2. Thaisetthawatkul P, *et al*. Muromonab-CD3-induced neurotoxicity: report of two siblings, one of whom had subsequent cyclosporin-induced neurotoxicity. *J Child Neurol* 2001; **16:** 825–31.
3. Pittock SJ, *et al*. OKT3 neurotoxicity presenting as akinetic mutism. *Transplantation* 2003; **75:** 1058–60.
4. Janssen-Ortho, Canada. Important new safety information on Orthoclone OKT*3 (muromonab-CD3) (issued 17 May 2004). Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/orthoclone_okt3_pa-ap-eng.pdf (accessed 18/02/08)

Pharmacokinetics

Therapeutic drug monitoring. US licensed product information states that serum concentrations of muromonab-CD3 are measurable using an enzyme-linked immunosorbent assay (ELISA). Studies in organ transplant recipients found that patients less than 10 years of age had higher concentrations than patients aged 10 to 50 years. Subsequent clinical experience has shown that serum concentrations of muromonab-CD3 greater than or equal to 800 nanograms/mL block the function of T-cells. Reduced T-cell clearance or low plasma concentrations of muromonab-CD3 provide a basis for adjusting muromonab dosage or stopping therapy.

In adults, periodic monitoring to ensure plasma muromonab-CD3 concentrations of 800 nanograms/mL or greater, or CD3-positive cells less than 25 cells/mm^3 is recommended. Paediatric patients are known to have higher CD3 lymphocyte counts than adults, and often require increased doses of muromonab-CD3 to achieve similar depletion of CD3-positive cells and therapeutic serum concentrations; both T-cell clearance and plasma muromonab-CD3 should be monitored daily in children.

Uses and Administration

Muromonab-CD3 is a murine monoclonal antibody to the T3 (CD3) antigen of human T-lymphocytes, which is essential to antigen recognition and response; the antibody thus specifically blocks T-cell generation and function, to exert an immunosuppressant effect without affecting the bone marrow.

It is used in the treatment of acute allograft rejection in organ transplant recipients, in doses of 5 mg daily by intravenous injection for 10 to 14 days. For children's doses, see Administration in Children, below. The dose of any other immunosuppressant therapy may need to be reduced. Patients should be monitored closely after the first few doses of muromonab-CD3 because of the risk of cytokine release syndrome and hypersensitivity reactions. The first dose may be preceded by intravenous methylprednisolone sodium succinate, in a dose of 8 mg/kg, 1 to 4 hours before muromonab-CD3. Paracetamol and antihistamines may also be given with muromonab-CD3 to reduce early reactions.

Muromonab-CD3 has also been given experimentally as part of regimens for the prophylaxis of graft rejection. For further details of the use of muromonab-CD3 in the treatment and prophylaxis of graft rejection see Organ and Tissue Transplantation, p.1810, *et seq*.

◊ References.

1. ten Berge IJM, *et al*. Guidelines for optimal use of muromonab CD3 in transplantation. *BioDrugs* 1999; **11:** 277–84.
2. Flechner SM. A randomized prospective trial of low-dose OKT3 induction therapy to prevent rejection and minimize side effects in recipients of kidney transplants. *Transplantation* 2000; **69:** 2374–81.
3. Henry ML, *et al*. A randomized prospective trial of OKT3 induction in the current immunosuppression era. *Clin Transplant* 2001; **15:** 410–14.
4. Benfield MR, *et al*. A randomized multicenter trial of OKT3 mAbs induction compared with intravenous cyclosporine in pediatric renal transplantation. *Pediatr Transplant* 2005; **9:** 282–92.
5. Knop S, *et al*. OKT3 muromonab as second-line and subsequent treatment in recipients of stem cell allografts with steroid-resistant acute graft-versus-host disease. *Bone Marrow Transplant* 2005; **36:** 831–7.
6. Sevmis S, *et al*. OKT3 treatment for steroid-resistant acute rejection in kidney transplantation. *Transplant Proc* 2005; **37:** 3016–18.
7. Wilmot I, *et al*. OKT3 treatment in refractory pediatric heart transplant rejection. *J Heart Lung Transplant* 2005; **24:** 1793–7.

Administration in children. The initial recommended doses in children given muromonab-CD3 for acute allograft rejection are as follows:

- those weighing 30 kg or less: 2.5 mg daily
- those weighing more than 30 kg: 5 mg daily

Doses are given by intravenous injection for 10 to 14 days.

Paediatric patients are known to have higher CD3 lymphocyte counts than adults, and often require doses to be titrated upwards. The initial dose may be subsequently adjusted in 2.5 mg increments to achieve T-cell clearance (CD3-positive cells less than 25 cells/mm^3) and ensure therapeutic serum concentrations of muromonab-CD3 (of 800 nanograms/mL or greater, see Therapeutic Drug Monitoring, above).

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Orthoclone OKT3; ***Belg.:*** Orthoclone OKT3; ***Braz.:*** Orthoclone OKT3; ***Canad.:*** Orthoclone OKT3; ***Chile:*** Ior T3†; ***Cz.:*** Cedetrin-T†; Orthoclone OKT3†; ***Fin.:*** Orthoclone OKT3; ***Fr.:*** Orthoclone OKT3; ***Ger.:*** Orthoclone OKT3; ***Gr.:*** Orthoclone; ***Hong Kong:*** Orthoclone OKT3†; ***Israel:*** Orthoclone OKT3; ***Ital.:*** Orthoclone OKT3; ***Malaysia:*** Orthoclone OKT3†; ***Mex.:*** Ior-T3; Orthoclone OKT3; ***Neth.:*** Orthoclone OKT3; ***Norw.:*** Orthoclone OKT3; ***NZ:*** Orthoclone OKT3; ***S.Afr.:*** Orthoclone; ***Swed.:*** Orthoclone OKT3; ***Switz.:*** Orthoclone OKT3; ***Thai.:*** Orthoclone OKT3†; ***Turk.:*** Orthoclone OKT3; ***USA:*** Orthoclone OKT3.

Mycophenolate

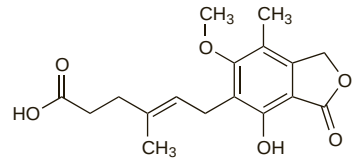
ATC — L04AA06.
ATC Vet — QL04AA06.

Mycophenolic Acid *(BAN, USAN, rINN)*

Acide Mycophénolique; Ácido micofenólico; Acidum Mycophenolicum; Lilly-68618; MPA; NSC-129185. (*E*)-6-(4-Hydroxy-6-methoxy-7-methyl-3-oxo-5-phthalanyl)-4-methyl-4-hexenoic acid.

Микофеноловая Кислота

$C_{17}H_{20}O_6$ = 320.3.
CAS — 24280-93-1.
ATC — L04AA06.
ATC Vet — QL04AA06.



Mycophenolate Mofetil *(BANM, USAN, rINNM)*

Micofenolato de mofetilo; Mikofenolat Mofetil; Mikofenolato mofetilis; Mofetilis Mycophenolas; Mofetil-mykofenolát; Mycophenolas Mofetil; Mycophenolas Mofetilum; Mycophenolasmofetil; Mycophénolate mofétil; Mycophénolate, Mofétil de; Mycophenolate Morpholinoethyl; Mykofenolaattimofetiili; Mykofenolatmofetil; RS-61443. 2-Morpholinoethyl (*E*)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-5-phthalanyl)-4-methyl-4-hexenoate.

Микофеноловая Мофетил

$C_{23}H_{31}NO_7$ = 433.5.
CAS — 115007-34-6.
ATC — L04AA06.
ATC Vet — QL04AA06.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Mycophenolate Mofetil). A white or almost white, crystalline powder. M.p. about 96°. Practically insoluble in water; sparingly soluble in dehydrated alcohol; freely soluble in acetone. Protect from light.
USP 31 (Mycophenolate Mofetil). A white or almost white, crystalline powder. Slightly soluble in water; sparingly soluble in alcohol; soluble in methyl alcohol; freely soluble in acetone. Store in airtight containers.

Mycophenolate Mofetil Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro del micofenolato de mofetilo; Mycophénolate, Mofétil Chlorhydrate de; Mycophenolati Mofetili Hydrochloridum; RS-61443-190. 2-Morpholinoethyl (*E*)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-5-phthalanyl)-4-methyl-4-hexenoate hydrochloride.

Микофеноловой Мофетила Гидрохлорид

$C_{23}H_{31}NO_7$,HCl = 470.0.
CAS — 116680-01-4.
ATC — L04AA06.
ATC Vet — QL04AA06.

Incompatibility. Solutions of mycophenolate mofetil hydrochloride were found to be physically compatible and chemically stable with solutions containing clinically relevant concentrations of cefepime, dopamine, noradrenaline, tacrolimus, and vancomycin, for up to 4 hours of simulated Y-site administration. However, combining ciclosporin and mycophenolate resulted in effervescence and chemical instability.[1]

1. Cochran BG, *et al*. Physical compatibility and chemical stability of mycophenolate mofetil during simulated Y-site administration with commonly coadministered drugs. *Am J Health-Syst Pharm* 2007; **64:** 1410–14.

Stability. UK and US licensed product information states that, after reconstitution of *mycophenolate mofetil oral suspension*, it may be stored at room temperature (15° to 30°) or in a refrigerator (2° to 8°) for up to 60 days; it should not be frozen.

UK licensed product information for *mycophenolate mofetil hydrochloride solution for infusion* states that the infusion should be started within 3 hours of reconstitution and dilution; solutions may be kept at room temperature (15° to 30°). A study found that solutions of mycophenolate mofetil hydrochloride in concentrations equivalent to mycophenolate mofetil 1, 5, or 10 mg/mL were stable for 7 days when stored at 4° or 25° in PVC infusion bags.[1] However, it was noted that a progressive discoloration occurred in bags unprotected from light and stored at 25°; further study was required to determine the source of the discoloration.

1. Certain E, *et al*. Stability of i.v. mycophenolate mofetil in 5% dextrose injection in polyvinyl chloride infusion bags. *Am J Health-Syst Pharm* 2002; **59:** 2434–9.

Mycophenolate Sodium *(BANM, USAN, rINNM)*

ERL-080; Micofenolato sódico; Mycophénolate de Sodium; Natrii Mycophenolas. Sodium 4(*E*)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxo-1,3-dihydroisobenzofuran-5-yl)-4-methylhex-4-enoate.

Натрий Микофеноловая

$C_{17}H_{19}NaO_6$ = 342.3.
CAS — 37415-62-6.
ATC — L04AA06.
ATC Vet — QL04AA06.

Adverse Effects, Treatment, and Precautions

Mycophenolate is associated with gastrointestinal disturbances, particularly diarrhoea and vomiting; gastrointestinal haemorrhage and perforation have occurred. Leucopenia may develop; as with other immunosuppressants there is an increased risk of infection and certain malignancies in patients receiving mycophenolate mofetil (see below). To minimise any risk of skin cancer, exposure to sunlight or ultraviolet light should be limited. Thrombocytopenia and anaemia are also common; there have been reports of aplastic anaemia and bone-marrow depression, sometimes fatal. Regular full blood counts are recommended during therapy, and treatment may need to be stopped if severe neutropenia develops. Other reported adverse effects include asthenia, fever, pain, headache, renal impairment, hypertension or hypotension, hyperglycaemia, disturbances of electrolytes and blood lipids, peripheral oedema, pleural effusion, dyspnoea, cough, acne, rash, alopecia, dizziness, insomnia or somnolence, paraesthesia, and tremor. Agitation, depression, anxiety, tachycardia, and arthralgia are also common. Abnormal hepatic function tests have also been reported. Hypersensitivity reactions, including angioedema and anaphylaxis, have occurred. Pancreatitis and hepatitis have been reported. There are rare reports of interstitial lung disorders, including fatal pulmonary fibrosis. Other less common adverse effects include renal tubular necrosis, haematuria, conjunctivitis, blurred vision, and impotence. Cases of progressive multifocal leukoencephalopathy (PML), sometimes fatal, have also been reported. Mycophenolate is teratogenic in *animals*; malformations, especially of the external ear, and other facial abnormalities, have been reported in infants after maternal exposure to mycophenolate (see below).

Mycophenolate should be given with care to patients with severe renal impairment or active disorders of the gastrointestinal tract. Intra-uterine devices should be used with caution in those given immunosuppressive treatment as there is an increased risk of infection. Live vaccines should be avoided in these patients for the same reason.

Mycophenolate mofetil and mycophenolate sodium should not be indiscriminately interchanged or substituted because of their differing pharmacokinetic profiles.

Effects on the gastrointestinal tract. The adverse effects of mycophenolate mofetil on the gastrointestinal tract appeared to be mostly of an irritative nature and included diarrhoea, abdominal pain, nausea and vomiting, anorexia, dyspepsia, and occasionally gastrointestinal haemorrhage or perforation.[1] Paediatric

patients tended to have a higher incidence of adverse gastrointestinal events than adults. There was some evidence that adverse effects were related to peak plasma concentrations of the drug.

A review comparing the adverse effect profile of enteric-coated mycophenolate sodium with that of mycophenolate mofetil found a similar incidence of gastrointestinal adverse effects with the two formulations. It was noted that the pathophysiology of the gastrointestinal disturbances seen with mycophenolate is complex and not fully understood. An increased incidence of diarrhoea has been seen with higher mycophenolic acid (MPA) concentrations, possibly due to a direct effect of MPA on intestinal enterocytes, caused by its inhibitory effect on inosine monophosphate dehydrogenase. While exposure to MPA may be higher with the enteric-coated formulation, studies have not shown an appreciable increase in gastrointestinal adverse effects with mycophenolate sodium; the enteric coating might have diminished the direct effect of MPA on enterocytes in the upper gastrointestinal tract.[2] Two studies found that gastrointestinal adverse effects decreased after patients were switched from mycophenolate mofetil to enteric-coated mycophenolate sodium.[3,4]

1. Behrend M. Adverse gastrointestinal effects of mycophenolate mofetil: aetiology, incidence and management. *Drug Safety* 2001; **24:** 645–63.
2. Behrend M, Braun F. Enteric-coated mycophenolate sodium: tolerability profile compared with mycophenolate mofetil. *Drugs* 2005; **65:** 1037–50.
3. Calvo N, *et al.* Renal transplant patients with gastrointestinal intolerability to mycophenolate mofetil: conversion to enteric-coated mycophenolate sodium. *Transplant Proc* 2006; **38:** 2396–7.
4. Boswell A, *et al.* Conversion from mycophenolate mofetil to enteric-coated mycophenolate sodium in patients with gastrointestinal side effects: case studies. *Prog Transplant* 2006; **16:** 138–40.

Handling. The UK licensed product information for film-coated gastro-resistant tablets of mycophenolate sodium (*Myfortic, Novartis*) warns that if it is necessary to crush the tablets, inhalation of the powder or direct contact of the powder with the skin or mucous membranes should be avoided.

Infection. The use of mycophenolate mofetil was not found to increase the risk of CMV infection in 2 small studies.[1,2] However, it did appear to be associated with an increased frequency[1] and severity[2] of CMV disease (defined as CMV infection plus evidence of viral syndrome). The number of organs affected in patients with CMV disease was also higher in those treated with mycophenolate mofetil.[2]

A retrospective study[3] found that the use of a protocol containing mycophenolate mofetil and tacrolimus was an independent risk factor for the development of CMV disease, but that the dose of mycophenolate mofetil was not. The authors interpreted this to mean that either the combination of mycophenolate mofetil and tacrolimus had an overall stronger immunosuppressive effect than other regimens, or that this protocol bore a specific risk for the development of CMV disease. The pharmacokinetics of mycophenolic acid (MPA), a metabolite of mycophenolate mofetil, and its interaction with tacrolimus, must be considered, with further studies taking MPA levels into account (see Immunosuppressants, under Interactions, below).

In contrast to these findings, another retrospective study[4] found that, although no patient developed CMV disease, the use of mycophenolate mofetil was an independent risk factor for the development of CMV infection in those patients initially seropositive for the CMV antigen.

In a study comparing the adverse effects of mycophenolate mofetil and enteric-coated mycophenolate sodium in renal transplant patients, the overall incidence of infections was similar. However, patients receiving mycophenolate sodium had significantly fewer serious infections. The incidence of CMV infection was very low and similar in both groups.[5]

In February 2008 the manufacturer in agreement with the EMEA warned[6] that isolated cases of progressive multifocal leukoencephalopathy (PML), sometimes fatal, had been reported in patients receiving mycophenolate mofetil (*CellCept, Roche*) for transplant rejection or SLE; a diagnosis of PML should be considered in patients who develop neurological symptoms while receiving mycophenolate mofetil. It was also recommended that consideration should be given to reducing the total immunosuppression in patients who develop PML but with a reminder that such a reduction may place the graft at risk in transplant patients.

1. ter Meulen CG, *et al.* The influence of mycophenolate mofetil on the incidence and severity of primary cytomegalovirus infections and disease after renal transplantation. *Nephrol Dial Transplant* 2000; **15:** 711–14.
2. Sarmiento JM, *et al.* Mycophenolate mofetil increases cytomegalovirus invasive organ disease in renal transplant patients. *Clin Transplant* 2000; **14:** 136–8.
3. Kuypers DRJ, *et al.* Role of immunosuppressive drugs in the development of tissue-invasive cytomegalovirus infection in renal transplant recipients. *Transplant Proc* 2002; **34:** 1164–70.
4. Hambach L, *et al.* Increased risk of complicated CMV infection with the use of mycophenolate mofetil in allogeneic stem cell transplantation. *Bone Marrow Transplant* 2002; **29:** 903–6.
5. Budde K, *et al.* Enteric-coated mycophenolate sodium can be safely administered in maintenance renal transplant patients: results of a 1-year study. *Am J Transplant* 2003; **4:** 237–43.
6. Roche, UK. Reports of progressive multifocal leukoencephalopathy (PML) in CellCept (mycophenolate mofetil) treated patients (issued 18th February 2008). Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON014106&RevisionSelectionMethod=Latest (accessed 19/05/08)

Pregnancy. There have been reports of spontaneous abortions and structural malformations in infants born to women taking mycophenolate. The manufacturers of mycophenolate mofetil (*Roche, USA*) have warned that use of the drug during pregnancy is associated with an increased risk of first trimester pregnancy loss and an increased risk of congenital malformations, especially external ear and other facial abnormalities including cleft lip and palate, and anomalies of the distal limbs, heart, oesophagus, and kidney.[1] Women of child-bearing potential should have a negative pregnancy test within 1 week of starting mycophenolate therapy. Women taking mycophenolate should use effective contraception, from at least 4 weeks before starting therapy, and until 6 weeks after stopping mycophenolate.

1. Roche, USA. Important changes in the CellCept (mycophenolate mofetil) prescribing information—use of CellCept is associated with increased pregnancy loss and congenital malformations/change from pregnancy category C to pregnancy category D (issued October 2007). Available at: http://www.fda.gov/Medwatch/SAFETY/2007/CellCept_dearhcpoct07.pdf (accessed 18/02/08)

Interactions

Mycophenolate may compete with other drugs that undergo active renal tubular secretion, resulting in increased concentrations of either drug. Antacids, polycarbophil calcium, sevelamer, or colestyramine may reduce absorption of mycophenolate. Rifampicin decreases exposure to mycophenolate (in patients not also taking ciclosporin); mycophenolic acid (MPA) concentrations should be monitored when rifampicin and mycophenolate are used together. See above for precautions about use with live vaccines.

Antacids. Although giving mycophenolate mofetil with an antacid mixture (aluminium and magnesium hydroxides) or food both resulted in reductions in peak plasma concentrations of mycophenolic acid (MPA), the differences were small compared with interindividual variation, and were considered unlikely to be clinically significant.[1]

UK licensed product information for mycophenolate sodium states that, although magnesium- or aluminium-containing antacids decrease MPA exposure and peak plasma concentrations, they may be used intermittently for the treatment of occasional dyspepsia; chronic use of antacids is not recommended.

1. Bullingham R, *et al.* Effects of food and antacid on the pharmacokinetics of single doses of mycophenolate mofetil in rheumatoid arthritis patients. *Br J Clin Pharmacol* 1996; **41:** 513–16.

Antibacterials. A selective bowel decontamination regimen of *tobramycin, cefuroxime,* and the antifungal *nystatin,* apparently inhibited the enterohepatic recycling of mycophenolic acid (MPA), thereby reducing the bioavailability of mycophenolate in liver transplant recipients.[1] *Norfloxacin, metronidazole,* or a combination of the two, reduced exposure to MPA and mycophenolic acid glucuronide (see Metabolism, below) when given to healthy subjects receiving mycophenolate mofetil. The effect of the antibacterials appeared to be additive.[2] Rapid reductions in MPA concentrations were seen after renal transplant patients stabilised on mycophenolate were given either *ciprofloxacin* or *amoxicillin with clavulanic acid*; MPA concentrations recovered to baseline within 3 days of stopping antibacterial therapy, and the effect was seen to wane with continued dosage of antibacterials for 14 days.[3] *Rifampicin* markedly reduced exposure to MPA in a heart-lung transplant recipient, possibly through induction of mycophenolate glucuronidation.[4] A study in renal transplant recipients given rifampicin confirmed this reduction in MPA exposure, concluding that the mechanism was induction of glucuronidation and inhibition of enterohepatic circulation.[5]

1. Schmidt LE, *et al.* The effect of selective bowel decontamination on the pharmacokinetics of mycophenolate mofetil in liver transplant recipients. *Liver Transpl* 2001; **7:** 739–42.
2. Naderer OJ, *et al.* The influence of norfloxacin and metronidazole on the disposition of mycophenolate mofetil. *J Clin Pharmacol* 2005; **45:** 219–26.
3. Borrows R, *et al.* The magnitude and time course of changes in mycophenolic acid 12-hour predose levels during antibiotic therapy in mycophenolate mofetil-based renal transplantation. *Ther Drug Monit* 2007; **29:** 122–6.
4. Kuypers DRJ, *et al.* Drug interaction between mycophenolate mofetil and rifampin: possible induction of uridine diphosphate-glucuronosyltransferase. *Clin Pharmacol Ther* 2005; **78:** 81–8.
5. Naesens M, *et al.* Rifampin induces alterations in mycophenolic acid glucuronidation and elimination: implications for drug exposure in renal allograft recipients. *Clin Pharmacol Ther* 2006; **80:** 509–21.

Immunosuppressants. Stopping *ciclosporin* therapy in renal transplant recipients was found to increase serum concentrations of mycophenolic acid (MPA),[1,2] leading to the hypothesis that ciclosporin inhibits the enterohepatic circulation of MPA. In contrast,[3,4] *tacrolimus* therapy increased serum concentrations of MPA, apparently by inhibiting conversion to mycophenolic acid glucuronide (MPAG). While the studies have been criticised,[5] it has been pointed out that an interaction cannot be excluded.[6] An increased incidence of CMV disease has been reported in renal transplant recipients given a triple therapy regimen containing tacrolimus and mycophenolate mofetil.[7] Based on a study[8] in children it has been recommended that mycophenolate mofetil be given in initial doses of 600 mg/m^2 twice daily with ciclosporin but 300 mg/m^2 twice daily with tacrolimus; 500 mg/m^2 twice daily was suggested if no calcineurin inhibitor was given. It is also recommended that dose adjustments are made using therapeutic drug monitoring. However, a pharmacokinetic study[9] showed that changes in MPA exposure with tacrolimus varied with the dose of mycophenolate mofetil used and that this effect was not adequately reflected by MPA trough concentrations (see Therapeutic Drug Monitoring, below). Another study found marked interindividual variability in MPA and MPAG pharmacokinetics when patients were given ciclosporin microemulsion or tacrolimus in the early stages after renal transplantation. This variability was greater in those given ciclosporin than in those given tacrolimus, and mean total MPA concentrations were about half that of patients in the tacrolimus group.[10] A randomised crossover study compared the effect of ciclosporin microemulsion or tacrolimus on the pharmacokinetics of MPA when each of these were given with enteric-coated mycophenolate sodium to stable renal transplant recipients.[11] In comparison with use with ciclosporin, giving mycophenolate sodium with tacrolimus resulted in a moderate increase in the total exposure of MPA and decreased maximum concentrations and total exposure to the metabolites MPAG and the acyl glucuronide. The results were not statistically significant, and the authors suggested that on this basis, doses of mycophenolate sodium need not be adjusted when converting stable renal transplant patients from one calcineurin inhibitor to the other. However, they recommended that mycophenolate sodium dose adjustments should be based on both the pharmacokinetic data and the clinical situation.

UK licensed product information has stated that ciclosporin reduces MPA exposure, and may decrease MPA concentrations when these two drugs are given together. The exact extent of the decrease is not known for mycophenolate sodium, but may be about 20%, extrapolated from data for mycophenolate mofetil. However, since efficacy studies used this combination, no dose adjustment of mycophenolate is considered necessary. If concomitant ciclosporin therapy is interrupted or stopped, an increase in MPA of about 30% is to be expected, and dosage should be re-evaluated depending on the immunosuppressive regimen. While not commenting on dose adjustment when used with tacrolimus, UK licensed product information for mycophenolate sodium stated that stable renal transplant patients showed increased MPA exposure and decreased MPAG when tacrolimus was substituted for ciclosporin.

Pharmacokinetic analyses found that use of *sirolimus* with mycophenolate led to greater MPA exposure,[12,13] but lower MPAG exposure,[14] when compared with ciclosporin plus mycophenolate. Therapeutic drug monitoring of MPA is recommended in transplant recipients given both mycophenolate and sirolimus;[12,13] guidelines are needed when switching patients from ciclosporin to sirolimus, since the same dose of mycophenolate mofetil would lead on average to a 50% increase in MPA exposure in patients receiving sirolimus compared with ciclosporin.[13]

1. Smak Gregoor PJH, *et al.* Effect of cyclosporine on mycophenolic acid trough levels in kidney transplant recipients. *Transplantation* 1999; **68:** 1603–6.
2. Shipkova M, *et al.* Effect of cyclosporine withdrawal on mycophenolic acid pharmacokinetics in kidney transplant recipients with deteriorating renal function: preliminary report. *Ther Drug Monit* 2001; **23:** 717–21.
3. Zucker K, *et al.* Unexpected augmentation of mycophenolic acid pharmacokinetics in renal transplant patients receiving tacrolimus and mycophenolate mofetil in combination therapy, and analogous in vitro findings. *Transpl Immunol* 1997; **5:** 225–32.
4. Hübner GI, *et al.* Drug interaction between mycophenolate mofetil and tacrolimus detectable within therapeutic mycophenolic acid monitoring in renal transplant patients. *Ther Drug Monit* 1999; **21:** 536–9.
5. van Gelder T, *et al.* [Drug interaction between mycophenolate mofetil and tacrolimus detectable within therapeutic mycophenolic acid monitoring in renal transplant patients]. *Ther Drug Monit* 2000; **22:** 639.
6. Hübner GI, Sziegoleit W. [Drug interaction between mycophenolate mofetil and tacrolimus detectable within therapeutic mycophenolic acid monitoring in renal transplant patients.] *Ther Drug Monit* 2000; **22:** 498–9.
7. Kuypers DRJ, *et al.* Role of immunosuppressive drugs in the development of tissue-invasive cytomegalovirus infection in renal transplant recipients. *Transplant Proc* 2002; **34:** 1164–70.
8. Filler G, *et al.* Pharmacokinetics of mycophenolate mofetil are influenced by concomitant immunosuppression. *Pediatr Nephrol* 2000; **14:** 100–104.
9. Kuypers DRJ, *et al.* Long-term changes in mycophenolic acid exposure in combination with tacrolimus and corticosteroids are dose dependent and not reflected by trough plasma concentration: a prospective study in 100 de novo renal allograft recipients. *J Clin Pharmacol* 2003; **43:** 866–80.

10. Atcheson BA, *et al.* Mycophenolic acid pharmacokinetics and related outcomes early after renal transplant. *Br J Clin Pharmacol* 2005; **59:** 271–80.
11. Kaplan B, *et al.* Randomized calcineurin inhibitor cross over study to measure the pharmacokinetics of co-administered enteric-coated mycophenolate sodium. *Clin Transplant* 2005; **19:** 551–8.
12. Büchler M, *et al.* Higher exposure to mycophenolic acid with sirolimus than with cyclosporine cotreatment. *Clin Pharmacol Ther* 2005; **78:** 34–42.
13. Picard N, *et al.* A comparison of the effect of ciclosporin and sirolimus on the pharmokinetics [sic] of mycophenolate in renal transplant patients. *Br J Clin Pharmacol* 2006; **62:** 477–84.
14. Pescovitz MD, *et al.* Pharmacokinetics, safety, and efficacy of mycophenolate mofetil in combination with sirolimus or ciclosporin in renal transplant patients. *Br J Clin Pharmacol* 2007; **64:** 758–71.

Iron. Absorption of mycophenolate mofetil after oral doses was markedly reduced by iron preparations in a study in 7 healthy subjects:[1] mean peak serum concentrations of mycophenolic acid were reduced from 20.1 to 1.3 micrograms/mL. However, in contrast, a study in 16 healthy subjects found no interaction between iron supplements and mycophenolate mofetil,[2] and 2 studies in renal transplant patients found no significant effect of oral iron supplements on the absorption of mycophenolate mofetil.[3,4]

1. Morii M, *et al.* Impairment of mycophenolate mofetil absorption by iron ion. *Clin Pharmacol Ther* 2000; **68:** 613–6.
2. Ducray PS, *et al.* Absence of an interaction between iron and mycophenolate mofetil absorption. *Br J Clin Pharmacol* 2005; **62:** 492–5.
3. Mudge DW, *et al.* The effect of oral iron admiinistration [sic] on mycophenolate mofetil absorption in renal transplant recipients: a randomized, controlled trial. *Transplantation* 2004; **77:** 206–9.
4. Lorenz M, *et al.* Ferrous sulfate does not affect mycophenolic acid pharmacokinetics in kidney transplant patients. *Am J Kidney Dis* 2004; **43:** 1098–1103.

Pharmacokinetics

Mycophenolate mofetil is rapidly and extensively absorbed from the gastrointestinal tract; enteric-coated mycophenolate sodium is also extensively absorbed. Mycophenolate undergoes presystemic metabolism to active mycophenolic acid (MPA). MPA undergoes enterohepatic recirculation and secondary increases in plasma MPA concentrations are seen; these have been reported at between 6 to 12 hours after a dose of mycophenolate mofetil, and at between 6 to 8 hours after a dose of mycophenolate sodium. MPA is metabolised by glucuronidation to the inactive mycophenolic acid glucuronide. The majority of a dose of mycophenolate is excreted in the urine as this glucuronide, with negligible amounts of MPA; about 6% of a dose is recovered in faeces. MPA is 97% bound to plasma albumin. The mean half-life of MPA after oral and intravenous doses of mycophenolate mofetil has been reported to be 17.9 hours and 16.6 hours, respectively; an MPA half-life of about 12 hours has been reported for mycophenolate sodium.

◊ References.

1. Bullingham RES, *et al.* Clinical pharmacokinetics of mycophenolate mofetil. *Clin Pharmacokinet* 1998; **34:** 429–55.
2. Gabardi S, *et al.* Enteric-coated mycophenolate sodium. *Ann Pharmacother* 2003; **37:** 1685–93.
3. Staatz CE, Tett SE. Clinical pharmacokinetics and pharmacodynamics of mycophenolate in solid organ transplant recipients. *Clin Pharmacokinet* 2007; **46:** 13–58.
4. Filler G, *et al.* Pharmacokinetics of mycophenolate mofetil and sirolimus in children. *Ther Drug Monit* 2008; **30:** 138–42.
5. Lévesque E, *et al.* Pharmacokinetics of mycophenolate mofetil and its glucuronide metabolites in healthy volunteers. *Pharmacogenomics* 2008; **9:** 869–79.

Bioavailability. A study in renal transplant patients found single doses of mycophenolate sodium 640 mg and 720 mg to be bioequivalent to mycophenolate mofetil 1 g. The 720-mg dose most closely approximated the mycophenolic acid (MPA) exposure of the mycophenolate mofetil dose.[1] The authors noted that since the study was conducted in patients given ciclosporin, bioequivalence of MPA exposure between these two formulations could not be assumed for patients receiving other immunosuppressants. A meta-analysis of 3 studies in stable renal transplant recipients concluded that mycophenolate mofetil and enteric-coated mycophenolate sodium give equivalent mycophenolate exposure in these patients.[2]

1. Arns W, *et al.* Enteric-coated mycophenolate sodium delivers bioequivalent MPA exposure compared with mycophenolate mofetil. *Clin Transplant* 2005; **19:** 199–206.
2. Johnston A, *et al.* Bioequivalence of enteric-coated mycophenolate sodium and mycophenolate mofetil: a meta-analysis of three studies in stable renal transplant recipients. *Transplantation* 2006; **82:** 1413–18.

Metabolism. Mycophenolate mofetil is rapidly de-esterified in the body to active mycophenolic acid (MPA), which is subsequently converted to inactive mycophenolic acid glucuronide (MPAG) in the gastrointestinal tract, liver and possibly kidney. This conversion to MPAG is considered to be the most important and rate limiting step.[1] MPA undergoes enterohepatic circulation, with MPAG formed in the liver being excreted into bile and converted back to MPA in the gastrointestinal tract. A further metabolite, the acyl glucuronide, has been shown to be active *in vitro*, inhibiting human inosine monophosphate dehydrogenase,[1,2] and may have implications in therapeutic drug monitoring (see below). MPA is extensively bound to albumin in patients with normal renal and hepatic function, but this binding may be affected in transplant patients by several factors such as hypoalbuminaemia, hyperbilirubinaemia, and uraemia. Accumulation of MPAG leads to an increase in unbound MPA, and a subsequent increase in MPA clearance.[2]

A crossover study to compare the metabolism of mycophenolate mofetil with mycophenolate sodium[3] found that the onset of MPA absorption was delayed with mycophenolate sodium, consistent with its enteric-coated formulation. However, MPA exposure was considered to be bioequivalent, and MPA metabolism did not differ significantly between the two formulations. MPAG was confirmed as being the principal metabolite of MPA, and the authors considered that acyl glucuronide exposure was of a sufficient magnitude to potentially contribute to immunosuppression and toxicity.

1. Shaw LM, *et al.* Pharmacokinetic, pharmacodynamic, and outcome investigations as the basis for mycophenolic acid therapeutic drug monitoring in renal and heart transplant patients. *Clin Biochem* 2001; **34:** 17–22.
2. Shaw LM, *et al.* Current issues in therapeutic drug monitoring of mycophenolic acid: report of a roundtable discussion. *Ther Drug Monit* 2001; **23:** 305–15.
3. Tedesco-Silva H, *et al.* Mycophenolic acid metabolite profile in renal transplant patients receiving enteric-coated mycophenolate sodium or mycophenolate mofetil. *Transplant Proc* 2005; **37:** 852–5.

Therapeutic drug monitoring. Mycophenolic acid (MPA) concentration appears to correlate with efficacy and toxicity.[1] Patients with low MPA concentrations may be at increased risk of transplant rejection,[2-5] or graft-versus-host disease,[5] and there is some evidence that a high MPA concentration correlates with increased adverse effects.[4,6] Fixed doses of mycophenolate mofetil have been reported to lead to variable MPA exposure,[7,8] and other immunosuppressants can affect MPA concentrations, see under Interactions, above. Therapeutic drug monitoring of mycophenolate mofetil is therefore considered necessary.[1]

Assay procedures to measure MPA concentrations include high performance liquid chromatography (HPLC) and an enzyme-multiplied immunoassay technique (EMIT). However, the acyl glucuronide metabolite of MPA (see Metabolism, above) may cross-react with the latter method, leading to higher measured concentrations than with HPLC.[8,9] This overestimation of MPA exposure using EMIT was reported to be about 24 to 35%, with the greatest bias seen in kidney recipients early after transplantation. However, in paediatric renal transplant patients, EMIT showed comparable diagnostic efficacy to HPLC, and is an acceptable assay for MPA in this population.[8] Another suggested approach is to measure inosine monophosphate dehydrogenase activity directly, (see Metabolism, above) but this has produced variable results.[10]

A review[9] concluded that while some studies show a correlation between MPA trough concentration (C_o) and acute allograft rejection, MPA area under the concentration-time curve (AUC) is predictive of the risk for rejection, and that both have limitations. An abbreviated AUC involving more practical blood sampling regimens may be more appropriate, and a trough concentration between 1 and 3.5 mg/litre has been proposed. For paediatric transplant recipients, a predose trough concentration, as measured by EMIT assay, of between 1.6 and 3.5 mg/litre has been recommended.[11] However, it has been pointed out[12] that the therapeutic range may be different at different time points after transplantation, and among different patient populations; concomitant drugs may also influence this range. The following target concentrations have been recommended for transplant patients taking mycophenolate mofetil:[13]

- MPA AUC 30 to 60 mg × hours/litre as determined by HPLC in the first 30 days post-transplantation
- for renal transplant recipients on a ciclosporin-based regimen, MPA C_0 greater than or equal to 1.3 mg/litre, as measured by HPLC
- for renal transplant recipients on a tacrolimus-based regimen, MPA C_0 greater than or equal to 1.9 mg/litre, as measured by HPLC
- for cardiac transplant recipients, MPA C_0 greater than or equal to 2 mg/litre, as measured by EMIT, or 1.2 to 3.5 mg/litre as measured by HPLC
- for liver transplant recipients, target concentrations could not be definitively recommended; similar targets to renal transplantation were suggested until more data are available

Some have stated that the contribution of MPA trough level monitoring during mycophenolate mofetil therapy is unproven, given the lack of data in paediatric renal transplant patients, and in cardiac and liver transplantation, and that adherence to recommended target ranges for MPA cannot ensure an improved clinical outcome.[14]

It has also been pointed out that, because of differing pharmacokinetic profiles, algorithms developed for mycophenolate mofetil cannot be used for patients treated with mycophenolate sodium.[15]

Measurements of unbound MPA concentrations may be of benefit in patients with renal or hepatic impairment, as factors such as hypoalbuminaemia and renal dysfunction affect the binding of MPA.[9] In liver transplant patients, plasma protein binding of MPA increased as albumin concentration increased and as bilirubin concentration decreased, leading to decreased unbound fraction of MPA, and contributing to large intra- and interindividual pharmacokinetic variability.[16] A population pharmacokinetic study considered the complexity in determining MPA pharmacokinetics to be underestimated.[17] Bayesian forecasting using only 3 samples has been reported to accurately predict MPA exposure.[18,19]

A study in 6 patients with psoriasis concluded that MPA trough concentrations (measured by EMIT) did not predict efficacy or toxicity, but instead were useful to evaluate compliance.[20]

For the view that MPA trough concentrations may not adequately reflect exposure in patients also receiving tacrolimus, see Interactions, Immunosuppressants, above.

1. Mourad M, *et al.* Therapeutic monitoring of mycophenolate mofetil in organ transplant recipients: is it necessary? *Clin Pharmacokinet* 2002; **41:** 319–27.
2. van Gelder T, *et al.* A randomized double-blind, multicenter plasma concentration controlled study of the safety and efficacy of oral mycophenolate mofetil for the prevention of acute rejection after kidney transplantation. *Transplantation* 1999; **68:** 261–6.
3. DeNofrio D, *et al.* Mycophenolic acid concentrations are associated with cardiac allograft rejection. *J Heart Lung Transplant* 2000; **19:** 1071–6.
4. Tredger JM, *et al.* Monitoring mycophenolate in liver transplant recipients: toward a therapeutic range. *Liver Transpl* 2004; **10:** 492–502.
5. Jacobson P, *et al.* Relationship of mycophenolic acid exposure to clinical outcome after hematopoietic cell transplantation. *Clin Pharmacol Ther* 2005; **78:** 486–500.
6. Mourad M, *et al.* Correlation of mycophenolic acid pharmacokinetic parameters with side effects in kidney transplant patients treated with mycophenolate mofetil. *Clin Chem* 2001; **47:** 88–94.
7. David-Neto E, *et al.* The need of mycophenolic acid monitoring in long-term renal transplants. *Clin Transplant* 2005; **19:** 19–25.
8. Jeong H, Kaplan B. Therapeutic monitoring of mycophenolate mofetil. *Clin J Am Soc Nephrol* 2007; **2:** 184–91.
9. Shaw LM, *et al.* Current issues in therapeutic drug monitoring of mycophenolic acid: report of a roundtable discussion. *Ther Drug Monit* 2001: **23:** 305–15.
10. Shaw LM, *et al.* Monitoring of mycophenolic acid in clinical transplantation. *Ther Drug Monit* 2002; **24:** 68–73.
11. Filler G. Value of therapeutic drug monitoring of MMF therapy in pediatric transplantation. *Pediatr Transplant* 2006; **10:** 707–11.
12. Venkataramanan R, Shaw LM. Therapeutic monitoring of mycophenolic acid in liver transplant patients. *Liver Transpl* 2004; **10:** 503–5.
13. van Gelder T, *et al.* Therapeutic drug monitoring of mycophenolate mofetil in transplantation. *Ther Drug Monit* 2006; **28:** 145–54.
14. Kaplan B. Mycophenolic acid trough level monitoring in solid organ transplant recipients treated with mycophenolate mofetil: association with clinical outcome. *Curr Med Res Opin* 2006; **22:** 2355–64.
15. Oellerich M, Armstrong VW. The role of therapeutic drug monitoring in individualizing immunosuppressive drug therapy: recent developments. *Ther Drug Monit* 2006; **28:** 720–5.
16. Pisupati J, *et al.* Intraindividual and interindividual variations in the pharmacokinetics of mycophenolic acid in liver transplant patients. *J Clin Pharmacol* 2005; **45:** 34–41.
17. Shum B, *et al.* Population pharmacokinetic analysis of mycophenolic acid in renal transplant recipients following oral administration of mycophenolate mofetil. *Br J Clin Pharmacol* 2003; **56:** 188–97.
18. Le Guellec C, *et al.* Population pharmacokinetics and Bayesian estimation of mycophenolic acid concentrations in stable renal transplant patients. *Clin Pharmacokinet* 2004; **43:** 253–66.
19. Zahr N, *et al.* Pharmacokinetic study of mycophenolate mofetil in patients with systemic lupus erythematosus and design of Bayesian estimator using limited sampling strategies. *Clin Pharmacokinet* 2008; **47:** 277–84.
20. Daudén E, *et al.* Plasma trough levels of mycophenolic acid do not correlate with efficacy and safety of mycophenolate mofetil in psoriasis. *Br J Dermatol* 2004; **150:** 132–5.

Uses and Administration

Mycophenolic acid is an immunosuppressant derived from *Penicillium stoloniferum*. It is a reversible inhibitor of inosine monophosphate dehydrogenase and thus inhibits purine synthesis, with potent cytostatic effects on both T- and B-lymphocytes. It is given with other immunosuppressants, for the prevention of graft rejection, and has also been tried in diseases with an autoimmune or immune-mediated inflammatory component.

It has been used mainly as the morpholinoethyl derivative, mycophenolate mofetil, or its hydrochloride salt; doses of both are expressed as mycophenolate mofetil. 1.08 g of mycophenolate mofetil hydrochloride is equivalent to about 1 g of mycophenolate mofetil. An enteric-coated formulation of mycophenolate sodium (the sodium salt of mycophenolic acid) is also available in some countries. Doses are expressed in terms of the acid; mycophenolate sodium 769 mg is equivalent to about 720 mg of mycophenolic acid.

In patients to whom oral therapy cannot initially be given, mycophenolate mofetil may be given for up to 14 days by intravenous infusion. Infusions are given as the hydrochloride salt. It is dissolved in glucose 5% to a final concentration equivalent to mycophenolate mofetil 6 mg/mL, and given over 2 hours through either a central or peripheral vein.

In the prophylaxis of acute **renal** graft rejection in adults, the conventional formulation of mycophenolate mofetil is given orally in doses of 1 g twice daily, usually within 72 hours of transplantation; the equivalent dose may be given by intravenous infusion, but is usually started within 24 hours after transplantation.

The enteric-coated formulation of mycophenolate sodium is also given for the prophylaxis of acute renal graft rejection to adults in a dose equivalent to mycophenolic acid 720 mg twice daily; the two formulations cannot be indiscriminately interchanged or substituted.

In the prophylaxis of **cardiac** graft rejection in adults, mycophenolate mofetil 1.5 g twice daily is given by mouth, within 5 days after transplantation, or by intravenous infusion at an equivalent dose.

For use in the prophylaxis of rejection in **hepatic** transplantation in adults, the equivalent of mycophenolate mofetil 1 g twice daily is given by intravenous infusion for the first 4 days after transplantation, with subsequent conversion to 1.5 g twice daily by mouth as soon as it can be tolerated.

For doses of mycophenolate used for organ transplantation in children see Administration in Children, below.

Patients should undergo regular blood counts; if neutropenia develops consideration should be given to interrupting mycophenolate treatment, reducing the dose, or stopping therapy.

Administration in children. Oral mycophenolate mofetil is licensed from the age of 2 years in the UK, and from 3 months of age in the USA. For prevention of **renal** graft rejection in patients up to 18 years of age, the recommended oral dose of mycophenolate mofetil is 600 mg/m^2 twice daily, up to a maximum of 1 g twice daily. Patients with a body-surface of 1.25 to 1.5 m^2 may be given 750 mg twice daily, whereas those with a body-surface of greater than 1.5 m^2 may be given the same dose as adults (see Uses and Administration, above). In the UK, the *BNFC* allows for use from 1 month to 18 years at 600 mg/m^2 twice daily orally or by infusion when used with ciclosporin and corticosteroids, but recommends 300 mg/m^2 twice daily when used with tacrolimus and corticosteroids; the maximum in both cases is 2 g daily.

UK licensed product information states that no data are available for paediatric cardiac and hepatic transplant patients. However, for prophylaxis of rejection in **hepatic** transplantation, the *BNFC* recommends mycophenolate mofetil 10 mg/kg twice daily, orally or by intravenous infusion, for children aged from 1 month to 18 years. This may be increased to 20 mg/kg twice daily, to a maximum of 2 g daily. The dose is the same whether used with either ciclosporin and corticosteroids, or tacrolimus and corticosteroids.

Administration in hepatic or renal impairment. Licensed product information in the UK and USA states that no dose adjustments of mycophenolate mofetil are needed for renal transplant recipients with severe *hepatic* parenchymal disease. However, it is not known whether dose adjustments are necessary for those with hepatic disease of differing aetiology. No data are available for cardiac transplant patients with severe hepatic parenchymal disease. UK licensed product information states that no dose adjustments are needed for mycophenolate sodium in renal transplant patients with hepatic impairment.

US licensed product information states that exposure to mycophenolic acid (MPA) is increased in patients with chronic *renal* impairment. Although mean MPA concentrations in patients with delayed renal graft function were comparable to those transplant patients without delayed renal graft function, there is a potential for a transient increase in MPA concentrations if renal graft function is delayed. However, dose adjustment does not appear to be necessary in these patients. UK licensed product information states that in renal transplant patients with severe chronic renal impairment (GFR less than 25 mL/minute per 1.73 m^2), oral or intravenous doses of mycophenolate mofetil above 1 g twice daily should be avoided outside the immediate post-transplantation period; the daily dose of mycophenolate sodium in these patients should not exceed 1.44 g. No dose adjustments of mycophenolate are needed in those with delayed renal graft function. No data are available for cardiac or hepatic transplant recipients with severe chronic renal impairment.

Chronic active hepatitis. Mycophenolate mofetil may be of benefit in patients with auto-immune hepatitis (p.1501) who are intolerant of or unresponsive to azathioprine or other standard therapy.[1-3]

1. Richardson PD, *et al.* Mycophenolate mofetil for maintenance of remission in autoimmune hepatitis in patients resistant to or intolerant of azathioprine. *J Hepatol* 2000; **33:** 371–5.
2. Devlin SM, *et al.* Mycophenolate mofetil for the treatment of autoimmune hepatitis in patients refractory to standard therapy. *Can J Gastroenterol* 2004; **18:** 321–6.
3. Inductivo-Yu I, *et al.* Mycophenolate mofetil in autoimmune hepatitis patients not responsive or intolerant to standard immunosuppressive therapy. *Clin Gastroenterol Hepatol* 2007; **5:** 799–802.

Eczema. Mycophenolate mofetil (typically 1 to 3 g daily by mouth) has been reported[1-3] to be safe and effective in the treatment of moderate-to-severe, refractory eczema (p.1579).

1. Neuber K, *et al.* Treatment of atopic eczema with oral mycophenolate mofetil. *Br J Dermatol* 2000; **143:** 385–91.
2. Grundmann-Kollmann M, *et al.* Mycophenolate mofetil is effective in the treatment of atopic dermatitis. *Arch Dermatol* 2001; **137:** 870–3.
3. Heller M, *et al.* Mycophenolate mofetil for severe childhood atopic dermatitis: experience in 14 patients. *Br J Dermatol* 2007; **157:** 127–32.

Eye disorders. Retrospective evaluations of treatment outcomes in patients with chronic inflammatory eye disease treated with mycophenolate mofetil found that it was effective in controlling inflammation and had a useful corticosteroid-sparing effect.[1,2] Mycophenolate mofetil, used either alone or adjunctively, has been reported[3-7] to be of benefit in refractory uveitis (p.1515). Oral doses of 600 mg/m^2 twice daily or 1 g twice daily have been used in children; the latter dose has also been used in adults with uveitis. There was some suggestion mycophenolate might be less effective in those patients initially unresponsive to azathioprine.[5]

1. Baltatzis S, *et al.* Mycophenolate mofetil as an immunomodulatory agent in the treatment of chronic ocular inflammatory disorders. *Ophthalmology* 2003; **110:** 1061–5.
2. Thorne JE, *et al.* Mycophenolate mofetil therapy for inflammatory eye disease. *Ophthalmology* 2005; **112:** 1472–7.
3. Zierhut M, *et al.* Immunsuppressive Therapie mit Mycophenolat Mofetil (CellCept) in der Behandlung der Uveitis. *Ophthalmologe* 2001; **98:** 647–51.
4. Greiner K, *et al.* Effizienz von Mycophenolat-Mofetil bei der Therapie der intermediären und posterioren Uveitis. *Ophthalmologe* 2002; **99:** 691–4.
5. Lau CH, *et al.* Long-term efficacy of mycophenolate mofetil in the control of severe intraocular inflammation. *Clin Experiment Ophthalmol* 2003; **31:** 487–91.
6. Siepmann K, *et al.* Mycophenolate mofetil is a highly effective and safe immunosuppressive agent for the treatment of uveitis: a retrospective analysis of 106 patients. *Graefes Arch Clin Exp Ophthalmol* 2006; **244:** 788–94.
7. Doycheva D, *et al.* Mycophenolate mofetil in the treatment of uveitis in children. *Br J Ophthalmol* 2007; **91:** 180–4.

Glomerular kidney disease. Mycophenolate mofetil, in usual oral doses of 1 to 2 g daily, has been reported[1-3] to be of benefit in various forms of glomerular kidney disease (p.1504); in childhood nephrotic syndrome, it was reported to have a significant corticosteroid-sparing effect, reduce relapse rates,[4] and benefit renal function.[5]

1. Choi MJ, *et al.* Mycophenolate mofetil treatment for primary glomerular diseases. *Kidney Int* 2002; **61:** 1098–1114.
2. Karim MY, Abbs IC. Mycophenolate mofetil in nonlupus glomerulonephropathy. *Lupus* 2005; **14** (suppl): s39–s41.
3. Segarra A, *et al.* Efficacy and safety of 'rescue therapy' with mycophenolate mofetil in resistant primary glomerulonephritis—a multicenter study. *Nephrol Dial Transplant* 2007; **22:** 1351–60.
4. Bagga A, *et al.* Mycophenolate mofetil and prednisolone therapy in children with steroid-dependent nephrotic syndrome. *Am J Kidney Dis* 2003; **42:** 1114–20.
5. Gellermann J, Querfeld U. Frequently relapsing nephrotic syndrome: treatment with mycophenolate mofetil. *Pediatr Nephrol* 2004; **19:** 101–4.

Idiopathic thrombocytopenic purpura. Mycophenolate mofetil has been reported[1-4] to be of benefit in small numbers of patients with refractory idiopathic thrombocytopenic purpura (p.1505).

1. Howard J, *et al.* Mycophenolate mofetil for the treatment of refractory auto-immune haemolytic anaemia and auto-immune thrombocytopenia purpura. *Br J Haematol* 2002; **117:** 712–15.
2. Hou M, *et al.* Mycophenolate mofetil (MMF) for the treatment of steroid-resistant idiopathic thrombocytopenic purpura. *Eur J Haematol* 2003; **70:** 353–7.
3. Kotb R, *et al.* Efficacy of mycophenolate mofetil in adult refractory auto-immune cytopenias: a single center preliminary study. *Eur J Haematol* 2005; **75:** 60–64.
4. Provan D, *et al.* Efficacy of mycophenolate mofetil as single-agent therapy for refractory immune thrombocytopenic purpura. *Am J Hematol* 2006; **81:** 19–25.

Inflammatory bowel disease. Mycophenolate mofetil has been investigated as an alternative to azathioprine in Crohn's disease (see Inflammatory Bowel Disease, p.1697). A randomised study in 70 patients compared therapy with corticosteroids plus mycophenolate mofetil or azathioprine in patients with moderate or severe Crohn's disease. The authors concluded that the mycophenolate regimen produced a clinical response earlier than the azathioprine regimen, and that mycophenolate should be considered in patients allergic or unresponsive to azathioprine or mercaptopurine.[1] However, it has been suggested[2] that the study may have been too short to draw definite conclusions, given the known delayed therapeutic effect of azathioprine. A beneficial effect for 5 out of 6 patients with severe Crohn's disease was reported[3] after 3 months of therapy with oral mycophenolate mofetil 1 g twice daily, but this effect was not sustained beyond 6 months.[4] Others have also noted relapse or lack of response to be relatively common;[5,6] while mycophenolate may have a role in those who cannot tolerate, or are refractory to, azathioprine, the latter remains the immunosuppressant of choice due to its greater ability to prevent flare-ups.[2]

1. Neurath MF, *et al.* Randomised trial of mycophenolate mofetil versus azathioprine for treatment of chronic active Crohn's disease. *Gut* 1999; **44:** 625–8.
2. Miehsler W, *et al.* Is mycophenolate mofetil an effective alternative in azathioprine-intolerant patients with chronic active Crohn's disease? *Am J Gastroenterol* 2001; **96:** 782–7.
3. Florin THJ, *et al.* Treatment of steroid refractory inflammatory bowel disease (IBD) with mycophenolate mofetil (MMF). *Aust N Z J Med* 1998; **28:** 344–5.
4. Radford-Smith GL, *et al.* Mycophenolate mofetil in IBD patients. *Lancet* 1999; **354:** 1386–7.
5. Ford AC, *et al.* Mycophenolate mofetil in refractory inflammatory bowel disease. *Aliment Pharmacol Ther* 2003; **17:** 1365–9.
6. Wenzl HH, *et al.* Mycophenolate mofetil for Crohn's disease: short-term efficacy and long-term outcome. *Aliment Pharmacol Ther* 2004; **19:** 427–34.

Multiple sclerosis. In a small open-label study, 5 out of 7 patients with multiple sclerosis (p.892) benefited from mycophenolate mofetil; 3 of these patients reported improved movement.[1] A retrospective review[2] of mycophenolate mofetil treatment (given either adjunctively or as monotherapy) in 79 patients, reported subjective improvements in 12 patients given adjunctive therapy.

1. Ahrens N, *et al.* Mycophenolate-mofetil in the treatment of refractory multiple sclerosis. *J Neurol* 2001; **248:** 713–14.
2. Frohman EM, *et al.* Mycophenolate mofetil in multiple sclerosis. *Clin Neuropharmacol* 2004; **27:** 80–83.

Myasthenia gravis. Mycophenolate mofetil has been investigated[1-4] in the treatment of myasthenia gravis (p.629). However negative results have been reported from controlled studies.

1. Meriggioli MN, *et al.* Mycophenolate mofetil for myasthenia gravis: a double-blind, placebo-controlled pilot study. *Ann N Y Acad Sci* 2003; **998:** 494–9.
2. Meriggioli MN, *et al.* Mycophenolate mofetil for myasthenia gravis: an analysis of efficacy, safety, and tolerability. *Neurology* 2003; **61:** 1438–40.
3. Ciafaloni E. Mycophenolate mofetil and myasthenia gravis. *Lupus* 2005; **14** (suppl): s46–s49.
4. Cahoon WD, Kockler DR. Mycophenolate mofetil treatment of myasthenia gravis. *Ann Pharmacother* 2006; **40:** 295–8.

Organ and tissue transplantation. Mycophenolate mofetil is used for the prophylaxis of graft rejection in kidney (p.1813), heart (p.1812), and liver transplantation (p.1815), and has also been used after transplantation of the lung (p.1815), pancreas (p.1816), and intestines (p.1813). It has been used as an alternative to, or replacement for, azathioprine, and may result in fewer rejections. However, in a small study of heart transplant recipients switched from standard immunosuppressive therapy with a calcineurin inhibitor, mycophenolate mofetil, and corticosteroids, to sirolimus with mycophenolate mofetil, there was an increased incidence of acute rejection; target sirolimus and mycophenolate concentrations may have been insufficient to maintain adequate immunosuppression. It has also been tried for the prophylaxis of graft-versus-host disease after bone marrow transplantation (see Haematopoietic Stem Cell Transplantation, p.1811).

A few selected references to the use of mycophenolate mofetil in transplantation are given below.

1. European Mycophenolate Mofetil Cooperative Study Group. Placebo-controlled study of mycophenolate mofetil combined with cyclosporin and corticosteroids for prevention of acute rejection. *Lancet* 1995; **345:** 1321–5.
2. Halloran P, *et al.* Mycophenolate mofetil in renal allograft recipients: a pooled efficacy analysis of three randomized, double-blind, clinical studies in prevention of rejection. *Transplantation* 1997; **63:** 39–47. Correction. *ibid.*; 618.
3. Mathew TH. A blinded, long-term, randomized multicenter study of mycophenolate mofetil in cadaveric renal transplantation: results at three years. *Transplantation* 1998; **65:** 1450–4. Correction. *ibid.*; **66:** 817.
4. Oh JM, *et al.* Comparison of azathioprine and mycophenolate mofetil for the prevention of acute rejection in recipients of pancreas transplantation. *J Clin Pharmacol* 2001; **41:** 861–9.
5. Salvadori M, *et al.* Enteric-coated mycophenolate sodium is therapeutically equivalent to mycophenolate mofetil in de novo renal transplant patients. *Am J Transplant* 2003; **4:** 231–6.
6. Sollinger HW. Mycophenolates in transplantation. *Clin Transplant* 2004; **18:** 485–92.
7. Remuzzi G, *et al.* Mycophenolate mofetil versus azathioprine for prevention of acute rejection in renal transplantation (MYSS): a randomised trial. *Lancet* 2004; **364:** 503–12.
8. Budde K, *et al.* Safety and efficacy after conversion from mycophenolate mofetil to enteric-coated mycophenolate sodium: results of a 1-year extension study. *Transplant Proc* 2005; **37:** 912–15.

9. Curran MP, Keating GM. Mycophenolate sodium delayed release: prevention of renal transplant rejection. *Drugs* 2005; **65:** 799–805.
10. Manzia TM, *et al.* Use of mycophenolate mofetil in liver transplantation: a literature review. *Transplant Proc* 2005; **37:** 2616–17.
11. Ciancio G, *et al.* Review of major clinical trials with mycophenolate mofetil in renal transplantation. *Transplantation* 2005; **80** (suppl 2): S191–S200.
12. Srinivas TR, *et al.* The impact of mycophenolate mofetil on long-term outcomes in kidney transplantation. *Transplantation* 2005; **80** (suppl 2): S211–S220.
13. Kobashigawa JA, Meiser BM. Review of major clinical trials with mycophenolate mofetil in cardiac transplantation. *Transplantation* 2005; **80** (suppl 2): S235–S243.
14. Kaplan B. Enteric-coated mycophenolate sodium (Myfortic): an overview of current and future use in transplantation. *Drugs* 2006; **66** (suppl 2): 1–8.
15. Kobashigawa JA, *et al.* Similar efficacy and safety of enteric-coated mycophenolate sodium (EC-MPS, Myfortic) compared with mycophenolate mofetil (MMF) in de novo heart transplant recipients: results of a 12-month, single-blind, randomized, parallel-group, multicenter study. *J Heart Lung Transplant* 2006; **25:** 935–41.
16. Zimmerhackl LB, *et al.* Mycophenolate mofetil (Cellcept) in pediatric renal transplantation. *Transplant Proc* 2006; **38:** 2038–40.
17. Schmeding M, *et al.* Mycophenolate mofetil in liver transplantation—is monotherapy safe? *Clin Transplant* 2006; **20** (suppl 17): 75–9.

Pemphigus and pemphigoid. Mycophenolate mofetil has been used successfully in the treatment of pemphigus and pemphigoid (p.1582), both with prednisolone[1-3] and alone.[4] In a randomised, non-blinded study,[5] adjuvant mycophenolate mofetil was found to be as effective as adjuvant azathioprine; corticosteroid-sparing effects were similar and there was a trend towards fewer adverse effects with mycophenolate.

1. Enk AH, Knop J. Mycophenolate is effective in the treatment of pemphigus vulgaris. *Arch Dermatol* 1999; **135:** 54–6.
2. Williams JV, *et al.* Use of mycophenolate mofetil in the treatment of paraneoplastic pemphigus. *Br J Dermatol* 2000; **142:** 506–8.
3. Powell AM, *et al.* An evaluation of the usefulness of mycophenolate mofetil in pemphigus. *Br J Dermatol* 2003; **149:** 138–45.
4. Bredlich R-O, *et al.* Mycophenolate mofetil monotherapy for pemphigus vulgaris. *Br J Dermatol* 1999; **141:** 934.
5. Beissert S, *et al.* A comparison of oral methylprednisolone plus azathioprine or mycophenolate mofetil for the treatment of pemphigus. *Arch Dermatol* 2006; **142:** 1447–54.

Polymyositis and dermatomyositis. Mycophenolate mofetil has been reported to be of benefit in refractory cases of polymyositis and dermatomyositis (p.1510), allowing for tapering of corticosteroid doses.[1-3] Despite benefit in 6 out of 10 patients in another study,[4] 3 patients developed opportunistic infection, which was fatal in 1 case. While acknowledging that other factors may have had a role in this, the authors advised caution in the use of mycophenolate in dermatomyositis.

1. Gelber AC, *et al.* Mycophenolate mofetil in the treatment of severe skin manifestations of dermatomyositis: a series of 4 cases. *J Rheumatol* 2000; **27:** 1542–5.
2. Majithia V, Harisdangkul V. Mycophenolate mofetil (CellCept): an alternative therapy for autoimmune inflammatory myopathy. *Rheumatology (Oxford)* 2005; **44:** 386–9.
3. Edge JC, *et al.* Mycophenolate mofetil as an effective corticosteroid-sparing therapy for recalcitrant dermatomyositis. *Arch Dermatol* 2006; **142:** 65–9.
4. Rowin J, *et al.* Mycophenolate mofetil in dermatomyositis: is it safe? *Neurology* 2006; **66:** 1245–7.

Primary biliary cirrhosis. Despite initial reports[1] of benefit with mycophenolate mofetil in the treatment of primary biliary cirrhosis (p.2408), a small study found no clinical benefit when it was given to patients with incomplete responses to ursodeoxycholic acid.[2]

1. Jones EA. Rationale for trials of long-term mycophenolate mofetil therapy for primary biliary cirrhosis. *Hepatology* 2002; **35:** 258–62.
2. Talwalkar JA, *et al.* Mycophenolate mofetil for the treatment of primary biliary cirrhosis in patients with an incomplete response to ursodeoxycholic acid. *J Clin Gastroenterol* 2005; **39:** 168–71.

Psoriasis. Mycophenolate mofetil has proved successful in some cases of psoriasis (p.1583) refractory to conventional therapies,[1-3] and topical application (as a 2% cream) has been investigated.[4]

1. Grundmann-Kollmann M, *et al.* Treatment of chronic plaque-stage psoriasis and psoriatic arthritis with mycophenolate mofetil. *J Am Acad Dermatol* 2000; **42:** 835–7.
2. Geilen CC, *et al.* Mycophenolate mofetil as a systemic antipsoriatic agent: positive experience in 11 patients. *Br J Dermatol* 2001; **144:** 583–6.
3. Zhou Y, *et al.* Mycophenolate mofetil (CellCept) for psoriasis: a two-center, prospective, open-label clinical trial. *J Cutan Med Surg* 2003; **7:** 193–7.
4. Wohlrab J, *et al.* Topical application of mycophenolate mofetil in plaque-type psoriasis. *Br J Dermatol* 2001; **144:** 1263–4.

Rheumatoid arthritis. Mycophenolate mofetil has been tried in rheumatoid arthritis (p.11); reports suggest it may effectively suppress synovial inflammation.[1]

1. McMurray RW, Harisdangkul V. Mycophenolate mofetil: selective T cell inhibition. *Am J Med Sci* 2002; **323:** 194–6.

Sarcoidosis. Mycophenolate mofetil has been used as an adjunct in the successful treatment of patients with mucocutaneous sarcoidosis (p.1512)[1] and neurosarcoidosis.[2] It was reported to have a significant corticosteroid-sparing effect in an adolescent with renal involvement,[3] and was effective in a case of severe, relapsing, corticosteroid-dependent gastrointestinal sarcoidosis.[4]

1. Kouba DJ, *et al.* Mycophenolate mofetil may serve as a steroid-sparing agent for sarcoidosis. *Br J Dermatol* 2003; **148:** 147–8.
2. Chaussenot A, *et al.* Neurosarcoïdose et mycophénolate mofétil. *Rev Neurol (Paris)* 2007; **163:** 471–5.
3. Moudgil A, *et al.* Successful steroid-sparing treatment of renal limited sarcoidosis with mycophenolate mofetil. *Pediatr Nephrol* 2006; **21:** 281–5.
4. O'Connor AS, *et al.* Pancreatitis and duodenitis from sarcoidosis: successful therapy with mycophenolate mofetil. *Dig Dis Sci* 2003; **48:** 2191–5.

Scleroderma. There are reports of response to mycophenolate in patients with scleroderma (p.1817).

References.

1. Nihtyanova SI, *et al.* Mycophenolate mofetil in diffuse cutaneous systemic sclerosis—a retrospective analysis. *Rheumatology (Oxford)* 2007; **46:** 442–5.
2. Vanthuyne M, *et al.* A pilot study of mycophenolate mofetil combined to intravenous methylprednisolone pulses and oral low-dose glucocorticoids in severe early systemic sclerosis. *Clin Exp Rheumatol* 2007; **25:** 287–92.
3. Shenin M, *et al.* The use of mycophenolate mofetil for the treatment of systemic sclerosis. *Endocr Metab Immune Disord Drug Targets* 2008; **8:** 11–14.

Systemic lupus erythematosus. Mycophenolate mofetil by mouth plus prednisolone, given for 12 months, was found to be as effective as oral cyclophosphamide plus prednisolone, for 6 months, followed by azathioprine plus prednisolone for 6 months,[1] in the treatment of Chinese patients with diffuse proliferative *lupus nephritis* (see Systemic Lupus Erythematosus, p.1513). However, some[2,3] have cautioned about generalising these findings to other patients since mycophenolate was compared with oral and not intravenous pulsed cyclophosphamide, which is considered the standard of care in those with diffuse proliferative disease. Patients with poorer prognoses were also considered to have been excluded or underrepresented in the study, and follow-up was short. However, in a 24-week unblinded study[4] oral mycophenolate mofetil was more effective in inducing complete remission than intermittent intravenous cyclophosphamide when used as induction therapy for active lupus nephritis and appeared to be better tolerated. Also, there have been reports of benefit with mycophenolate mofetil in patients with various forms of refractory lupus nephritis, including proliferative disease and membranous nephropathy,[5-7] and some consider it a good therapeutic alternative.[8,9] A review[10] concluded that limited data support induction with cyclophosphamide followed by maintenance with azathioprine or mycophenolate; in selected patients induction with mycophenolate is a reasonable alternative. Meta-analyses concluded that daily oral mycophenolate mofetil, in average or median doses of 1 to 2 g, was more effective than pulsed intravenous or oral cyclophosphamide,[11] and that mycophenolate reduced the risk of failure to induce remission during induction therapy when compared with cyclophosphamide.[12] However, the role of racial and ethnic differences in lupus remain poorly understood, and enrolment of varying ethnic populations in studies can significantly affect results of therapy.[13] Furthermore, it has been pointed out that subjects in studies included in one meta-analysis had relatively preserved renal function, and results cannot be generalised to patients with moderate to severe renal impairment and rapidly progressive glomerulonephritis.[14] While acknowledging data of mycophenolate use in children are limited, another review[15] concluded that from data in adults, mycophenolate is an acceptable alternative to intravenous cyclophosphamide in the induction phase for newly diagnosed patients with mild to moderate nephritis and intact renal function; it may also be suitable if there is concern about a patient's future fertility. However, the optimal dose and length of induction treatment with mycophenolate are still unknown.

Mycophenolate mofetil has been used to control extra-renal manifestations of SLE,[16,17] although it was ineffective in a small number of patients with severe refractory cutaneous disease.[18] Oral mycophenolate sodium 1.44 g daily has been reported to be effective in the treatment of patients with subacute cutaneous lupus erythematosus resistant to standard therapy.[19]

1. Chan TM, *et al.* Efficacy of mycophenolate mofetil in patients with diffuse proliferative lupus nephritis. *N Engl J Med* 2000; **343:** 1156–62.
2. Falk RJ. Treatment of lupus nephritis—a work in progress. *N Engl J Med* 2000; **343:** 1182–3.
3. Karassa FB, Isenberg DA. Efficacy of mycophenolate mofetil in patients with diffuse proliferative lupus nephritis. *N Engl J Med* 2001; **344:** 382–3. Correction. *ibid.*; 1176.
4. Ginzler EM, *et al.* Mycophenolate mofetil or intravenous cyclophosphamide for lupus nephritis. *N Engl J Med* 2005; **353:** 2219–28.
5. Kingdon EJ, *et al.* The safety and efficacy of MMF in lupus nephritis: a pilot study. *Lupus* 2001; **10:** 606–11.
6. Kapitsinou PP, *et al.* Lupus nephritis: treatment with mycophenolate mofetil. *Rheumatology (Oxford)* 2004; **43:** 377–80.
7. Spetie DN, *et al.* Mycophenolate therapy of SLE membranous nephropathy. *Kidney Int* 2004; **66:** 2411–15.
8. Ginzler EM, Aranow C. Mycophenolate mofetil in lupus nephritis. *Lupus* 2005; **14:** 59–64.
9. Pisoni CN, *et al.* Mycophenolate mofetil in systemic lupus erythematosus: efficacy and tolerability in 86 patients. *J Rheumatol* 2005; **32:** 1047–52.
10. Lenz O, *et al.* Defining the role of mycophenolate mofetil in the treatment of proliferative lupus nephritis. *Drugs* 2005; **65:** 2429–36.
11. Moore RA, Derry S. Systematic review and meta-analysis of randomised trials and cohort studies of mycophenolate mofetil in lupus nephritis. *Arthritis Res Ther* 2006; **8:** R182.
12. Walsh M, *et al.* Mycophenolate mofetil for induction therapy of lupus nephritis: a systematic review and meta-analysis. *Clin J Am Soc Nephrol* 2007; **2:** 968–75.
13. Dooley MA. Mycophenylate [sic] mofetil: what role in the treatment of lupus? *Lupus* 2006; **15:** 179–82.
14. Contreras G, Sosnov J. Role of mycophenolate mofetil in the treatment of lupus nephritis. *Clin J Am Soc Nephrol* 2007; **2:** 879–82.
15. Paredes A. Can mycophenolate mofetil substitute cyclophosphamide treatment of pediatric lupus nephritis? *Pediatr Nephrol* 2007; **22:** 1077–82.
16. Karim MY, *et al.* Mycophenolate mofetil for systemic lupus erythematosus refractory to other immunosuppressive agents. *Rheumatology (Oxford)* 2002; **41:** 876–82.
17. Pisoni CN, *et al.* Mycophenolate mofetil and systemic lupus erythematosus: an overview. *Lupus* 2005; **14** (suppl): s9–s11.
18. Pisoni CN, *et al.* Skin manifestations of systemic lupus erythematosus refractory to multiple treatment modalities: poor results with mycophenolate mofetil. *Clin Exp Rheumatol* 2005; **23:** 393–6.
19. Kreuter A, *et al.* Mycophenolate sodium for subacute cutaneous lupus erythematosus resistant to standard therapy. *Br J Dermatol* 2007; **156:** 1321–7.

Vasculitic syndromes. Mycophenolate mofetil has been tried in a number of the vasculitic syndromes, including Churg-Strauss syndrome (p.1501), polyarteritis nodosa and microscopic polyangiitis (p.1510), Takayasu's arteritis (p.1514), and Wegener's granulomatosis (p.1515).

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: CellCept; Imuxgen; Munotras; Myfortic; ***Austral.:*** CellCept; Myfortic; ***Austria:*** CellCept; Myfortic; ***Belg.:*** CellCept; Myfortic; ***Braz.:*** CellCept; Myfortic; Refrat†; ***Canad.:*** CellCept; Myfortic; ***Chile:*** CellCept; Myfortic; ***Cz.:*** CellCept; Myfenax; Myfortic; ***Denm.:*** CellCept; Myfortic; ***Fin.:*** CellCept; Myfortic; ***Fr.:*** CellCept; Myfortic; ***Ger.:*** CellCept; Myfortic; ***Gr.:*** CellCept; Myfortic; ***Hong Kong:*** CellCept; Myfortic; ***Hung.:*** CellCept; Myfortic; ***India:*** Cellmune; Mycept; ***Indon.:*** CellCept; Myfortic; ***Irl.:*** CellCept; Myfortic; ***Israel:*** CellCept; Myfortic; ***Ital.:*** CellCept; Myfortic; ***Jpn:*** CellCept; ***Malaysia:*** CellCept; Myfortic; ***Mex.:*** CellCept; Myfortic; ***Neth.:*** CellCept; Myfortic; ***Norw.:*** CellCept; Myfortic; ***NZ:*** CellCept; ***Philipp.:*** CellCept; Myfortic; ***Pol.:*** CellCept; Myfortic; ***Port.:*** CellCept; Myfortic; ***Rus.:*** Myfortic (Майфортик); ***S.Afr.:*** CellCept; Myfortic; ***Singapore:*** CellCept; ***Spain:*** CellCept; Myfortic; ***Swed.:*** CellCept; Myfortic; ***Switz.:*** CellCept; Myfortic; ***Thai.:*** CellCept; Myfortic; ***Turk.:*** CellCept; ***UK:*** CellCept; Myfortic; ***USA:*** CellCept; Myfortic; ***Venez.:*** CellCept; Myfortic.

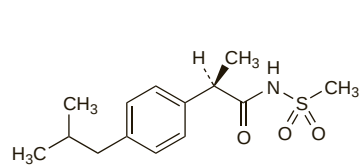
Reparixin *(USAN, rINN)*

DF-1681Y; Reparixina; Réparixine; Reparixinum; Repertaxin. (2*R*)-2-[4-(2-Methylpropyl)phenyl]-*N*-methylsulfonylpropanamide.

Репариксин

$C_{14}H_{21}NO_3S$ = 283.4.

CAS — 266359-83-5.



Reparixin Lysine *(rINNM)*

Reparixin L-Lysine; Reparixina lisina; Réparixine Lysine; Reparixinum Lysinum; Repertaxin L-Lysine. Reparixin compound with L-lysine (1:1); .

Репариксин Лизин

$C_{14}H_{21}NO_3S,C_6H_{14}N_2O_2$; = 429.6.

CAS — 266359-93-7.

Profile

Reparixin is an inhibitor of interleukin-8. Reparixin and reparixin lysine are under investigation for the prevention of delayed graft function in organ transplantation.