk minimization measure.

	Veterinary Medicinal Products - Other variation				
PSUSA/2099/201405	Periodic Safety Update EU Single assessment - mycophenolate mofetil	04/12/2014	n/a		PRAC Recommendation - maintenance
IG/0497	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	18/11/2014	n/a		
IB/0117	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	09/07/2014	n/a		
IB/0115/G	This was an application for a group of variations. 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 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 B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation 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.h - Change in the specification parameters	09/05/2014	n/a		

	and/or limits of the finished product - Update of the dossier to comply with the provisions of an updated general monograph of the Ph. Eur. for the finished product B.II.d.1.i - Change in the specification parameters and/or limits of the finished product - Ph. Eur. 2.9.40 uniformity of dosage units is introduced to replace the currently registered method, either Ph. Eur. 2.9.5 or Ph. Eur. 2.9.6 B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
IB/0116/G	This was an application for a group of variations. B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition) B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method	28/04/2014	n/a		
IB/0114/G	This was an application for a group of variations. B.II.b.1.e - Replacement or addition of a	16/04/2014	n/a		

	manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation 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 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				
IA/0113/G	This was an application for a group of variations. B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer B.III.1.b.2 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer	22/08/2013	n/a		
II/0111	Update of section 4.4 of the SmPC in order to include a warning regarding hepatitis B and C reactivation associated with CellCept.	25/07/2013	18/07/2014	SmPC, Annex II, Labelling	Following cumulative review of the MAH global drug safety database and the published preclinical and clinical literature the data on association of MMF causing hepatitis B or C

	In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is being brought in line with the latest QRD template. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data			and PL	reactivation appears limited. However, reactivation of hepatitis B and C with immunosuppressants is well documented. Overall, a causal relationship of MMF in isolation with hepatitis B or C reactivation cannot be proven but MMF may contribute to reactivation by the virtue of being an immunosuppressant or by increasing the overall potency of immnunosupression. Therefore the proposed amendments to the PI are acceptable. Taking into consideration that most guidelines recommend testing for hepatitis B before immunosuppressant's are started or prior to transplantation and initiation of antiviral prophylaxis/therapy is advised and neither a guideline nor an effective prophylaxis exists for hepatitis C reactivation routine pharmacovigilance for these events are acceptable at this point in time.
IG/0311	B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	28/06/2013	n/a		
IA/0110/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.7 - Administrative change - Deletion of manufacturing sites 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	13/12/2012	n/a		

IG/0228	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/11/2012	n/a		
II/0106	Update of section 4.5 of the SmPC to include information regarding the interaction with proton pump inhibitors following the outcome of PSUR 18 assessment (covering the period: 01.05.08 - 30.04.11). The package leaflet has been updated accordingly. The MAH also adjusted the pharmaceutical form according to QRD template throughout the annexes for CellCept 500 mg film-coated tablets. Furthermore, the MAH changed section 4 of the package leaflet to correct the location of information on "Fighting infections". In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. 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	21/06/2012	20/07/2012	SmPC, Labelling and PL	Routine monitoring of literature publications by the MAH identified reports of reduction in mycophenolic acid (MPA) exposure when PPIs were given concomitantly with MMF. This has the potential to reduce the clinical effectiveness of MMF therapy. The available data could not rule out the occurrence of clinically relevant effects. This was not considered a new or significant safety finding as reference to an interaction with antacids were already included in the SmPC, and as patients during development and dose selection were using antacids. The MAH therefore updated section 4.5 of the SmPC to include information regarding the interaction with proton pump inhibitors (PPIs) administered with mycophenolate mofetil (MMF).
IB/0108	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	19/03/2012	n/a		

IA/0107/G	This was an application for a group of variations. 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 B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	27/01/2012	n/a		
IG/0115/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer	16/12/2011	n/a		
IB/0104/G	This was an application for a group of variations. B.II.b.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions B.II.b.4.b - Change in the batch size (including batch	07/11/2011	n/a		

	size ranges) of the finished product - Downscaling down to 10-fold B.II.a.3.a.2 - Changes in the composition (excipients) of the finished product - Changes in components of the flavouring or colouring system - Increase or reduction B.III.1.b.2 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer				
IB/0103	B.II.e.1.a.2 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Semi-solid and non-sterile liquid pharmaceutical forms	16/06/2011	n/a		
IB/0102/G	This was an application for a group of variations. B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method	04/03/2011	n/a		
IA/0101/G	This was an application for a group of variations. B.III.1.b.2 - Submission of a new or updated Ph. Eur.	08/12/2010	n/a		

	TSE Certificate of suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.3 - Submission of a new or updated Ph. Eur. TSE Certificate of suitability - Updated certificate from an already approved manufacturer				
IB/0100	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	20/10/2010	n/a	Labelling and PL	Changes to the PIL section 2. BEFORE YOU TAKE CELLCEPT - Take special care with CellCept and Pregnancy and breast-feeding recommended by the CHMP following the assessment of FU2 032. The MAH is also introducing harmonised terms for the 'expiry date' and 'batch No' printed on small vial labels of parental formulations of a number of our products in all languages.
IA/0099/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.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	15/09/2010	n/a		
II/0097	Addition of an alternative manufacturing site for the	18/02/2010	01/03/2010		

	active substance and minor changes in the manufacturing process Change(s) to the manufacturing process for the active substance				
IB/0098	To replace the manufacturer responsible for bulk production and primary packaging IB_07_c_Replacement/add. of manufacturing site: All other manufacturing operations ex. batch release IA_07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms	13/01/2010	n/a		
II/0093	Update of sections 4.8 of the SPC to include information on isolated reports of ILD and pulmonary fibrosis further to the CHMP's request following the assessment of the additional pharmacovigilance Follow-up measure 30.1, follow-up information to PSUR 17. The MAH used the opportunity of this variation to update section 4 of the PL of the powder for concentrate for infusion to correct inconsistencies resulting from variation EMEA/H/C/0082/II/24 (removal of the term "dehydration"). As a new packaging design for CellCept has been introduced, Annex IIIA has been updated as well. Update of Summary of Product Characteristics, Labelling and Package Leaflet	24/09/2009	13/10/2009	SmPC, Labelling and PL	In the course of routine safety surveillance of this product, cases of interstitial lung disease (ILD) and pulmonary fibrosis have been reported. A causal contribution of CellCept was found to be a reasonable possibility in at least some of these cases. Therefore, it was regarded as necessary to include this information in the Summary of Product Characteristics (SPC). Pulmonary side effects were already included in the Package Leaflet (PL).
IA/0096	IA_37_a_Change in the specification of the finished product - tightening of specification limits	29/09/2009	n/a		

IA/0095	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	29/09/2009	n/a		
IA/0094	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	29/09/2009	n/a		
II/0086	Update of section 4.4 and 4.8 of the SPC to include information on pure red cell aplasia. Update of sections 4.8 of the SPC to include information on acquired Pelger-Huet anomaly and to include the term "gingival hyperplasia". Update of section 4.5 of the SPC to include possible drug-drug interaction of CellCept in combination with ciprofloxacin or amoxicillin plus clavulanic acid. The MAH has also taken the opportunity to correct an error in the PL of the three formulations for oral use. Update of Summary of Product Characteristics and Package Leaflet	23/04/2009	25/05/2009	SmPC and PL	Forty-one cases of PRCA have been reported worldwide to date in patients treated with CellCept. In 16 of the reported cases, dose reduction (in 4 cases) or discontinuation (in 12 cases) of CellCept led to resolution of the condition. A causal association between CellCept and PRCA could not be excluded. The review of the isolated cases of acquired Pelger-Huet anomaly and abnormal neutrophil morphology reported in patients treated with CellCept shows that a causal association between abnormal neutrophil morphological abnormalities, including the acquired Pelger-Huet anomaly and CellCept can not be excluded. The assessment of the pharmacokinetic data shows an interaction between CellCept and ciprofloxacin or amoxicillin plus clavulanic acid which can lead to a reduction in pre-dose concentration of mycophenolic acid of about 50% compared to baseline pre-antibiotic concentrations. Gum hyperplasia, swelling or gingival hyperplasia are expected adverse drug reactions for CellCept. "Gingival hyperplasia" is listed in the Company Core Data Sheet of the MAH. The CellCept's product information has been updated accordingly.
IB/0088	IB_37_a_Change in the specification of the finished	06/05/2009	n/a		

	product - tightening of specification limits				
IB/0087	IB_14_b_Change in manuf. of active substance without Ph. Eur. certificate - new manufacturer	06/05/2009	n/a		
IB/0092	IB_38_c_Change in test procedure of finished product - other changes	27/04/2009	n/a		
IA/0090	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	27/04/2009	n/a		
IA/0091	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	23/04/2009	n/a		
IA/0089	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	22/04/2009	n/a		
IA/0085	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	10/11/2008	n/a		
II/0084	Update of sections 4.4 "Special warnings and precautions for use" and 4.8 "Undesirable effects" of the summary of product characteristics (SPC) to implement the warning on BK virus-associated nephropathy (BKVN) and JC virus associated progressive multifocal leukoencephalopathy (PML) requested by the CHMP in July 2008. The MAH also took the opportunity to include information on the excipient sorbitol in the SPC and package leaflet (PL) of the powder for oral suspension formulation, to comply with the EU guideline on "Excipients in the label and package	25/09/2008	23/10/2008	SmPC and PL	More than half of the confirmed cases of BKVN were reported in patients receiving the approved combination of mycophenolate mofetil with ciclosporin and steroids. Although the risk of BKVN may be related to the total burden of immunosuppression, an association specifically with MMF is biologically plausible and cannot be ruled out. It is therefore considered important to make physicians fully aware of the risks of opportunistic infections that may occur under potent immunosuppression. Thus physicians should consider BKVN and PML in the differential diagnosis in immunosuppressed patients with deteriorating renal

	leaflet on medicinal products for human use". Update of Summary of Product Characteristics and Package Leaflet				function and neurological symptoms.
II/0083	To update section 4.6 of the SPC to include that cases of spontaneous abortions have been reported in patients exposed to CellCept. The PL was updated accordingly. Furthermore the contact details of the Estonian and Finnish local representatives in the PL have been updated. Update of Summary of Product Characteristics and Package Leaflet	24/01/2008	28/02/2008	SmPC and PL	Based on the assessment of the annual Drug Safety Report on pregnancy the CHMP noted that among the 191 pregnancy cases received by the MAH since CellCept has been first marketed, 38 cases had been reported as spontaneous abortion. Thus, the CHMP concluded that spontaneous abortion should be included in section 4.6 of the SPC.
II/0082	To update sections 4.4 and 4.8 of the SPC to include information that cases of Progressive Multifocal Leukoencephalopathy (PML), sometimes fatal, have been reported in CellCept treated patients and that physicians should consider PML in the differential diagnosis in patients reporting neurological symptoms. The PL was updated accordingly. Furthermore, the Marketing Authorisation Holder took the opportunity to amend the storage condition for the capsules in the SPC and labelling in line with the wording in the PL. Update of Summary of Product Characteristics, Labelling and Package Leaflet	24/01/2008	28/02/2008	SmPC, Labelling and PL	Cases of Progressive Multifocal Leukoencephalopathy (PML), sometimes fatal, have been reported in CellCept treated patients based on a safety review of all PML cases reported with mycophenolate mofetil in the company safety database. In the reported cases patients generally had risk factors for PML, including immunosuppressant therapies and impairment of immune function. Nevertheless based on the temporal relationship observed in some cases, the contributory role of CellCept cannot be excluded. Thus, in immunosuppressed patients, physicians should consider PML in the differential diagnosis in patients reporting neurological symptoms and consultation with a neurologist should be considered as clinically indicated. Furthermore, in patients who develop PML, physicians should consider the reduction of the total immunosuppression. In transplant patients, however, reduced immunosuppression may place

					the graft at risk.
II/0079	To update sections 4.6 and 4.8 of the SPC to include information on congenital malformations reported in children of patients exposed to CellCept, in combination with other immunosuppressants, during pregnancy. Section 2 of the PL was updated accordingly. Update of Summary of Product Characteristics and Package Leaflet	20/09/2007	19/10/2007	SmPC and PL	Based on a publication (Sifontis et al, 2006) and a cumulative review of pregnancy outcomes from the company safety database, section 4.6 of the SPC was updated to include that congenital malformations (including ear malformations, i.e. abnormally formed or absent external/middle ear) were reported in children of patients exposed to CellCept, in combination with other immunosuppressants, during pregnancy. Section 4.8 of the SPC was updated to include a cross-reference to section 4.6 for congenital disorders. Finally, section 2 of the PL was updated in order to reflect the changes in the SPC and to re-inforce the message that CellCept should not be used during pregnancy unless clearly indicated by doctors.
IA/0081	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	05/10/2007	n/a		
II/0077	To update section 4.5 of the SPC to include new data on potential interaction with other medicinal products. The PL has been updated accordingly. To reword section 4.9 of the SPC in order to include information on signs and symptoms of overdose and on treatment of overdose. Furthermore, to introduce minor linguistic changes and to update the Product Information in line with the latest EMEA/QRD template. To amend the storage condition for CellCept Tablets from "protect from moisture" to "protect from light" throughout the Product Information. Update of Summary of Product Characteristics,	21/06/2007	10/08/2007	SmPC, Annex II, Labelling and PL	Section 4.5 "Interaction with other medicinal products and other forms of interaction" of the SPC has been updated to include new data on potential interaction with the following medicinal products: - tacrolimus: in hepatic transplant patients, the exposure of MPA (mycophenolic acid), which is the active metabolite of CellCept, was not significantly affected by the coadministration of tacrolimus; - ciclosporin A: if concomitant ciclosporin treatment is stopped, an increase in the concentration of MPA should be expected; - sirolimus: in renal transplant patients, concomitant administration of CellCept and ciclosporin A resulted in

	Labelling and Package Leaflet				reduced MPA exposures by 30 50% compared with patients receiving the combination of sirolimus and similar doses of CellCept; - norfloxacin and metronidazole: in healthy volunteers, no significant interaction was observed when CellCept was administered with - norfloxacin and metronidazole separately. However, norfloxacin and metronidazole combined reduced the MPA exposure by approximately 30 % following a single dose of CellCept; - rifampicin: in patients not also taking ciclosporin, concomitant administration of CellCept and rifampicin resulted in a decrease in MPA exposure; - sevelamer: decrease in MPA exposure was observed when CellCept was concomitantly administered with sevelamer without any clinical consequences (i.e. graft rejection). The PL has been updated accordingly. Additionally, the MAH took the opportunity to reword section 4.9 "Overdose" of the SPC in order to include information on signs and symptoms of overdose and on treatment of overdose.
IB/0080	IB_10_Minor change in the manufacturing process of the active substance	10/05/2007	n/a		
N/0076	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/04/2007	n/a	PL	
IB/0078	IB_10_Minor change in the manufacturing process of the active substance	22/03/2007	n/a		

IA/0075	IA_05_Change in the name and/or address of a manufacturer of the finished product	15/12/2006	n/a	Annex II and PL	
IB/0074	IB_10_Minor change in the manufacturing process of the active substance	27/11/2006	n/a		
IB/0073	IB_25_a_01_Change to comply with Ph. - compliance with EU Ph. - active substance	27/11/2006	n/a		
IB/0072	IB_10_Minor change in the manufacturing process of the active substance	27/11/2006	n/a		
II/0071	Change(s) to the test method(s) and/or specifications for the finished product	21/09/2006	27/09/2006		
IA/0070	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	04/05/2006	n/a		
R/0069	Renewal of the marketing authorisation.	26/01/2006	13/03/2006	SmPC, Annex II, Labelling and PL	
II/0066	This variation relates to an update of section 4.8 "Undesirable effects" of the Summary of Product Characteristics (SPC) to include "aplastic anaemia" and "bone marrow depression" following the CHMP assessment of PSUR n. 15 (covering the period from 1 May 2003 to 30 April 2004). Additionally the list of local representatives (Iceland) in the Package Leaflet has been updated.	13/10/2005	15/11/2005	SmPC and PL	Following the CHMP assessment of PSUR n. 15 (covering the period from 1 May 2003 to 30 April 2004), on the basis of a detailed examination of the cases reported by the MAH, it is reasonable to conclude that aplastic anaemia and bone marrow depression are potential adverse drug reactions attributable to Cellcept. Therefore the MAH has amended the list of undesirable effects from post-marketing experience in the SPC to include that there have been isolated reports of aplastic anaemia and bone marrow

	Update of Summary of Product Characteristics and Package Leaflet				depression in patients treated with CellCept, some of which have been fatal.
IA/0068	IA_01_Change in the name and/or address of the marketing authorisation holder	11/10/2005	n/a	SmPC, Labelling and PL	
IA/0067	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	08/09/2005	n/a		
II/0065	Update of section 4.3 `Contraindications' to add `breastfeeding' and section 4.6 "Pregnancy and lactation" of the Summary of Product Characteristics (SPC). Additionally the MAH has proposed to align the Product Information (SPC, Labelling and Package Leaflet) to the latest QRD recommendations and to use INN names where relevant in the Product Information. Update of Summary of Product Characteristics, Labelling and Package Leaflet	16/03/2005	27/04/2005	SmPC, Labelling and PL	In line with the CHMP recommendations following the review of PSUR n. 14 (covering the period from 01.05.02 to 30.04.03) and PSUR n. 15 (covering the period from 01.05.03 to 30.04.04) the MAH has proposed to contraindicate the use of Cellcept in nursing mothers: section 4.3 `Contraindications' of the Summary of Product Characteristics (SPC) was updated to add `breastfeeding'. Section 4.6 "Pregnancy and lactation" of the SPC has been updated to include information on pregnancy and lactation. Additionally the MAH has proposed to align the Product Information (SPC, Labelling and Package Leaflet) to the latest QRD recommendations and to use INN names where relevant in the Product Information. Minor changes to the list of local representatives (Malta, Slovenija, Slovenská republika) in the Package Leaflet have been proposed.
IB/0064	IB_33_Minor change in the manufacture of the finished product	27/09/2004	n/a		
II/0059	This variation relates to an update of section 4.8 of the Summary of Product Characteristics to add the	22/04/2004	02/08/2004	SmPC and PL	Angioedema:. The MAH has performed an adequate search of its safety database for cases consistent with

	terms "angioedema", and "anaphylaxis" following the evaluation of the fourteenth CellCept Periodic Safety Update Report (PSUR). Sections 4.3 and 4.8 have been modified to include the term "hypersensitivity"instead of "allergic reaction". The Package Leaflet section 4 have been updated accordingly. The list of the local representatives in the Package Leaflet has been updated. Update of Summary of Product Characteristics and Package Leaflet				angioedema. A total of 19 case reports were retrieved. These figures give a crude estimated incidence of angioedema of approximately 3:100,000 (i.e. <1:10,000 - very rare). Anaphylaxis: A total of 19 case reports were retrieved. No rate estimates were possible but the figures suggest a rate that is likely to be less that the estimated incidence of angioedema. Allergic reaction: The Meddra-preferred term "hypersensitivity" has been proposed by the MAH instead of "allergic reaction" in section 4.8. For consistency section 4.3 was also amended.
IB/0063	IB_10_Minor change in the manufacturing process of the active substance	26/07/2004	n/a		
IB/0062	IB_10_Minor change in the manufacturing process of the active substance	26/07/2004	n/a		
IA/0061	IA_13_a_Change in test proc. for active substance - minor change	29/06/2004	n/a		
IA/0060	IA_13_a_Change in test proc. for active substance - minor change	29/06/2004	n/a		
II/0058	Change(s) to the manufacturing process for the finished product	24/07/2003	28/07/2003		
I/0057	23_Change in storage conditions	18/10/2002	02/12/2002	SmPC, Labelling and PL	

II/0055	Update of Summary of Product Characteristics	25/07/2002	18/10/2002	SmPC	
I/0056	15_Minor changes in manufacture of the medicinal product	23/08/2002	10/09/2002		
I/0054	12_Minor change of manufacturing process of the active substance 11b_Change in supplier of an intermediate compound used in manufacture of the active substance	14/08/2002	10/09/2002		
I/0053	12_Minor change of manufacturing process of the active substance	14/08/2002	10/09/2002		
II/0036	Update of Summary of Product Characteristics	13/12/2001	15/05/2002	SmPC	
I/0051	25_Change in test procedures of the medicinal product	04/02/2002	13/02/2002		
I/0039	01_Withdrawal of the manufacturing authorisation for a site of manufacture	23/11/2001	06/02/2002	Annex II and PL	
I/0046	32_Change of imprints/bossing/marking on tablets/printing on capsules, incl. addition/change of inks	23/11/2001	05/02/2002	SmPC and PL	
II/0037	Change(s) to shelf-life or storage conditions	13/12/2001	21/12/2001		
I/0049	25_Change in test procedures of the medicinal product	30/11/2001	10/12/2001		

I/0048	15_Minor changes in manufacture of the medicinal product	30/11/2001	10/12/2001		
II/0034	Update of Summary of Product Characteristics	23/08/2001	06/12/2001	SmPC	
I/0050	16_Change in the batch size of finished product	30/11/2001	n/a		
I/0047	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	19/11/2001	28/11/2001		
I/0045	26_Changes to comply with supplements to pharmacopoeias	23/11/2001	28/11/2001		
I/0044	16_Change in the batch size of finished product	23/11/2001	28/11/2001		
I/0043	16_Change in the batch size of finished product	23/11/2001	28/11/2001		
I/0042	15a_Change in IPCs applied during the manufacture of the product	23/11/2001	28/11/2001		
I/0041	15_Minor changes in manufacture of the medicinal product	23/11/2001	28/11/2001		
I/0040	04_Replacement of an excipient with a comparable excipient	23/11/2001	28/11/2001		
I/0038	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	23/11/2001	28/11/2001		
II/0032	Update of Summary of Product Characteristics	29/03/2001	16/07/2001	SmPC	

II/0027	Update of Summary of Product Characteristics and Package Leaflet	29/03/2001	16/07/2001	SmPC and PL	
I/0033	01_Change in the name of a manufacturer of the medicinal product	18/05/2001	23/05/2001		
II/0029	Update of or change(s) to the pharmaceutical documentation	25/04/2001	04/05/2001		
II/0031	Update of Summary of Product Characteristics	25/01/2001	27/04/2001	SmPC	
II/0024	Extension of Indication	27/07/2000	09/11/2000	SmPC and PL	
I/0025	11_Change in or addition of manufacturer(s) of active substance	07/03/2000	30/03/2000		
II/0022	Update of Summary of Product Characteristics and Package Leaflet	30/07/1999	08/12/1999	SmPC, Labelling and PL	
I/0023	15_Minor changes in manufacture of the medicinal product	04/08/1999	n/a		
X/0014	X-3-iv_Change or addition of a new pharmaceutical form	19/11/1998	26/02/1999	SmPC, Annex II, Labelling and PL	
I/0019	04_Replacement of an excipient with a comparable excipient	30/10/1998	07/12/1998	SmPC and PL	
I/0016	16_Change in the batch size of finished product	30/10/1998	09/11/1998		

I/0015	01_Change following modification(s) of the manufacturing authorisation(s)	30/10/1998	09/11/1998		
I/0021	16_Change in the batch size of finished product	30/10/1998	n/a		
I/0018	08_Change in the qualitative composition of immediate packaging material	30/10/1998	n/a		
I/0017	17_Change in specification of the medicinal product	30/10/1998	n/a		
X/0013	X-3-iv_Change or addition of a new pharmaceutical form	27/05/1998	20/10/1998	SmPC, Annex II, Labelling and PL	
II/0020	Update of Summary of Product Characteristics and Package Leaflet	27/05/1998	18/09/1998	SmPC and PL	
II/0010	Extension of Indication	22/04/1998	17/08/1998	SmPC and PL	
I/0008	12_Minor change of manufacturing process of the active substance 14_Change in specifications of active substance	09/09/1997	n/a		
I/0012	14_Change in specifications of active substance	20/08/1997	n/a		
I/0011	14_Change in specifications of active substance 24_Change in test procedure of active substance	20/08/1997	n/a		
I/0009	14_Change in specifications of active substance	20/08/1997	n/a		
I/0005	20_Extension of shelf-life as foreseen at time of authorisation	23/05/1997	14/07/1997		

II/0003	New presentation(s)	20/11/1996	13/05/1997	SmPC, Labelling and PL	
II/0004	Update of Summary of Product Characteristics and Package Leaflet	19/12/1996	02/05/1997	SmPC and PL	
I/0001	15_Minor changes in manufacture of the medicinal product	20/03/1996	n/a		