VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Kidney transplantation is the act of transferring a kidney from a living-donor or a deceased-donor into a patient with end-stage renal disease. Renal transplants, depending on whether a biological relationship exists between the donor and recipient, can be characterized as genetically related (living- related) or non-related (living-unrelated) transplants. However, the immune system has developed elaborate and effective mechanisms to combat foreign agents which are also involved in the rejection of transplanted organs. Transplant rejection is when transplanted tissue is recognized as foreign by the recipient's immune system which destroys the transplanted tissue and, in the case of kidney transplantation, causes kidney rejection. Acute rejection may appear within the first 6 months after transplantation, the risk being highest in the first three months, and affects approximately 15% of transplanted kidneys.

VI.2.2 Summary of treatment benefits

The safety and efficacy of mycophenolic acid in combination with cyclosporine and corticosteroids for the prevention of organ (kidney) rejection was assessed in two multicentre, randomized, double-blind trials in patients with new kidney transplant and in patients with previously transplanted kidney who received the study drug for maintenance therapy compared to mycophenolate mofetil (total number of patients = 745; ages 18-75 years). The main measure of effectiveness was the proportion of patients whose new organ had been rejected after six months. These clinical trials have demonstrated that mycophenolic acid in combination with cyclosporine and corticosteroids is as effective as mycophenolate mofetil in preventing the rejection of transplanted kidneys after six months.

VI.2.3 Unknowns relating to treatment benefits

- Limited information on interactions with other immunosuppressants (e.g. tacrolimus and azathioprine)
- Limited data are available on the use of mycophenolic acid in children and adolescents.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability

Birth defects and spontaneous miscarriages (related to exposure to mycophenolate during pregnancy)	The use of mycophenolic acid (mycophenolate sodium) in pregnancy may harm the foetus and increase the risk of pregnancy loss. Because mycophenolic acid (mycophenolate sodium) may harm the foetus and increase the risk of pregnancy loss, mycophenolic acid (mycophenolate sodium)should not be used during pregnancy unless clearly necessary.	If you are a woman you should make sure that you are not pregnant, by means of a negative pregnancy test, before you start taking mycophenolate sodium. If you are a woman, your doctor should advise you about contraception before you start taking mycophenolate sodium. You must use contraception before and while taking it and for 6 weeks after you have stopped taking it. Tell your doctor straight away if you become pregnant during treatment with mycophenolate sodium. If you are a sexually active man it is recommended to use condoms during treatment, and for a total of 13 weeks after your last dose of mycophenolate sodium. In addition, your female partners are recommended to use highly effective contraception during your treatment and for a total of 13 weeks after the last dose of mycophenolate sodium.

Risk	**What is known**	**Preventability**
Malignancies (lymphomas and other malignancies, particularly of the skin)	Patients receiving immunosuppressive regimens involving combinations of drugs, including mycophenolic acid (mycophenolate sodium) are at increased risk of developing lymphomas and other malignancies, particularly of the skin. The risk appears to be related to the intensity and duration of immunosuppression rather than to the use of any specific agent.	As general advice to minimise the 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.
Serious bacterial, fungal, protozoal and viral (including BK virus associated kidney disease and JC virus associated progressive damage or inflammation of the white matter of the brain at multiple locations (progressive multifocal leukoencephalopathy, PML)) infections and sepsis	Immunosuppressants, including mycophenolic acid (mycophenolate sodium) reduce your body's own defence mechanisms to stop you rejecting your transplanted organ. Consequently your body will not be as good as normal at fighting infections. If you are taking mycophenolic acid (mycophenolate sodium), you may therefore catch more infections than usual such as infections of the brain, skin, mouth, stomach and intestines, lungs and urinary tract.	If you get any signs of infection (such as fever or a sore throat) you should tell your doctor straight away.

Blood and lymphatic system disorders including type of anaemia called pure red cell aplasia (PRCA) and a rare blood disorder called acquired Pelger-Huët anomaly	Cases of pure red cell aplasia (PRCA) have been reported in patients treated with mycophenolate derivatives (which include mycophenolate mofetil and mycophenolate sodium) in combination with other immunosuppressants. Isolated cases of abnormal neutrophil white blood cells, including the acquired Pelger-Huet anomaly, have been observed in patients treated with mycophenolic acid derivatives.	PRCA may resolve with dose reduction or cessation of therapy. Changes to mycophenolate sodium therapy should only be undertaken under appropriate medical supervision.
Ulcerations and bleedings of gastrointestinal tract	Mycophenolic acid (mycophenolate sodium) can cause serious vomiting blood, black or bloody stools, stomach or intestinal ulcer. Additional side effects have been reported with the group of medicines that mycophenolic acid (mycophenolate sodium) belongs to: development of a hole in the intestinal wall, resulting in severe abdominal pain with possible bleeding, stomach or duodenal ulcers.	Talk to your doctor, pharmacist or nurse before taking this medicine if you have or have ever had serious digestive problems, such as a stomach ulcer. If you experience serious vomiting blood, black or bloody stools, stomach or intestinal ulcer after taking mycophenolic acid (mycophenolate sodium), talk to your doctor straight away.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Serious adverse reactions in breast-fed babies (related to exposure during breastfeeding)	It is not known whether mycophenolic acid (mycophenolate sodium) passes into breast milk. Do not breast-feed during treatment with mycophenolic acid (mycophenolate sodium) or for 6 weeks after you have stopped taking mycophenolic acid (mycophenolate sodium).

Missing information

Risk	What is known
Interaction with other immunosuppressants (e.g. tacrolimus and azathioprine)	The efficacy and safety of the use of mycophenolic acid (mycophenolate sodium) with other immunosuppressive agents (for example, tacrolimus) have not been studied. It is recommended that mycophenolate sodium not be administered concomitantly with azathioprine because concomitant administration of these drugs has not been evaluated.
Use in children	The use of mycophenolic acid (mycophenolate sodium) in children and adolescents is not recommended due to lack of data.

VI.2.5 Summary of risk minimisation measures by safety concern

No additional risk minimisation measures are proposed.

VI.2.6 Planned post authorisation development plan

Not applicable.

VI.2.7 Summary of changes to the risk management plan over time

Not applicable. This is the first RMP version.