CellCept®

Mycophenolate mofetil

1. DESCRIPTION
1.1 Therapeutic/Pharmacologic Class of Drug
Selective immunosuppressive agent – mycophenolic acid.

ATC code: L04AA06.

1.2 Type of Dosage Form
CellCept is supplied as film-coated caplets.

1.3 Route of Administration
Oral.

1.4 Sterile/Radioactive Statement
Not applicable.

1.5 Qualitative and Quantitative Composition
Active ingredient: mycophenolate mofetil.
Each film-coated caplets contains 500 mg mycophenolate mofetil.

2. CLINICAL PARTICULARS
2.1 Therapeutic Indication(s)
Transplant patients
CellCept is indicated for the prophylaxis of acute organ rejection in patients receiving allogeneic renal transplants.
CellCept is indicated for the prophylaxis of acute organ rejection and increased graft and patient survival in patients receiving allogeneic cardiac transplants.

CellCept should be used concomitantly with ciclosporin and corticosteroids.

Lupus nephritis patients
CellCept is indicated for induction and maintenance therapy of adult patients with WHO Class III, IV, V lupus nephritis. This indication is based on the evidence in literature reports of studies of treatment in patients with lupus nephritis, the majority of whom were ISN/RPS (2003) Class IV. The evidence for efficacy was based on surrogate endpoints.

2.2 Dosage and Administration
CellCept oral dosage forms **should not be switched with mycophenolic acid delayed-release tablets without supervision of a physician with experience in immunosuppressive therapy** because the rates of absorption following the administration of CellCept oral dosage forms and mycophenolic acid delayed-release tablets are not equivalent.

Please refer to full prescribing information for corticosteroids and ciclosporin, which are used in combination with CellCept.

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Transplant patients
Standard dosage for prophylaxis of renal rejection
The initial dose of CellCept should be given orally within 72 hours following transplantation. Although a dose of 1.5 g administered twice daily (daily dose of 3 g) was used in clinical trials and was shown to be safe and effective, no efficacy advantage could be established for renal transplant patients. Patients receiving 2 g per day of CellCept demonstrated an overall better safety profile compared to patients receiving 3 g per day of CellCept.

Standard dosage for prophylaxis of cardiac rejection
The initial dose of CellCept should given orally within 5 days following transplantation. A dose of 1.5 g administered twice a day (daily dose of 3 g) is recommended for use in cardiac transplant patients.

Oral administration (see *3.2.1 Pharmacokinetic Properties, Absorption*)
The initial dose of CellCept should be given as soon as possible following renal or cardiac transplantation.

Lupus nephritis patients
Standard dosage for induction therapy
Adults: A dose of 750 mg–1.5 g administered orally twice a day (daily dose of up to 3 g) is recommended.

Standard dosage for maintenance therapy
Adults: A dose of 500 mg–1 g administered orally twice a day is recommended.

CellCept should be used in combination with corticosteroids. Doses should be introduced gradually and adjusted according to clinical response. Therapeutic drug monitoring could help prevent subtherapeutic exposure ($C_{min} \geq 3.0$ mg/L or inter-dose AUC ≥ 35 h*mg/L).

2.2.1 Special Dosage Instructions
Pediatric use
Safety and efficacy in pediatric patients have not been established. Very limited pharmacokinetic data are available for pediatric renal transplant patients. No data are available for pediatric patients receiving cardiac transplants.

Geriatric use
For transplant patients, no oral dosage adjustment is recommended (see *2.4 Warnings and Precautions*).

For lupus nephritis patients, no recommendation is available.

Renal impairment
For renal transplant patients with severe chronic renal impairment (glomerular filtration rate (GFR) < 25 mL/min/1.73 m^2), outside of the immediate post-transplant period or after treatment of acute or refractory rejection, administration of doses greater than 1 g twice daily should be avoided (see *3.2. Pharmacokinetic Properties*).

For cardiac transplant patients with severe chronic renal impairment, no data are available.

Patients with delayed renal graft function posttransplant
For post-transplant patients with delayed renal graft function, no dose adjustment is recommended but patients should be carefully monitored (see *3.2 Pharmacokinetics Properties*).

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Hepatic impairment
For renal transplant patients with severe hepatic parenchymal disease, no dose adjustments are recommended (see *3.2 Pharmacokinetic Properties*).

For cardiac transplant patients and lupus nephritis patients with severe hepatic parenchymal disease, no data are available.
Patients with neutropenia
For patients that develop neutropenia (absolute neutrophil count < 1.3 x 10^3/µL), dosing with CellCept should be interrupted or the dose should be reduced (see *2.4 Warnings and Precautions*). Physician should perform appropriate diagnostic test and manage the patients appropriately.

2.3 Contraindications
Allergic reactions to CellCept have been observed. Therefore, CellCept is contraindicated in patients with hypersensitivity to mycophenolate mofetil or mycophenolic acid (MPA).

CellCept is contraindicated during pregnancy due to its mutagenic and teratogenic potential (see *2.5.2 Pregnancy*).

CellCept is contraindicated in women of childbearing potential not using highly effective contraceptive methods (see *2.5.1 Females and Males of Reproductive Potential*).

CellCept is contraindicated in women who are breastfeeding (see *2.5.3 Lactation*).

2.4 Warnings and Precautions
2.4.1 General
Neoplasms
As in all patients receiving immunosuppressive regimens involving combinations of drugs, patients receiving CellCept as part of an immunosuppressive regimen are at increased risk of developing lymphomas and other malignancies, particularly of the skin (see *2.6 Undesirable Effects*). The risk appears to be related to the intensity and duration of immunosuppression rather than to the use of any specific agent.

As with all patients at an increased risk for skin cancer, exposure to sunlight and UV light should be limited by wearing protective clothing and using a sunscreen with a high protection factor.

Infections
Oversuppression of the immune system can also increase susceptibility to infection including opportunistic infections, fatal infections and sepsis (see *2.6 Undesirable Effects*). Such infections include latent viral reactivation, such as hepatitis B or hepatitis C reactivation, or infections caused by polyomaviruses. Cases of hepatitis due to reactivation of hepatitis B or hepatitis C have been reported in carrier patients treated with immunosuppressants. Cases of Progressive Multifocal Leukoencephalopathy (PML) associated with the JC virus, sometimes fatal, have been reported in CellCept-treated patients. The reported cases generally had risk factors for PML, including immunosuppressant therapies and impairment of immune function. 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.

BK virus-associated nephropathy has been observed during the use of CellCept in patients post- renal transplant. This infection can be associated with serious outcomes, sometimes leading to renal graft loss. Patient monitoring may help detect patients at risk for BK virus-associated nephropathy. Due to the cytostatic effect of CellCept on B- and T-lymphocytes, increased severity of COVID-19 may occur. Dose

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reduction or discontinuation of CellCept should be considered for patients who develop evidence of BK virus-associated nephropathy, or in cases of clinically significant COVID-19.

Blood and immune system
Cases of pure red cell aplasia (PRCA) have been reported in patients treated with CellCept in combination with other immunosuppressive agents. The mechanism for mycophenolate mofetil induced PRCA is unknown; the relative contribution of other immunosuppressants and their combinations in an immunosuppression regimen are also unknown. In some cases PRCA was found to be reversible with dose reduction or cessation of CellCept therapy. In transplant patients however reduced immunosuppression may place the graft at risk.

Patients receiving CellCept should be instructed to report immediately any evidence of infection, unexpected bruising, bleeding or any other manifestation of bone marrow depression.

Patients on CellCept should have complete blood counts weekly during the first month of treatment, twice monthly for the second and third months, then monthly through the first year. In particular, patients receiving CellCept should be monitored for neutropenia. The development of neutropenia may be related to CellCept, concomitant medications, viral infection or some combination of these causes (see *2.2.1 Special Dosage Instructions*). If neutropenia develops (absolute neutrophil count < $1.3 \times 10^3/\mu L$), dosing with CellCept should be interrupted or the dose should be reduced and the patient carefully observed (see *2.2.1 Special Dosage Instructions*).

Blood donation
Patients should not donate blood during therapy and for at least 6 weeks following discontinuation of CellCept.

Vaccination
Patients should be advised that during treatment with CellCept vaccinations may be less effective and the use of live attenuated vaccines should be avoided (see *2.8 Interactions with Other Medicinal Products and Other Forms of Interaction*). Influenza vaccination may be of value. Prescribers should refer to national guidelines for influenza vaccination.

Gastrointestinal
CellCept has been associated with an increased incidence of digestive system adverse events, including infrequent cases of gastrointestinal tract ulceration, hemorrhage, and perforation. CellCept should be administered with caution in patients with active digestive system disease.

CellCept is an inosine monophosphate dehydrogenase (IMPDH) inhibitor; therefore it should be avoided in patients with rare hereditary deficiency of hypoxanthine-guanine phosphoribosyl-transferase (HGPRT) such as Lesch-Nyhan and Kelley-Seegmiller syndrome.

Interactions
Caution should be exercised when switching combination therapy from regimens containing immunosuppressants, which interfere with MPA enterohepatic recirculation e.g. ciclosporin to others devoid of this effect e.g. sirolimus, belatacept, or vice versa, as this might result in changes of MPA exposure (see *2.8 Interactions with Other Medicinal Products and Other Forms of Interaction*). Therapeutic drug monitoring of MPA may be appropriate when switching combination therapy or to ensure adequate immunosuppression in patients with high immunological risk (e.g. risk of rejection, treatment with antibiotics, addition or removal of an interacting medication).

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Drugs which interfere with MPA's enterohepatic cycle (e.g. cholestyramine, sevelamer, antibiotics) should be used with caution due to their potential to reduce the plasma levels and efficacy of CellCept (see *2.8 Interactions with Other Medicinal Products and Other Forms of Interaction*). Sevelamer and other calcium-free phosphate binders should be taken 2 hours after CellCept intake to minimise the impact on the absorption of MPA.

It is recommended that CellCept should not be administered concomitantly with azathioprine because both have the potential to cause bone marrow suppression and such concomitant administration has not been studied.

Special populations
Geriatric population
Geriatric patients may be at an increased risk of adverse events such as certain infections (including cytomegalovirus tissue invasive disease) and possibly gastrointestinal hemorrhage and pulmonary edema, compared with younger individuals (see *2.6 Undesirable Effects*).

Pregnancy and breastfeeding
CellCept is contraindicated in pregnancy and during breastfeeding (see *2.5.2 Pregnancy* and *2.5.3 Lactation*).

Semen donation
Men should not donate semen during therapy and for 90 days following discontinuation of CellCept.

2.4.2 Drug Abuse and Dependence
There is no data available to show that CellCept has the potential for drug abuse or dependence.

2.4.3 Ability to Drive and Use Machines
CellCept may have a moderate influence on the ability to drive and use machines.

Patients should be advised to use caution when driving or using machines if they experience adverse drug reactions such as somnolence, confusion, dizziness, tremor or hypotension during treatment with CellCept (see *2.6 Undesirable Effects*).

2.5 Use in Special Populations
2.5.1 Females and Males of Reproductive Potential
Fertility
CellCept is contraindicated in women of childbearing potential not using highly effective contraceptive methods (see *2.3 Contraindications*). Malformations (including anophthalmia, agnathia, and hydrocephaly) occurred in the first generation offspring of female rats treated with oral doses of mycophenolate mofetil in the absence of maternal toxicity (see *3.3.3 Impairment of Fertility*). No effect was seen on the fertility of male rats treated with mycophenolate mofetil.

Pregnancy testing
Prior to starting therapy with CellCept, female patients of childbearing potential must have a negative serum or urine pregnancy test with a sensitivity of at least 25 mIU/mL. A second test should be performed 8-10 days later.

Repeat pregnancy tests should be performed during routine follow-up visits. Results of all pregnancy tests should be discussed with the patient. Patients should be instructed to consult their physician immediately should pregnancy occur.

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Contraception
Females
CellCept is contraindicated in women of childbearing potential not using highly effective contraceptive methods (see *2.3 Contraindications)*.

Before the start of treatment, female patients of reproductive potential must be made aware of the increased risk of pregnancy loss and congenital malformations and must be counseled regarding pregnancy prevention and planning. Women of childbearing potential should use two reliable forms of contraception simultaneously, at least one of which must be highly effective, before beginning CellCept therapy, during therapy, and for six weeks following discontinuation of therapy, unless abstinence is the chosen method of contraception.

Males
Limited clinical evidence is currently available on paternal exposure to CellCept. This evidence does not indicate an increased risk of malformations or miscarriage following paternal exposure to mycophenolate.

Nonclinical evidence shows that the dose of mycophenolate that could be transferred via the seminal fluid to a potentially pregnant partner is 30-fold lower than the concentration without teratogenic effects in animals and 200-fold lower than the lowest teratogenic concentration in animals. However, genotoxic effects have been observed in animal studies at exposures exceeding the human therapeutic exposures by approximately 2.5 times. Thus, the risk of genotoxic effects on sperm cells cannot completely be excluded.

In absence of sufficient data to exclude a risk of harm to the fetus conceived during or directly after the treatment of the father, the following precautionary measure is recommended: sexually active male patients and/or their female partners are recommended to use effective contraception during treatment of the male patient and for at least 90 days after cessation of treatment.

2.5.2 Pregnancy
CellCept is contraindicated during pregnancy due to its mutagenic and teratogenic potential (see *2.3 Contraindications)*. CellCept is a human teratogen, with an increased risk of spontaneous abortions (mainly in the first trimester) and congenital malformations in case of maternal exposure during pregnancy (see *2.6.2 Undesirable Effects, Postmarketing*). In the medical literature, the risk of spontaneous abortions has been reported as 45 to 49% following mycophenolate mofetil exposure, compared to a reported rate between 12 and 33% in solid organ transplant patients treated with other immunosuppressants.

Congenital malformations (including multiple malformations in individual newborns) have been reported in 23 to 27% of live births in mycophenolate mofetil exposed pregnancies in published literature. For comparison the risk of malformations is estimated at approximately 2% of live births in the overall population and at approximately 4 to 5% in solid organ transplant patients treated with immunosupressants other than mycophenolate mofetil.

The following malformations were most frequently reported postmarketing, in children of patients exposed to mycophenolate mofetil in combination with other immunosuppressants during pregnancy:

- Facial malformations such as cleft lip, cleft palate, micrognathia and hypertelorism of the orbits;
- Abnormalities of the ear (e.g. abnormally formed or absent external/middle ear) and eye (e.g. coloboma, microphthalmos);
- Malformations of the fingers (e.g. polydactyly, syndactyly, brachydactyly);
- Cardiac abnormalities such as atrial and ventricular septal defects;
- Oesophageal malformations (e.g. oesophageal atresia);
- Nervous system malformations (such as spina bifida).

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These findings were consistent with teratology studies performed in rats and rabbits where fetal resorptions and malformations occurred in absence of maternal toxicity (see *3.3.4 Reproductive Toxicity).*

Labor and delivery
The safe use of CellCept during labor and delivery has not been established.

2.5.3 Lactation
It is not known whether CellCept is excreted in human milk. Due to the potential for serious adverse reactions in nursing infants, CellCept is contraindicated during breastfeeding (see section *2.3 Contraindications*).
Although the relevance to humans is unknown, studies in rats have shown mycophenolate mofetil to be excreted in milk.

2.5.4 Pediatric Use
See *2.2 Dosage and Administration*, *2.6 Undesirable Effects*, and *3.2.5 Pharmacokinetics in Special Populations*.

2.5.5 Geriatric Use
See *2.2 Dosage and Administration*, *2.4 Warnings and Precautions*, *2.6 Undesirable Effects*, and *3.2.5 Pharmacokinetics in Special Populations*.

2.5.6 Renal Impairment
See *2.2 Dosage and Administration* and *3.2.5 Pharmacokinetics in Special Populations.*

2.5.7 Hepatic Impairment
See *2.2 Dosage and Administration* and *3.2.5 Pharmacokinetics in Special Populations.*

2.6 Undesirable Effects
The safety profile presented in this section is based on data from both clinical trials and postmarketing experience and has been shown to be consistent across transplant and lupus nephritis patient populations.

2.6.1 Clinical Trials
An estimated total of 1557 patients received CellCept during pivotal clinical trials in the prevention of acute organ rejection. Of these, 991 were included in the pooled renal studies ICM1866, MYC022, MYC023, and 289 were included in the cardiac study MYC1864. Patients in all study arms also received ciclosporin and corticosteroids.

Diarrhoea, leukopenia, sepsis, and vomiting were among the most common and/or serious adverse drug reactions associated with the administration of CellCept in the pivotal trials. There was also evidence of a higher frequency of certain types of infection, e.g. opportunistic infections (see *2.4 Warnings and Precautions).*

In the three pivotal trials for prevention of renal transplant rejection, patients receiving 2 g per day of CellCept demonstrated an overall better safety profile than patients receiving 3 g CellCept. The safety profile of CellCept in patients treated for refractory renal transplant rejection was similar to that observed in the pivotal trials for prevention of renal rejection at doses of 3 g per day. Diarrhoea and leukopenia, followed by anemia, nausea, abdominal pain, sepsis, nausea and vomiting, and dyspepsia were the predominant adverse events reported more frequently in patients receiving CellCept in comparison to patients receiving i.v. corticosteroids.

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Tabulated summary of adverse drug reactions

Adverse drug reactions from clinical trials and postmarketing experience (*Table 1*) are listed by MedDRA system organ class along with their incidence. The corresponding frequency category for each adverse drug reaction is based on the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1000 to < 1/100); rare (≥ 1/10000 to < 1/1000); very rare (< 1/10000). Due to the large differences observed in the frequency of certain ADRs across the different transplant indications, the frequency is presented separately for renal and cardiac transplant patients.

Table 1 Summary of adverse drug reactions occurring in patients treated with CellCept reported from clinical trials and postmarketing experience

Adverse drug reaction (MedDRA) System organ class	**Renal transplant n=991**	**Cardiac transplant n=289**
	Frequency	**Frequency**
Infections and infestations		
Bacterial infections	Very common	Very common
Fungal infections	Common	Very common
Protozoal infections	Uncommon	Uncommon
Viral infections	Very common	Very common
Neoplasms benign, malignant and unspecified (including cysts and polyps)		
Benign neoplasm of skin	Common	Common
Lymphoma	Uncommon	Uncommon
Lymphoproliferative disorder	Uncommon	Uncommon
Neoplasm	Common	Common
Skin cancer	Common	Common
Blood and lymphatic system disorders		
Anemia	Very common	Very common
Aplasia pure red cell	Uncommon	Uncommon
Bone marrow failure	Uncommon	Uncommon
Ecchymosis	Common	Very common
Leukocytosis	Common	Very common
Leukopenia	Very common	Very common
Pancytopenia	Common	Uncommon
Pseudolymphoma	Uncommon	Common
Thrombocytopenia	Common	Very common
Metabolism and nutrition disorders		
Acidosis	Common	Very common
Hypercholesterolemia	Very common	Very common
Hyperglycemia	Common	Very common
Hyperkalemia	Common	Very common
Hyperlipidemia	Common	Very common
Hypocalcemia	Common	Common

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Adverse drug reaction (MedDRA) System organ class	**Renal transplant n=991**	**Cardiac transplant n=289**
Hypokalemia	Common	Very common
Hypomagnesemia	Common	Very common
Hypophosphatemia	Very common	Common
Hyperuricemia	Common	Very common
Gout	Common	Very common
Weight decreased	Common	Common
Psychiatric disorders		
Confusional state	Common	Very common
Depression	Common	Very common
Insomnia	Common	Very common
Agitation	Uncommon	Very common
Anxiety	Common	Very common
Thinking abnormal	Uncommon	Common
Nervous system disorders		
Dizziness	Common	Very common
Headache	Very common	Very common
Hypertonia	Common	Very common
Paresthesia	Common	Very common
Somnolence	Common	Very common
Tremor	Common	Very common
Convulsion	Common	Common
Dysgeusia	Uncommon	Common
Cardiac disorders		
Tachycardia	Common	Very common
Vascular disorders		
Hypertension	Very common	Very common
Hypotension	Common	Very common
Lymphocele	Uncommon	Uncommon
Venous thrombosis	Common	Common
Vasodilatation	Common	Very common
Respiratory, thoracic and mediastinal disorders		
Bronchiectasis	Uncommon	Uncommon
Cough	Very common	Very common
Dyspnoea	Very common	Very common
Interstitial lung disease	Uncommon	Very rare
Pleural effusion	Common	Very common
Pulmonary fibrosis	Very rare	Uncommon
Gastrointestinal disorders		
Abdominal distension	Common	Common

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Adverse drug reaction (MedDRA) System organ class	**Renal transplant n=991**	**Cardiac transplant n=289**
Abdominal pain	Very common	Very common
Colitis	Common	Common
Constipation	Very common	Very common
Decreased appetite	Common	Very common
Diarrhoea	Very common	Very common
Dyspepsia	Very common	Very common
Esophagitis	Common	Common
Eructation	Uncommon	Common
Flatulence	Common	Very common
Gastritis	Common	Common
Gastrointestinal hemorrhage	Common	Common
Gastrointestinal ulcer	Common	Common
Gingival hyperplasia	Common	Common
Ileus	Common	Common
Mouth ulceration	Common	Common
Nausea	Very common	Very common
Pancreatitis	Uncommon	Uncommon
Stomatitis	Common	Common
Vomiting	Very common	Very common
Immune system disorders		
Hypersenstivity	Uncommon	Common
Hypogammaglobulinemia	Uncommon	Very rare
Hepatobiliary disorders		
Blood alkaline phosphatase increased	Common	Common
Blood lactate dehydrogenase increased	Common	Very common
Hepatic enzyme increased	Common	Very common
Hepatitis	Common	Uncommon
Hyperbilirubinemia	Common	Very common
Jaundice	Uncommon	Common
Skin and subcutaneous tissue disorders		
Acne	Common	Very common
Alopecia	Common	Common
Rash	Common	Very common
Skin hypertrophy	Common	Very common
Musculoskeletal and connective tissue disorders		
Arthralgia	Common	Very common
Muscular weakness	Common	Very common
Renal and urinary disorders		
Blood creatinine increased	Common	Very common

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Adverse drug reaction (MedDRA) System organ class	Renal transplant n=991	Cardiac transplant n=289
Blood urea increased	Uncommon	Very common
Hematuria	Very common	Common
Renal impairment	Common	Very common
General disorders and administration site conditions		
Asthenia	Very common	Very common
Chills	Common	Very common
Edema	Very common	Very common
Hernia	Common	Very common
Malaise	Common	Common
Pain	Common	Very common
Pyrexia	Very common	Very common
De novo purine synthesis inhibitors associated acute inflammatory syndrome	Uncommon	Uncommon

Note: 991 (2 g/3 g CellCept daily), 289 (3 g CellCept daily) and 277 (2 g IV/3 g oral CellCept daily) patients were treated in Phase III studies for the prevention of rejection in renal, cardiac and hepatic transplantation, respectively.

Description of selected adverse drug reactions

Infections
All patients treated with immunosuppressants are at increased risk of bacterial, viral, and fungal infections (some of which may lead to a fatal outcome), including those caused by opportunistic agents and latent viral reactivation. The risk increases with total immunosuppressive load (see *2.4 Warnings and Precautions*). The most serious infections were sepsis and peritonitis. The most common opportunistic infections in patients receiving CellCept with other immunosuppressants were mucocutaneous candida, CMV viremia/syndrome, and herpes simplex. The proportion of patients with CMV viremia/syndrome was 13.5%.

Malignancies
Patients receiving CellCept as part of an immunosuppressive regimen are at increased risk of developing lymphomas and other malignancies, particularly of the skin (see *2.4 Warnings and Precautions*).

Three-year safety data in renal and cardiac transplant patients did not reveal any unexpected changes in the incidence of malignancy compared to the 1-year data. In supportive clinical trials of treatment of refractory renal rejection, the lymphoma rate was 3.9% at an average follow-up of 42 months.

Blood and lymphatic disorders
Cytopenias, including leukopenia, anemia, thrombocytopenia and pancytopenia, are a known risk associated with mycophenolate and may lead or contribute to the occurrence of infections and hemorrhages (see *2.4 Warnings and Precautions*).

Gastrointestinal disorders
The most serious gastrointestinal disorders were ulceration and hemorrhage which are known risks associated with CellCept. Mouth, esophageal, gastric, duodenal, and intestinal ulcers often complicated by hemorrhage, as well as hematemesis, melena, and hemorrhagic forms of gastritis and colitis were commonly reported during the pivotal clinical trials. The most common gastrointestinal disorders however, were

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diarrhoea, nausea and vomiting. Endoscopic investigation of patients with CellCept-related diarrhoea have revealed isolated cases of intestinal villous atrophy (see *2.4 Warnings and Precautions*).

General disorders and administration site conditions
Edema, including peripheral, face and scrotal edema, was reported very commonly during the pivotal trials. Musculoskeletal pain such as myalgia, and neck and back pain were also very commonly reported.

Special populations
Elderly patients (≥ 65 years)
Elderly patients, particularly those who are receiving CellCept as part of a combination immunosuppressive regimen, may be at greater increased risk of certain infections (including cytomegalovirus tissue invasive disease) and possibly gastrointestinal hemorrhage and pulmonary edema, compared to younger individuals (see *2.4 Warnings and Precautions*).

2.6.2 Postmarketing Experience
Infections
Serious life-threatening infections such as meningitis and infectious endocarditis have been reported occasionally and there is evidence of a higher frequency of certain types of infections such as tuberculosis and atypical mycobacterial infection.

Progressive Multifocal Leukoencephalopathy (PML) and BK virus-associated nephropathy, have been reported in CellCept-treated patients (see *2.4 Warnings and Precautions*).

Congenital disorders and pregnancy, puerperium and perinatal conditions
See *2.5.2 Pregnancy* for further information.

General disorders and administration site conditions
De novo purine synthesis inhibitors-associated acute inflammatory syndrome is a newly described paradoxical pro-inflammatory reaction associated with mycophenolate and other purine synthesis inhibitors, characterized by fever, arthralgias, arthritis, muscle pain and elevated inflammatory markers. Anecdotal literature reports showed rapid improvements following discontinuation of the drug.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Pusat Farmakovigilans/MESO Nasional
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Address: Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR

PT Roche Indonesia
Patient Safety
Email: indonesia.safety@roche.com
Phone: +62 21 3041 3000
Website: https://medinfo.roche.com/id/id.html

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2.7 Overdose

Reports of overdoses with mycophenolate mofetil have been received from clinical trials and during postmarketing experience. In many of these cases no adverse events were reported. In those overdose cases in which adverse events were reported, the events fall within the known safety profile of the drug.

It is expected that an overdose of mycophenolate mofetil could possibly result in over-suppression of the immune system and increase susceptibility to infections and bone marrow suppression (see *2.4 Warnings and Precautions*). If neutropenia develops, dosing with CellCept should be interrupted or the dose reduced (see *2.4 Warnings and Precautions*).

MPA cannot be removed by haemodialysis. However, at high MPAG plasma concentrations (> 100 µg/mL), small amounts of MPAG are removed. Bile acid sequestrants, such as cholestyramine, can remove MPA by increasing excretion of the drug (see *3.2 Pharmacokinetic Properties*).

2.8 Interactions with Other Medicinal Products and Other Forms of Interaction

DNA Polymerase Inhibitors (acyclovir, ganciclovir)

Acyclovir: Higher MPAG (the phenolic glucuronide of MPA) and acyclovir plasma concentrations were observed when mycophenolate mofetil was administered with acyclovir than when the drugs were administered alone. Because MPAG plasma concentrations are increased in the presence of renal impairment, as are acyclovir concentrations, the potential exists for mycophenolate and acyclovir or its prodrugs e.g. valacyclovir to compete for tubular secretion, further increasing the concentrations of both drugs.

Ganciclovir: Based on the results of a single-dose administration study of recommended doses of oral mycophenolate and i.v. ganciclovir and the known effects of renal impairment on the pharmacokinetics of MMF (see *3.2 Pharmacokinetic Properties* and *2.4 Warnings and Precautions*) and ganciclovir, it is anticipated that coadministration of these agents (which compete for mechanisms of renal tubular secretion) will result in increases in MPAG and ganciclovir concentration. No substantial alteration of MPA pharmacokinetics is anticipated and MMF dose adjustment is not required. In patients with renal impairment in whom MMF and ganciclovir or its prodrugs e.g. valganciclovir are coadministered, patients should be monitored carefully.

Antacids and proton pump inhibitors (PPIs)

Decreased mycophenolic acid (MPA) exposure has been observed when antacids, such as magnesium and aluminium hydroxides, and PPIs, including lansoprazole and pantoprazole were administered with CellCept. When comparing rates of transplant rejection or rates of graft loss between CellCept patients taking PPIs vs. CellCept patients not taking PPIs, no significant differences were seen. These data support extrapolation of this finding to all antacids because the reduction in exposure when CellCept was coadministered with magnesium and aluminium hydroxides is considerably lower than when CellCept was coadministered with PPIs. PPIs and antacids should be used with caution when coadministered with CellCept.

Sequestrants

Cholestyramine: Following single-dose administration of 1.5 g of mycophenolate mofetil to normal healthy subjects pretreated with 4 g three times daily of cholestyramine for 4 days, there was a 40% reduction in the AUC of MPA. Caution should be used during concomitant administration of drugs that interfere with enterohepatic circulation (see *2.4 Warnings and Precautions*).

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Sevelamer: Concomitant administration of sevelamer and CellCept in adults and pediatric patients decreased the MPA C_{max} and AUC_{0-12} by 30% and 25%, respectively (see *2.4 Warnings and Precautions, Interactions*).

Immunosuppressants
Ciclosporin A: Ciclosporin A (CsA) pharmacokinetics were unaffected by mycophenolate mofetil. However, CsA interferes with MPA enterohepatic recycling, resulting in reduced MPA exposures by 30-50% in renal transplant patients treated with CellCept and CsA compared with patients receiving sirolimus or belatacept and similar doses of Cellcept. Conversely, changes of MPA exposure should be expected when switching patients from CsA to one of the immunosuppressants which do not interfere with MPA's enterohepatic cycle (see *2.4 Warnings and Precautions)*.

Tacrolimus: Exposure to tacrolimus concomitantly administered with CellCept had no effect on the AUC or C_{max} of MPA in liver transplant recipients. A similar finding was observed in a recent study in kidney transplant recipients.

Antibiotics
Rifampicin: After correction for dose a 70% decrease in MPA exposure (AUC_{0-12h}) has been observed with concomitant rifampicin administration in a single heart-lung transplant patient. It is therefore recommended to monitor MPA exposure levels and to adjust CellCept doses accordingly to maintain clinical efficacy when the drugs are administered concomitantly. Alternatively a change in antimycobacterial therapy might have to be considered.

Antibiotics eliminating β-glucuronidase-producing bacteria in the intestine (e.g. aminoglycoside, cephalosporin, fluoroquinolone, and penicillin classes of antibiotics) may interfere with MPAG/MPA enterohepatic recirculation thus leading to reduced systemic MPA exposure (see *2.4.1 Warnings and Precautions, Interactions*).

Information concerning the following antibiotics is available:

Ciprofloxacin or amoxicillin plus clavulanic acid: Reductions in predose (trough) MPA concentrations of 54% have been reported in renal transplant recipients in the days immediately following commencement of oral ciprofloxacin or amoxicillin plus clavulanic acid. Effects tended to diminish with continued antibiotic use and cease after discontinuation. The change in predose level may not accurately represent changes in overall MPA exposure therefore clinical relevance of these observations is unclear.

Norfloxacin and metronidazole: Norfloxacin in combination with metronidazole reduced the MPA AUC_{0-48} by 30% following a single-dose of CellCept. No such effect on the systemic exposure of MPA with either of these antibiotics occurred when they were administered separately.

Trimethoprim/sulphamethoxazole: No effect on the systemic exposure of MPA (AUC, C_{max}) was seen with the combination trimethoprim/sulfamethoxazole.

Oral contraceptives
A study of coadministration of CellCept (1 g twice daily) and combined oral contraceptives containing ethinylestradiol (0.02-0.04 mg) and levonorgestrel (0.05-0.20 mg), desogestrel (0.15 mg) or gestodene (0.05-0.10 mg) conducted in 18 women with psoriasis over 3 menstrual cycles showed no clinically relevant influence of CellCept on serum levels of progesterone, LH and FSH, thus indicating no influence of CellCept on the ovulation-suppressing action of the oral contraceptives. The pharmacokinetics of oral contraceptives were not affected to a clinically relevant degree by coadministration of CellCept (see *2.5.1 Females and Males of Reproductive Potential*).

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Other interactions
Drugs affecting glucuronidation: Concomitant administration of drugs inhibiting glucuronidation of MPA may increase MPA exposure (e.g. increase of MPA $AUC_{0-\infty}$ by 35% was observed with concomitant administration of isavuconazole). Caution is therefore recommended when administering these drugs concomitantly with CellCept.

Telmisartan: Concomitant administration of telmisartan and CellCept resulted in an approximately 30% decrease of mycophenolic acid (MPA) concentrations. Telmisartan changes MPA's elimination by enhancing PPAR gamma (peroxisome proliferator-activated receptor gamma) expression which in turn results in an enhanced UGT1A9 expression and activity, enhancing glucuronidation. When comparing rates of transplant rejection, rates of graft loss or adverse event profiles between CellCept patients with and without concomitant telmisartan medication, no clinical consequences of the pharmacokinetic DDI were seen. However, caution should be exercised when CellCept is coadministered with telmisartan and monitoring of CellCept levels may be considered.

Probenecid: Coadministration of probenecid with mycophenolate mofetil in monkeys raises the plasma AUC of MPAG 3-fold. Thus, other drugs known to undergo renal tubular secretion may compete with MPAG and thereby raise plasma concentrations of MPAG or the other drug undergoing tubular secretion.

Live vaccines: Live vaccines should not be given to patients with an impaired immune response. The antibody response to other vaccines may be diminished (see 2.*4 Warnings and Precautions*).

3. PHARMACOLOGICAL PROPERTIES AND EFFECTS
3.1 Pharmacodynamic Properties
3.1.1 Mechanism of Action
Mycophenolate mofetil (MMF) is the 2-morpholinoethyl ester of mycophenolic acid (MPA). MPA is a potent, selective, uncompetitive and reversible inhibitor of inosine monophosphate dehydrogenase (IMPDH), and therefore inhibits the *de novo* pathway of guanosine nucleotide synthesis without incorporation into DNA. The mechanism by which MPA inhibits the enzymatic activity of IMPDH appears to be related to the ability of MPA to structurally mimic both nicotinamide adenine dinucleotide cofactor and a catalytic water molecule. This prevents the oxidation of IMP to xanthose-5'-monophosphate which is the committed step in *de novo* guanosine nucleotide biosynthesis. Two IMPDH isoforms have been identified, isoform type I, which is present in most known cells (including resting human lymphocytes) and isoform type II, which is strongly and predominantly expressed in activated human B- and T-lymphocytes. The type II isoform is nearly five times more sensitive to inhibition by MPA than is the type I isoform. MPA has more potent cytostatic effects on lymphocytes than on other cells because T- and B-lymphocytes are critically dependent for their proliferation on *de novo* synthesis of purines whereas other cell types can utilise salvage pathways. CellCept is effective in the prophylaxis of organ rejection in patients receiving allogeneic renal transplants and in the prophylaxis of organ rejection in patients receiving allogeneic cardiac transplants.

In addition to its inhibition of IMPDH and the resulting deprivation of lymphocytes, MPA also influences cellular checkpoints responsible for metabolic programming of lymphocytes. It has been shown, using human CD4+ T-cells, that MPA shifts transcriptional activities in lymphocytes from a proliferative state to catabolic processes relevant to metabolism and survival leading to an anergic state of T-cells, whereby the cells become unresponsive to their specific antigen.

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3.1.2 Clinical/Efficacy Studies

Transplant studies

CellCept has been administered in combination with the following agents in clinical trials for the prevention of renal and cardiac rejection episodes: antithymocyte globulin, OKT3, ciclosporin and corticosteroids. CellCept has also been administered in combination with ciclosporin and corticosteroids for the treatment of refractory renal rejection episodes. Prior to treatment with CellCept, patients may have also received antilymphocyte globulin, antithymocyte globulin and OKT3. CellCept has further been used in clinical trials together with daclizumab and tacrolimus.

Prevention of organ rejection

The safety and efficacy of CellCept in combination with corticosteroids and ciclosporin for the prevention of organ rejection were assessed in renal transplant patients in three randomized, double-blind, multicenter trials and in cardiac patients in one randomized double-blind, multicenter trial.

Renal transplant

The three studies compared two dose levels of oral CellCept (1 g twice daily and 1.5 g twice daily) with azathioprine (2 studies) or placebo (1 study) when administered in combination with ciclosporin and corticosteroids to prevent acute rejection episodes.

The primary efficacy endpoint was the proportion of patients in each treatment group who experienced treatment failure within the first 6 months after transplantation (defined as biopsy-proven acute rejection on treatment or the occurrence of death, graft loss or early termination from the study for any reason without prior biopsy-proven rejection). CellCept was studied in the following three therapeutic regimens: (1) antithymocyte globulin induction/MMF or azathioprine/ ciclosporin/corticosteroids, (2) MMF or azathioprine/ciclosporin/corticosteroids, and (3) MMF or placebo/ciclosporin/corticosteroids.

CellCept, in combination with corticosteroids and ciclosporin reduced (statistically significant at the < 0.05 level) the incidence of treatment failure within the first 6 months following transplantation. The following tables summarise the results of these studies. Patients who prematurely discontinued treatment were followed for the occurrence of death or graft loss, and the cumulative incidence of graft loss and patient death are summarised separately. Patients who prematurely discontinued treatment were not followed for the occurrence of acute rejection after termination. More patients receiving CellCept discontinued (without prior biopsy-proven rejection, death or graft loss) than discontinued in the control groups, with the highest rate in the CellCept 3 g/day group. Therefore, the acute rejection rates may be underestimates, particularly in the CellCept 3 g/day group.

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Renal Transplant Studies
Incidence of Treatment Failure
(Biopsy-proven Rejection or Early Termination for Any Reason)

USA Study* **(n=499 patients)**	**CellCept 2 g/day (n=167 patients)**	**CellCept 3 g/day (n=166 patients)**	**Azathioprine 1 to 2 mg/kg/day (n=166 patients)**
All treatment failures	31.1%	31.3%	47.6%
Early termination without prior acute rejection**	9.6%	12.7%	6.0%
Biopsy-proven rejection episode on treatment	19.8%	17.5%	38.0%

* antithymocyte globulin induction/MMF or azathioprine/ciclosporin/corticosteroids

Europe/Canada/ Australia Study* (n=503 patients)	**CellCept 2 g/day (n=173 patients)**	**CellCept 3 g/day (n=164 patients)**	**Azathioprine 100 to 150 mg/day (n=166 patients)**
All treatment failures	38.2%	34.8%	50.0%
Early termination without prior acute rejection**	13.9%	15.2%	10.2%
Biopsy-proven rejection episode on treatment	19.7%	15.9%	35.5%

* MMF or azathioprine/ciclosporin/corticosteroids

Europe Study* (n=491 patients)	**CellCept 2 g/day (n=165 patients)**	**CellCept 3 g/day (n=160 patients)**	**Placebo (n=166 patients)**
All treatment failures	30.3%	38.8%	56.0%
Early termination without prior acute rejection**	11.5%	22.5%	7.2%
Biopsy-proven rejection episode on treatment	17.0%	13.8%	46.4%

* MMF or placebo/ciclosporin/corticosteroids
** Does not include death and graft loss as reason for early termination

Cumulative incidence of 12-month graft loss and patient death are presented below. No advantage of CellCept with respect to graft loss and patient death was established. Numerically, patients receiving CellCept 2 g/day and 3 g/day experienced a better outcome than controls in all three studies; patients receiving CellCept 2 g/day experienced a better outcome than CellCept 3 g/day in two of the three studies.

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Patients in all treatment groups who terminated treatment early were found to have a poor outcome with respect to graft loss and patient death at 1 year.

Renal Transplant Studies
Cumulative Incidence of Combined Graft Loss
and Patient Death at 12 Months

Study	CellCept 2 g/day	CellCept 3 g/day	Control (Azathioprine or Placebo)
USA	8.5%	11.5%	12.2%
Europe/Canada/Australia	11.7%	11.0%	13.6%
Europe	8.5%	10.0%	11.5%

Cardiac transplant
A double-blind, randomized, comparative, parallel-group, multicenter study was performed in primary cardiac transplant recipients. The total number of patients enrolled was 650; 72 never received study drug and 578 received study drug. Patients received CellCept 1.5 g b.i.d. (n=289) or azathioprine 1.5 to 3 mg/kg/day (n=289), in combination with ciclosporin and corticosteroids as maintenance immunosuppressive therapy. The two primary efficacy endpoints were: (1) the proportion of patients who, after transplantation, had at least one endomyocardial biopsy-proven rejection with haemodynamic compromise, or were re-transplanted or died, within the first 6 months, and (2) the proportion of patients who died or were transplanted during the first 12 months following transplantation. Patients who prematurely discontinued treatment were followed for the occurrence of allograft rejection for up to 6 months and for the occurrence of death for 1 year.

1. *Rejection:* No difference was established between CellCept and azathioprine (AZA) with respect to biopsy-proven rejection with haemodynamic compromise, as presented below.

	Rejection at 6 Months			
	All Patients		Treated Patients	
	AZA n=323	CellCept n=327	AZA n=289	CellCept n=289
Biopsy-proven rejection with haemodynamic compromise*	121 (38%)	120 (37%)	100 (35%)	92 (32%)

* Haemodynamic compromise occurred if any of the following criteria were met: pulmonary capillary wedge pressure ≥ 20 mm or a 25% increase; cardiac index < 2.0 L/min/m^2 or a 25% decrease; ejection fraction ≤ 30%; pulmonary artery oxygen saturation ≤ 60% or a 25% decrease; presence of new S_3 gallop; fractional shortening was ≤ 20% or a 25% decrease; inotropic support required to manage the clinical condition.

2. *Survival:* In the enrolled patients, there were no statistically significant differences between patients randomized to MMF and patients randomized to AZA for death and re-transplantation. In patients who received study drug, the lower limit of the 97.5% confidence interval of the difference of death and re-transplantation was 0.9 at 1 year, indicating that MMF was superior to AZA in these patients, as presented below.

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	Death or Re-transplantation at 1 Year			
	All Patients		Treated Patients	
	AZA n=323	CellCept n=327	AZA n=289	CellCept n=289
Death or Re-transplantation	49 (15.2%)	42 (12.8%)	33 (11.4%)	18 (6.2%)
Weighted Treatment Difference	2.6%		5.3%	
Lower Limit of 97.5% one-sided Confidence Interval	-2.5%		+0.9%	

Lupus nephritis studies

Studies comparing the use of mycophenolate mofetil with intravenous cyclophosphamide (IVC) and azathioprine (AZA) in patients with proliferative lupus nephritis have been reported in the literature and a Cochrane review including over 5000 patients supports the use of MMF for induction and maintenance therapy (Tunnicliffe D., 2018). Results from the two pivotal published studies with MMF in induction and maintenance therapy are given below:

The ALMs study (Appel et al., 2009) compared MMF and IVC as induction treatment for active lupus nephritis in a 24-week open-label parallel group multicenter study. 370 patients with Class III to V lupus nephritis were randomly assigned to a target dose of 3 g/day MMF or 0.5 to 1.0 g/m^2 IVC. Both groups received prednisone, tapered from a maximum starting dose of 60 mg/day. The primary endpoint was a prespecified decrease in urine protein/creatinine ration and stabilization or improvement in serum creatinine. Secondary endpoints included complete renal remission, systemic disease activity and damage, and safety. No significant difference in response rate between the two groups was detected. The primary efficacy endpoint was achieved in 104 (56.2%) patients receiving MMF, compared with 98 (53.0%) patients receiving IVC. No significant differences were detected between the MMF and IVC groups with regards to the rates of adverse events, serious adverse events or infections.

Dooley et al., 2011 conducted a 36-month randomized, double-blind, double-dummy study comparing MMF (2 g/day) plus placebo and AZA (2 mg/kg/day) plus placebo for the maintenance of remission in 227 patients who met the response criteria during the ALMS 6-month induction trial with either MMF or IVC. 116 patients were randomly assigned to MMF and 111 to AZA. The primary endpoint was the time to treatment failure measured as the time until the first event defined as death, end-stage renal disease, sustained doubling of the serum creatinine level, renal flare, or the need for rescue therapy. Secondary assessment included the time to the individual components of treatment failure and adverse events. MMF was superior to AZA with respect to the primary endpoint, time to treatment failure (hazard ratio, 0.04; 95% confidence interval, 0.25 to 0.77; p=0.003), and with respect to time to renal flare and time to rescue therapy (hazard ratio, < 1.00; p < 0.05). Observed rates of treatment failure were 16.4% (19 of 116 patients) in the MMF group and 32.4% (36 of 111) in the AZA. Adverse events, most commonly minor infections and gastrointestinal disorders, occurred in more than 95% of the patients in both groups (p=0.68). Serious adverse events occurred in 33.3% of the patients in the AZA group and in 23.5% of those in the MMF group (p=0.11), and the rate of withdrawal due to adverse events was higher with AZA than with MMF (39.6% vs. 25.2%, p=0.02).

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3.1.3 Immunogenicity
No data available.
3.2 Pharmacokinetic Properties
The pharmacokinetics of MMF have been studied in renal and cardiac transplant patients and in patients with lupus nephritis.

In general, the pharmacokinetic profile of MPA is similar in renal and in cardiac transplant patients.

The pharmacokinetic profile of MPA in lupus nephritis is similar to that reported in transplantation (including the high variability in exposure to active drug observed) but is complicated by more unpredictable changes in renal function in lupus nephritis patients.

3.2.1 Absorption
Following oral and intravenous administration, mycophenolate mofetil undergoes rapid and extensive absorption and complete presystemic metabolism to the active metabolite, MPA. The mean bioavailability of oral mycophenolate mofetil, based on MPA AUC, is 94% relative to i.v. mycophenolate mofetil. Mycophenolate mofetil can be measured systemically during intravenous infusion; however, after oral administration it is below the limit of quantitation (0.4 μg/mL).

Immediately posttransplant (< 40 days), renal and cardiac transplant patients had mean MPA AUCs approximately 30% lower and C_{max} approximately 40% lower compared to the late transplant period (3-6 months posttransplant). This is referred to as non-stationarity of MPA pharmacokinetics. MPA AUC values obtained following administration of 1 g twice daily intravenous CellCept at the recommended infusion rate to renal patients in the immediate posttransplant phase are comparable to those observed following oral dosing.

Food had no effect on the extent of absorption (MPA AUC) of mycophenolate mofetil administered at doses of 1.5 g twice daily to renal transplant patients. However, MPA C_{max} was decreased by 40% in the presence of food.

3.2.2 Distribution
Secondary increases in plasma MPA concentrations are usually observed at approximately 6-12 hours post-dose, consistent with enterohepatic recirculation. A reduction of approximately 40% in the AUC of MPA is associated with coadministration of cholestyramine (4 g three times daily), consistent with interruption of enterohepatic recirculation.

At clinically relevant concentrations, MPA is 97% bound to plasma albumin. This value is dependent on renal function; changes in albumin binding after initiating therapy may explain the non-stationarity in the pharmacokinetics of MPA.

3.2.3 Metabolism
MPA is conjugated primarily by glucuronyltransferase (isoform UGT1A9) to form the inactive phenolic glucuronide of MPA (MPAG). *In vivo*, MPAG is converted back to free MPA via enterohepatic recirculation. A minor acylglucuronide (AcMPAG) is also formed. AcMPAG is pharmacologically active and is suspected to be responsible for some of MMF's side effects (diarrhoea, leukopenia).

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3.2.4 Elimination

Oral administration of radiolabelled mycophenolate mofetil resulted in complete recovery of the administered dose, with 93% of the dose recovered in the urine and 6% recovered in the feces. Most (about 87%) of a dose is excreted in the urine as MPAG. A negligible amount of drug (< 1% of dose) is excreted as MPA in the urine.

Enterohepatic recirculation interferes with accurate determination of MPA's disposition parameters; only apparent values can be indicated. In healthy volunteers and patients with autoimmune disease approximate clearance values of 10.6 L/h and 8.27 L/h respectively and half-life values of 17 h were observed. In transplant patients mean clearance values were higher (range 11.9-34.9 L/h) and mean half-life values shorter (5-11 h) with little difference between renal, hepatic or cardiac transplant patients. In the individual patients, these elimination parameters vary based on type of cotreatment with other immunosuppressants, time posttransplantation, plasma albumin concentration and renal function. These factors explain why reduced exposure is seen when CellCept is coadministered with ciclosporin (see section *2.8 Interactions with Other Medicinal Products and Other Forms of Interaction*) and why plasma concentrations tend to increase over time compared to what is observed immediately after transplantation (see non-stationarity in sections *3.2.1 Absorption* and *3.2.2 Distribution*).

At clinically encountered concentrations, MPA and MPAG are not removed by haemodialysis. However, at high MPAG concentrations (> 100 µg/mL), small amounts of MPAG are removed. By interfering with enterohepatic circulation of the drug, bile acid sequestrants, such as cholestyramine, reduce MPA AUC (see *2.7 Overdose*).

MPA's disposition depends on several transporters. Organic anion-transporting polypeptides (OATPs) and multidrug resistance-associated protein 2 (MRP2) are involved in MPA's disposition; OATP isoforms, MRP2 and breast cancer resistance protein (BCRP) are transporters associated with the glucuronides' biliary excretion. Multidrug resistance protein 1 (MDR1) is also able to transport MPA, but its contribution seems to be confined to the absorption process. In the kidney MPA and its metabolites potently interact with renal organic anion transporters.

3.2.5 Pharmacokinetics in Special Populations

Renal impairment

In a single-dose study (6 subjects per group), mean plasma MPA AUCs observed after oral dosing in subjects with severe chronic renal impairment (glomerular filtration rate (GFR) < 25 mL/min/1.73 m^2) were 28-75% higher than those observed in normal healthy subjects or subjects with lesser degrees of renal impairment. The mean single-dose MPAG AUC was 3- to 6-fold higher in subjects with severe renal impairment than in subjects with mild renal impairment and normal healthy subjects, consistent with the known renal elimination of MPAG.

Multiple dosing of mycophenolate mofetil in patients with severe chronic renal impairment has not been studied.

There is also a paucity of information available for lupus nephritis patients with severe renal impairment. Therapeutic drug monitoring in lupus nephritis patients with GFR < 30 mL/min is advisable.

Patients with delayed renal graft function posttransplant

In patients with delayed renal graft function post-transplant, mean MPA AUC_{0-12} was comparable to that seen in post-transplant patients without delayed renal graft function. There may be a transient increase in the free-fraction and concentration of plasma MPA in patients with delayed renal graft function. Dose adjustment of CellCept does not appear to be necessary (see *2.2.1 Special Dosage Instructions*). Mean

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plasma MPAG AUC_{0-12} was 2- to 3-fold higher than in post-transplant patients without delayed renal graft function.

In patients with primary nonfunctioning graft following renal transplantation, plasma concentrations of MPAG accumulated; accumulation of MPA, if any, was much smaller.

Hepatic impairment
Overall, the pharmacokinetics of MPA and MPAG were relatively unaffected by hepatic parenchymal disease in volunteers with alcoholic cirrhosis dosed with oral or intravenous MMF. Effects of hepatic disease on these processes probably depend on the particular disease. Hepatic disease with predominantly biliary damage, such as primary biliary cirrhosis, may show a different effect.

Geriatric population (≥ 65 years)
The pharmacokinetics of mycophenolate mofetil and its metabolites have not been found to be altered in geriatric transplant patients when compared to younger transplant patients.

3.3 Nonclinical Safety
The haematopoietic and lymphoid systems were the primary organs affected in toxicology studies conducted with mycophenolate mofetil in the rat, mouse, dog and monkey. These effects occurred at systemic exposure levels that are equivalent to or less than the clinical exposure at the recommended dose of 2 g/day for renal transplant recipients. Gastrointestinal effects were observed in the dog at systemic exposure levels equivalent to or less than the clinical exposure at the recommended doses. Gastrointestinal and renal effects consistent with dehydration were also observed in the monkey at the highest dose (systemic exposure levels equivalent to or greater than clinical exposure). The nonclinical toxicity profile of mycophenolate mofetil appears to be consistent with adverse events observed in human clinical trials which now provide safety data of more relevance to the patient population (see *2.6 Undesirable Effects*).

3.3.1 Carcinogenicity
In experimental models, mycophenolate mofetil was not tumorigenic. The highest dose tested in the animal carcinogenicity studies resulted in approximately 2-3 times the systemic exposure (AUC or C_{max}) observed in renal transplant patients at the recommended clinical dose of 2 g/day and 1.3-2 times the systemic exposure (AUC or C_{max}) observed in cardiac transplant patients at the recommended clinical dose of 3 g/day.

3.3.2 Genotoxicity
Two genotoxicity assays (the mouse lymphoma/thymidine kinase assay and the mouse micronucleus aberration assay) indicated a potential of mycophenolate mofetil to cause chromosomal instability at severely cytotoxic dose levels. Other genotoxicity tests (the bacterial mutation assay, the yeast mitotic gene conversion assay or the Chinese hamster ovary cell chromosomal aberration assay) did not demonstrate mutagenic activity.

3.3.3 Impairment of Fertility
Mycophenolate mofetil had no effect on fertility of male rats at oral doses up to 20 mg/kg/day. The systemic exposure at this dose represents 2 to 3 times the clinical exposure at the recommended clinical dose of 2 g/day in renal transplant patients and 1.3–2 times the clinical exposure at the recommended clinical dose of 3 g/day in cardiac transplant patients. In a female fertility and reproduction study conducted in rats, oral doses of 4.5 mg/kg/day caused malformations (including anophthalmia, agnathia, and hydrocephaly) in the first generation offspring in the absence of maternal toxicity. The systemic exposure at this dose was approximately 0.5 times the clinical exposure at the recommended clinical dose of 2 g/day for renal transplant patients and approximately 0.3 times the clinical exposure at the recommended clinical dose of

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3 g/day for cardiac transplant patients. No effects on fertility or reproductive parameters were evident in the dams or in the subsequent generation.

3.3.4 Reproductive Toxicity
In teratology studies in rats and rabbits, fetal resorptions and malformations occurred in rats at 6 mg/kg/day (including anophthalmia, agnathia, and hydrocephaly) and in rabbits at 90 mg/kg/day (including cardiovascular and renal anomalies, such as ectopia cordis and ectopic kidneys, and diaphragmatic and umbilical hernia), in the absence of maternal toxicity. The systemic exposure at these levels are approximately equivalent to or less than 0.5 times the clinical exposure at the recommended clinical dose of 2 g/day for renal transplant patients and approximately 0.3 times the clinical exposure at the recommended clinical dose of 3 g/day for cardiac transplant patients.

Refer to section *2.5.2 Pregnancy*.

4. PHARMACEUTICAL PARTICULARS

4.1 Storage and shelf life
Store below 30°C, store in the original package in order to protect from moisture.

This medicine should not be used after the expiry date (EXP) shown on the pack. See also outer pack for storage remark.

4.2 Special Instructions for Use, Handling and Disposal
Mycophenolate mofetil has demonstrated teratogenic effects (see *2.5.2 Pregnancy*), therefore CellCept caplets should not be crushed to avoid inhalation or direct contact with skin or mucous membranes. If such contact occurs, wash thoroughly with soap and water; rinse eyes with plain water.

4.3 Packs
Film-coated caplets 500 mg
Box, 5 blisters @ 10 film-coated caplets Reg No.: DKI2157510309A1

5. Date of Latest Marketing Authorisation
Date of latest marketing authorisation: 07 October 2022

6. Date of Revision of the Product Information
Date of revision of the Product Information:

Medicine: keep out of reach and sight of children
Obat: Jauhkan dari jangkauan dan pandangan anak-anak
On medical prescription only
Harus dengan resep dokter

Made by:
Delpharm Milano S.r.l.
Segrate, Italy

Released by:
F. Hoffmann-La Roche Ltd.
Basel, Switzerland

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Imported by:
PT Menarini Indria Laboratories
Bekasi, Indonesia

Distributed by:
PT Roche Indonesia
Jakarta, Indonesia

This PI draft has been reviewed and approved by Asri Mega Putri on 18 Jul 2025

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INFORMASI PRODUK UNTUK PASIEN

CELLCEPT
Mikofenolat mofetil
Kaplet salut selaput
500 mg

Bacalah seluruh brosur ini dengan saksama sebelum Anda mulai menggunakan obat ini karena brosur ini berisi informasi yang penting bagi Anda.

- Simpan brosur ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan pada dokter, apoteker atau perawat Anda.
- Obat ini hanya diresepkan untuk Anda. Jangan memberikannya kepada orang lain. Obat ini dapat membahayakan mereka, walaupun tanda-tanda penyakit mereka serupa dengan penyakit Anda.
- Jika Anda mengalami efek samping, bicarakanlah dengan dokter, apoteker atau perawat Anda. Hal ini termasuk efek samping yang mungkin terjadi di luar dari apa yang tercantum pada brosur ini. Lihat bagian 4.

Apa yang terdapat di dalam brosur ini

1. Apa itu CellCept dan kegunaannya
Nama lengkap obat Anda adalah CellCept kaplet salut selaput 500 mg.
- Pada brosur ini digunakan nama singkat yaitu CellCept.

CellCept mengandung mikofenolat mofetil.
- Kandungan tersebut termasuk ke dalam golongan “imunosupresan”.

CellCept digunakan untuk:
- mencegah tubuh Anda menolak organ transplan (ginjal atau jantung)
- induksi dan pemeliharaan pada pengobatan penyakit lupus nefritis, pada orang dewasa

CellCept sebaiknya digunakan bersama obat lainnya:
- bersama siklosporin dan kortikosteroid untuk pencegahan penolakan transplan ginjal atau jantung
- bersama kortikosteroid untuk pengobatan lupus nefritis

2. Apa yang perlu Anda ketahui sebelum mengonsumsi CellCept
PERINGATAN
Mikofenolat menyebabkan cacat lahir dan keguguran. Jika Anda adalah perempuan yang memiliki potensi untuk hamil, Anda harus menunjukkan hasil tes kehamilan yang negatif sebelum memulai pengobatan dan harus menggunakan kontrasepsi seperti yang disarankan oleh dokter Anda.

Jangan mengonsumsi CellCept:
- Jika Anda alergi (memiliki hipersensitivitas) terhadap mikofenolat mofetil, asam mikofenolat, atau kandungan lain yang terdapat dalam obat ini (tercantum di bagian 6)
- Jika Anda adalah perempuan yang memiliki potensi untuk hamil dan tidak menunjukkan hasil

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negatif dari tes kehamilan sebelum menerima resep pertama, karena mikofenolat dapat menyebabkan cacat lahir dan keguguran
- Jika Anda sedang hamil atau sedang merencanakan kehamilan atau berpikir Anda sedang hamil
- Jika Anda tidak menggunakan kontrasepsi yang efektif (lihat bagian Kehamilan, kontrasepsi, dan menyusui)
- Jika Anda sedang menyusui

Jangan mengonsumsi obat ini jika salah satu kondisi di atas berlaku untuk Anda. Jika Anda tidak yakin, hubungi dokter, apoteker atau perawat Anda sebelum mengonsumsi CellCept.

Peringatan dan perhatian

Segera hubungi dokter Anda sebelum mengonsumsi CellCept:
- Jika Anda berusia lebih dari 65 tahun karena terdapat kemungkinan adanya peningkatan risiko terjadinya efek samping dibandingkan dengan pasien yang lebih muda seperti infeksi virus, perdarahan saluran cerna dan edema paru-paru
- Jika Anda memiliki tanda infeksi, seperti demam atau sakit tenggorokan
- Jika Anda memiliki memar atau perdarahan yang tidak terduga
- Jika Anda pernah memiliki permasalahan dengan sistem pencernaan seperti tukak lambung
- Jika Anda berencana untuk hamil atau mengalami kehamilan ketika mengonsumsi CellCept
- Jika Anda memiliki keturunan defisiensi enzim seperti sindrom Lesch-Nyhan dan Kelley-Seegmiller

Jika salah satu kondisi di atas berlaku pada Anda (atau Anda tidak yakin), segera hubungi dokter Anda sebelum mengonsumsi CellCept.

Efek sinar matahari

CellCept menurunkan daya tahan tubuh Anda. Sebagai akibatnya, terdapat peningkatan risiko kanker kulit. Batasi jumlah sinar matahari dan sinar UV dengan cara:
- Memakai pakaian pelindung yang menutupi kepala, leher, lengan, dan tungkai
- Menggunakan tabir surya dengan faktor proteksi (SPF) yang tinggi

Obat lainnya dan CellCept

Segera hubungi dokter, apoteker atau perawat Anda jika Anda sedang menggunakan, belum lama telah menggunakan, atau mungkin akan menggunakan obat-obatan lainnya; termasuk obat yang didapat tanpa resep dan obat herbal. Hal ini karena CellCept dapat memengaruhi cara kerja obat lainnya. Selain itu, obat lain mungkin dapat memengaruhi cara kerja CellCept.

Secara khusus, hubungi dokter, apoteker atau perawat Anda jika Anda sedang mengonsumsi obat di bawah ini sebelum mulai mengonsumsi CellCept:
- azathioprin atau obat lainnya yang menekan sistem imun Anda – diberikan setelah operasi transplantasi
- kolestiramin – digunakan untuk menangani kolesterol tinggi
- rifampisin – antibiotik yang digunakan untuk mencegah dan mengobati infeksi seperti tuberkulosis (TBC)
- antasida atau penghambat pompa proton – digunakan untuk masalah asam lambung seperti gangguan pencernaan
- pengikat fosfat – digunakan pada pasien dengan gagal ginjal kronik untuk menurunkan kadar fosfat yang diserap darah
- antibiotik – digunakan untuk mengobati infeksi bakteri
- isavukonazol – digunakan untuk mengobati infeksi jamur
- telmisartan – digunakan untuk mengobati tekanan darah tinggi

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Vaksin
Jika Anda membutuhkan vaksin (vaksin hidup) ketika mengonsumsi CellCept, hubungi dokter, apoteker atau perawat Anda terlebih dahulu. Dokter Anda yang akan menentukan vaksin yang dapat Anda gunakan.

Anda tidak boleh mendonorkan darah selama dalam pengobatan dengan CellCept dan paling tidak 6 (enam) minggu setelah penghentian pengobatan. Pasien laki-laki tidak boleh mendonasikan sperma atau air mani selama pengobatan dengan CellCept dan paling tidak 90 hari setelah penghentian pengobatan.

Konsumsi CellCept dengan makanan dan minuman
Konsumsi makanan dan minuman tidak memberikan pengaruh terhadap pengobatan CellCept Anda.

Kehamilan, kontrasepsi, dan menyusui

Kontrasepsi pada perempuan yang mengonsumsi CellCept
Jika Anda adalah perempuan yang memiliki potensi untuk hamil, Anda harus menggunakan metode kontrasepsi yang efektif selama pengobatan dengan CellCept. Hal tersebut termasuk:
- Sebelum Anda mulai mengonsumsi CellCept
- Selama masa pengobatan dengan CellCept
- Selama 6 minggu setelah menghentikan pengobatan CellCept

Konsultasikan dengan dokter Anda tentang kontrasepsi yang paling sesuai untuk Anda. Hal ini tergantung dari situasi individual Anda. Penggunaan dua jenis kontrasepsi lebih dianjurkan karena dapat menurunkan kemungkinan kehamilan yang tidak diinginkan. **Hubungi dokter Anda sesegera mungkin jika Anda berpikir bahwa kontrasepsi Anda mungkin tidak efektif atau Anda lupa mengonsumsi pil kontrasepsi**.

Anda dikategorikan sebagai perempuan yang tidak dapat hamil apabila kondisi berikut ada pada Anda:
- Anda sudah mengalami menopause, yaitu berusia paling tidak 50 tahun dan menstruasi terakhir Anda terjadi lebih dari 1 tahun lalu (jika menstruasi Anda berhenti karena pengobatan kanker, maka masih ada kemungkinan bagi Anda untuk dapat hamil)
- Kedua tuba falopi dan ovarium Anda sudah diangkat melalui operasi (salpingo-ooforektomi bilateral)
- Uterus/rahim Anda sudah diangkat melalui operasi (histerektomi)
- Kedua ovarium Anda sudah tidak berfungsi (kegagalan ovarium dini yang sudah dikonfirmasi oleh spesialis ginekologi)
- Anda dilahirkan dengan kondisi langka dimana kehamilan tidak mungkin terjadi: genotipe XY, sindrom Turner, atau agenesis uterus
- Anda adalah anak-anak atau remaja yang belum menstruasi

Kontrasepsi pada laki-laki yang mengonsumsi CellCept
Bukti yang saat ini ada tidak mengindikasikan terjadinya peningkatan risiko malformasi atau keguguran jika sang ayah yang mengonsumsi CellCept. Namun, risiko tidak dapat sepenuhnya ditiadakan. Sebagai pencegahan, Anda atau pasangan perempuan Anda sebaiknya menggunakan metode kontrasepsi yang efektif selama pengobatan dan selama 90 hari setelah Anda berhenti dari pengobatan CellCept.

Jika Anda berencana untuk mempunyai anak, diskusikan dengan dokter Anda mengenai potensi risikonya.

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Kehamilan dan menyusui
Jika Anda sedang hamil atau menyusui, berpikir bahwa Anda mungkin hamil atau sedang merencanakan kehamilan, hubungi dokter atau apoteker Anda sebelum memulai pengobatan. Dokter Anda akan memaparkan risiko jika terjadi kehamilan dan alternatif yang dapat Anda lakukan untuk pengobatan Anda jika:
- Anda merencanakan kehamilan
- Menstruasi Anda terlambat atau Anda merasa menstruasi Anda terlambat, atau Anda mengalami perdarahan menstruasi yang tidak biasa, atau Anda curiga bahwa Anda hamil
- Anda melakukan hubungan seksual tanpa menggunakan metode kontrasepsi yang efektif

Jika Anda menjadi hamil pada saat pengobatan dengan CellCept, Anda harus segera memberitahukan dokter Anda. Namun, tetaplah mengonsumsi CellCept sampai dengan jadwal Anda berkonsultasi.

Kehamilan
Mikofenolat sangat sering menyebabkan keguguran (50%) dan cacat lahir yang parah (23-27%) pada janin. Cacat lahir yang telah dilaporkan mencakup kelainan telinga, mata, wajah (bibir sumbing atau celah langit-langit), serta kelainan pada perkembangan jari, jantung, kerongkongan, ginjal, dan sistem saraf (contohnya spina bifida: ketika tulang pada tulang belakang tidak berkembang dengan baik). Bayi Anda mungkin dapat mengalami satu atau lebih dari kelainan tersebut.

Jika Anda perempuan yang memiliki potensi untuk hamil, Anda harus memberikan hasil tes kehamilan yang negatif sebelum memulai pengobatan dan harus mengikuti saran kontrasepsi yang diberikan dokter Anda. Dokter Anda mungkin meminta lebih dari satu tes untuk memastikan Anda tidak hamil sebelum memulai pengobatan.

Menyusui
Jangan mengonsumsi CellCept jika Anda sedang menyusui. Karena sejumlah kecil obat ini dapat tersalurkan ke air susu ibu (ASI).

Mengemudi dan menggunakan mesin
CellCept mungkin memengaruhi kemampuan mengemudi dan menggunakan mesin.

Anda disarankan untuk berhati-hati saat mengemudi atau menggunakan mesin jika mengalami efek samping seperti mengantuk, kebingungan, pusing, tremor atau hipotensi selama perawatan dengan CellCept.

3. Cara mengonsumsi CellCept

CellCept kaplet oral tidak boleh digantikan dengan tablet asam mikofenolat pelepasan-tertunda lain tanpa pengawasan dokter dengan pengalaman dalam terapi imunosupresif karena tingkat penyerapan setelah mengonsumsi CellCept kaplet oral dan tablet asam mikrokenolat pelepasan-tertunda tidak setara.

Selalu konsumsi CellCept sama seperti instruksi dokter. Anda harus memastikan kepada dokter, apoteker atau perawat Anda jika tidak yakin.

Jumlah yang harus dikonsumsi
Berikut adalah dosis yang lazim digunakan. Pengobatan akan berlanjut selama diperlukan untuk mencegah penolakan organ transplantasi.

Transplantasi ginjal
- Dosis pertama diberikan dalam rentang waktu 3 hari setelah operasi transplantasi.
- Dosis harian adalah 4 kaplet (2 gram obat) yang dikonsumsi dalam 2 dosis terpisah.
- Minum 2 kaplet di pagi hari dan 2 kaplet di malam hari.

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Transplantasi jantung
- Dosis pertama diberikan dalam rentang waktu 5 hari setelah operasi transplantasi.
- Dosis harian adalah 6 kaplet (3 gram obat) yang dikonsumsi dalam 2 dosis terpisah.
- Minum 3 kaplet di pagi hari dan 3 kaplet di malam hari.

Lupus nefritis
- Dosis harian untuk induksi adalah hingga 3-6 kaplet (dosis harian maksimum 3 gram) yang dikonsumsi dalam 2 dosis terpisah (minum 2 atau 3 kaplet di pagi hari dan 1 atau 3 kaplet di malam hari).
- Dosis harian untuk pemeliharaan adalah 2-4 kaplet (dosis harian maksimum 2 gram) yang dikonsumsi dalam 2 dosis terpisah (minum 1 atau 2 kaplet di pagi hari dan 1 atau 2 kaplet di malam hari).

Dosis untuk anak
Belum terdapat data keamanan dan khasiat yang cukup terkait penggunaan CellCept pada anak.

Cara minum obat
- Telan kaplet secara utuh dengan segelas air.
- Jangan membelah atau menggerus kaplet tersebut.

Jika Anda mengonsumsi CellCept lebih dari yang seharusnya
Jika Anda mengonsumsi CellCept lebih dari yang seharusnya, segera hubungi dokter atau pergi ke rumah sakit. Lakukan hal yang sama ketika ada seseorang yang tidak sengaja menelan obat tersebut. Selalu bawa kemasan obat bersama Anda.

Jika Anda lupa mengonsumsi CellCept
Jika Anda lupa mengonsumsi obat ini, segeralah konsumsi begitu Anda ingat. Lalu, lanjutkan konsumsi pada waktu biasa. Jangan mengonsumsi dosis dua kali lipat untuk mengganti dosis yang terlupakan.

Jika Anda berhenti mengonsumsi CellCept
Jangan berhenti mengonsumsi CellCept kecuali jika dokter meminta Anda untuk berhenti.

Untuk pasien penerima transplan: Jika Anda menghentikan pengobatan, Anda dapat meningkatkan risiko penolakan organ transplantasi.

Jika Anda memiliki pertanyaan lebih lanjut tentang penggunaan produk ini, tanyakan pada dokter, apoteker, atau perawat Anda.

4. Efek samping yang mungkin terjadi

Seperti semua obat, CellCept dapat menyebabkan efek samping, walaupun tidak semua pasien mengalaminya.

Segera hubungi dokter jika Anda mengetahui atau merasakan adanya efek samping serius seperti di bawah ini – Anda mungkin memerlukan pengobatan segera:
- Anda mengalami tanda infeksi seperti demam atau sakit tenggorokan
- Anda mengalami memar atau perdarahan yang tidak terduga
- Anda mengalami ruam, bengkak pada wajah, bibir, lidah, atau tenggorokan dengan kesulitan bernafas – Anda mungkin memiliki reaksi alergi serius akibat obat ini (seperti anafilaksis, angioedema)

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Masalah yang umum terjadi
Masalah yang lebih umum terjadi antara lain diare, penurunan jumlah sel darah putih atau sel darah merah, infeksi, nyeri pada perut, mual, muntah, dan gangguan asam lambung. Dokter Anda akan melakukan tes darah rutin untuk memeriksa perubahan pada:
- Jumlah sel darah Anda
- Jumlah zat lain pada darah Anda, seperti kadar gula, lemak, atau kolesterol

Melawan infeksi
CellCept menurunkan sistem pertahanan tubuh Anda. Untuk pasien penerima transplan, hal ini untuk mencegah tubuh Anda menolak organ transplantasi. Sebagai akibatnya, tubuh Anda tidak dapat melawan infeksi sebaik biasanya. Hal ini memungkinkan Anda mendapat infeksi lebih sering daripada biasanya. Hal ini termasuk infeksi pada otak, kulit, mulut, lambung dan usus, paru-paru, dan saluran kemih.

Kanker kelenjar getah bening dan kulit
Seperti yang dapat terjadi pada pasien yang mengonsumsi obat jenis ini (imunosupresan), terdapat pasien CellCept dengan jumlah yang sangat sedikit yang mengalami kanker pada kelenjar getah bening dan kulit.

Efek samping umum yang tidak diinginkan
Anda mungkin mengalami efek samping umum di seluruh tubuh Anda, termasuk reaksi alergi serius (seperti anafilaksis, angioedema), demam, merasa sangat lelah, sakit kepala, nyeri (misalnya pada perut, dada, sendi dan punggung), sakit kepala, gejala seperti flu, dan bengkak.

Efek lain yang tidak diinginkan meliputi:
Masalah kulit misalnya:
- jerawat, herpes mulut/oral, sinanaga (herpes zoster), pertumbuhan kulit, kerontokan rambut, ruam, gatal.

Masalah saluran kemih seperti:
- masalah ginjal atau rasa sangat ingin berkemih.

Masalah sistem pencernaan dan mulut seperti:
- pembengkakan gusi dan luka pada mulut (seriawan),
- radang pada pankreas, usus besar, atau lambung,
- masalah usus termasuk perdarahan, masalah hepar/hati,
- konstipasi, mual, gangguan pencernaan, kehilangan nafsu makan, kembung/sering buang gas.

Masalah sistem saraf seperti:
- merasa pusing, mengantuk, atau mati rasa,
- gemetar (tremor), spasme otot, kejang,
- merasa cemas atau depresi, perubahan suasana hati atau pikiran.

Masalah jantung dan pembuluh darah seperti:
- perubahan tekanan darah, detak jantung yang tidak biasa, pelebaran pembuluh darah.

Masalah paru-paru seperti:
- pneumonia, bronkitis,
- sesak napas, batuk, yang bisa disebabkan oleh bronkiektasis (kondisi dimana saluran napas dalam paru-paru melebar secara abnormal) atau fibrosis paru (luka pada paru-paru). Hubungi dokter Anda jika Anda mengalami batuk terus-menerus atau sulit bernapas;
- cairan dalam paru-paru atau rongga dada,
- masalah sinus.

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Masalah lainnya seperti:
- penurunan berat badan, asam urat (gout), peningkatan gula darah, perdarahan, memar.

Pelaporan efek samping
Bila Anda mengalami efek samping, beri tahu dokter, apoteker atau perawat Anda. Termasuk efek samping apa pun yang mungkin terjadi tetapi tidak tertera pada brosur ini. Anda juga dapat melaporkan efek samping langsung melalui:

PT Roche Indonesia – Patient Safety
Email: Indonesia.safety@roche.com
Tel: +62 21 3041 3000
Situs web: https://medinfo.roche.com/id/id.html

Dengan melaporkan efek samping, Anda dapat membantu memberikan lebih banyak informasi mengenai keamanan obat ini.

5. Cara penyimpanan CellCept
- Jauhkan dari pandangan dan jangkauan anak-anak.
- Jangan minum kaplet setelah melewati tanggal kedaluwarsa yang tertera pada dus setelah tulisan "EXP". Tanggal kedaluwarsa tersebut mengacu pada hari terakhir pada bulan tersebut.
- Jangan simpan pada suhu lebih dari 30°C.
- Simpan obat di dalam dus untuk melindungi obat dari kelembaban.
- Obat tidak boleh dibuang melalui sistem pembuangan limbah rumah tangga. Tanyakan pada apoteker Anda bagaimana cara pembuangan obat yang sudah tidak digunakan lagi. Upaya-upaya ini akan membantu melindungi lingkungan.

6. Isi kemasan dan informasi lainnya
CellCept kaplet salut selaput mengandung
- Zat aktif berupa mikofenolat mofetil.
- Bahan-bahan lainnya yaitu:
  - ✓ Inti kaplet: selulosa mikrokristalin, polividon (K-90), natrium kroskarmelosa, magnesium stearat
  - ✓ Selaput kaplet: hidroksipropil metilselulosa, hidroksipropil selulosa, titanium dioksida (E171), polietilen glikol 400, *indigo carmine aluminium lake* (E132), *red iron oxide* (E172)

Tampilan CellCept dan isi dalam kemasan
- Kaplet CellCept berwarna lavender (ungu) dan berbentuk kaplet. Terdapat tulisan "CellCept 500" yang terukir pada satu sisi dan "Roche" pada sisi lainnya
- Tersedia dalam kemasan 50 kaplet (dikemas dalam blister masing-masing berisi 10 kaplet)

Kemasan
Dus, 5 blister @ 10 kaplet salut selaput

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Obat: jauhkan dari jangkauan dan pandangan anak-anak
Harus dengan Resep Dokter

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Diproduksi oleh:
Delpharm Milano S.r.l.
Segrate, Italia

Dirilis oleh:
F. Hoffmann-La Roche Ltd.
Basel, Swiss

Diimpor oleh:
PT Menarini Indria Laboratories
Bekasi, Indonesia

Didistribusikan oleh:
PT Roche Indonesia
Jakarta, Indonesia

This PIL draft has been reviewed and approved by Deny Yanes Souisa on 18 November 2024

DISETUJUI OLEH BPOM: 31/07/2025 ID: EREG100437VR12400295