Shared Care Guideline for Immunosuppression after Kidney and Pancreas Transplantation
1 Introduction

Renal transplantation is now a comparatively routine procedure that can dramatically improve the quality of life for patients and has considerable cost-savings for purchasers. In September 2004 NICE issued a technology appraisal of the clinical and cost effectiveness of immunosuppressive therapy for renal transplantation in adults (1). The protocols for immunosuppression at Manchester Renal Transplant Unit are supported by local transplant teams at non-transplanting renal centres. These protocols have been designed to be in-line with NICE guidance. Full prescribing information is available in the summary of product characteristics for each individual product.

This protocol includes all main immunosuppressant drugs currently used by the transplant teams (TT), including Neoral® (Ciclosporin), Prograf® (Tacrolimus), Advagraf® (Tacrolimus MR), Cellcept® (Mycophenolate mofetil), Myfortic® (Mycophenolate sodium), and Rapamune® (Sirolimus). Greater Manchester Medicines Management Group has advised that these drugs may all be considered for shared care arrangements between Primary and Secondary care.

Ciclosporin and tacrolimus remain the most frequently prescribed immunosuppressant therapies. Immunosuppressive therapy is patient specific and may include one or a number of different agents in addition or in
place of ciclosporin or tacrolimus. Prednisolone, azathioprine, mycophenolate
and/or sirolimus may be added to therapy. Mycophenolate is considered to
be similar to azathioprine but with a more specific targeted mode of action.

Patients taking ciclosporin, tacrolimus and sirolimus will require blood level
monitoring to ensure efficacy and safety.

In most circumstances blood sample monitoring will be carried out in the
hospital clinic unless alternative arrangements have been made with the
Primary Care Team. Blood samples for drug level monitoring are not required
to be taken or interpreted by GPs.
2 Scope

This shared care guideline is intended for any adult patient who has had a renal or pancreas transplant and is under the care of renal transplant consultants at Central Manchester University Hospitals NHS Foundation Trust (CMFT) or Salford Royal NHS Foundation Trust (SRFT).

The purpose of this shared care protocol is to ensure the safety of the patient by ensuring that the individual signing the prescriptions is fully aware of their responsibilities. This includes ensuring that the necessary monitoring has been undertaken and to be aware of the results of this.

Throughout this guideline the following terms are used:

- **Transplant Consultant (TC)** refers to the Consultant Transplant Surgeon or Consultant Nephrologist who is ultimately responsible for the transplant related care of the patient. This includes consultants at CMFT and SRFT hospitals.
- **The Transplant Team (TT)** refers to the team of senior medical and nursing personnel at the base hospital responsible for transplant related care of the patient. This includes teams at CMFT and SRFT.

3 Clinical condition being treated

The immunosuppressant medicines discussed in this document are all licensed for immunosuppression following renal transplantation. Only ciclosporin is licensed for pancreatic transplantation but the vast majority of patients having a pancreas transplant have a dual renal and pancreas transplant. All patients prescribed these immunosuppressants could be considered for shared care if the conditions for assuming responsibility are met at least 3 months post transplantation.

4 Product information and treatment regimen to be used

*The medicines below should be prescribed by brand name to reduce the risk of prescribing and dispensing errors*

4.1 Licensed Indications

**Prograf®** (Standard release (twice daily) Tacrolimus)
Prophylaxis of transplant rejection in liver, kidney or heart allograft recipients.
Treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products.

**Advagraf®** (Tacrolimus MR (once daily))
Prophylaxis of transplant rejection in kidney or liver allograft recipients.
Treatment of allograft rejection resistant to treatment with other immunosuppressive medicinal products in adult patients.
Neoral® (Ciclosporin)
Prevention of graft rejection following kidney, liver, heart, combined heart-lung, lung or pancreas transplants. Treatment of transplant rejection in patients previously receiving other immunosuppressive agents.

Cellcept® (Mycophenolate mofetil)
Indicated in combination with ciclosporin (or tacrolimus) and corticosteroids for the prophylaxis of acute transplant rejection in patients receiving allogenic renal, cardiac or hepatic transplants.

Myfortic® (Mycophenolate sodium)
Prophylaxis of organ rejection in patients receiving allogenic renal transplants, administered in combination with ciclosporin and corticosteroids.

Rapamune® (Sirolimus)
The prophylaxis of organ rejection in adult patients at low to moderate immunological risk receiving a renal transplant. Sirolimus should be used in combination with ciclosporin and corticosteroids for the first 2 to 3 months post transplant. Sirolimus may be continued as maintenance therapy with corticosteroids only if ciclosporin microemulsion can be progressively discontinued.

4.2 Treatment Regimen

The current, primary immunosuppressive regimen comprises the calcineurin inhibitor (CNI) tacrolimus. Many patients transplanted prior to May 2006 will have received the alternative CNI ciclosporin. Low risk renal transplants patients may be maintained on tacrolimus monotherapy, but in other patients additional therapy with steroids, mycophenolate, azathioprine or sirolimus may be indicated dependent on the risk of rejection and renal function post transplant (see table one). The initiation of any immunosuppressive regimen will be undertaken by the Transplant Team.

In general the immunosuppressive strategy may be summarised as follows:

<table>
<thead>
<tr>
<th>Category</th>
<th>Main regimen</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk first cadaveric grafts</td>
<td>Monotherapy with tacrolimus</td>
<td></td>
</tr>
<tr>
<td>Living donor transplants</td>
<td>Tacrolimus, mycophenolate, and prednisolone</td>
<td>Evidence from our own data shows higher rejection in this group</td>
</tr>
<tr>
<td>First cadaveric grafts with delayed graft function</td>
<td>Tacrolimus, mycophenolate and prednisolone</td>
<td>In line with NICE recommendations</td>
</tr>
<tr>
<td>Extended criteria donors with high risk of nephrotoxicity</td>
<td>Tacrolimus, mycophenolate and prednisolone</td>
<td>In line with NICE recommendations</td>
</tr>
<tr>
<td>Second and subsequent transplants</td>
<td>Monotherapy with tacrolimus unless other risk factors dictate extra immunosuppression</td>
<td></td>
</tr>
</tbody>
</table>
• Patients should not receive tacrolimus and ciclosporin together, they are mutually exclusive drugs.
• Patients should not receive azathioprine with mycophenolate, they are mutually exclusive drugs.
• No patient should ever be advised to discontinue their immunosuppressive drug(s) unless this is under the direct guidance and supervision of the TC.
• Prednisolone is usually weaned down to a low dose and then discontinued according the patient’s clinical condition and the function of the transplant. Adjustment of steroid doses should be done by or on the advice of the TT.
• Even where available, patients should never be prescribed generic formulations of any of the above. This is because of varying bioavailability and pharmacokinetics that may compromise their transplant.
• **In all settings both tacrolimus and ciclosporin must be prescribed by brand name to reduce the risk of generic substitution.**
• **Standard release tacrolimus (Prograf) and tacrolimus MR (Advagraf) are not equivalent and can not be interchanged without additional monitoring.**
• Live vaccines should not be given to patients with an impaired immune response. The response to other vaccines may be diminished.

### 4.3 Care Plan for the Patient Post-transplantation

Clinic visits become less frequent as the graft function is stabilised and the drug therapy is established. An approximate timetable for outpatient visits is detailed below.

- **Month 0-1**  twice / three times a week
- **Month 1-2**  once weekly
- **Month 3-5**  fortnightly
- **Month 6-12**  monthly
- **Month 12 onwards**  2-4 monthly

Frequency of visits may depend on clinical condition of patient and their graft.

At each appointment, in addition to blood pressure and weight measurements, the following blood tests will be checked:

- Full blood count
- Urea and electrolytes including bicarbonate
- Calcium and phosphate
- Liver function tests
- Blood Glucose
- Blood drug levels
- Midstream urine sample – infection, blood, protein, glucose
Further tests are performed as required. See Appendix One (CMFT) and Appendix Two (SRFT) for further details of clinic visits and annual reviews.
4.4 Dosage and administration

Ciclosporin (Neoral)

Ciclosporin should be prescribed by brand name and in the vast majority of cases this will be Neoral. Treatment is initiated within 12 hours after transplantation at a dose of 10 to 15mg/kg body weight given in two divided doses. After a week doses are gradually reduced until a maintenance dose of about 2 to 6mg/kg per day is reached. Doses should maintain blood trough levels of 100-200ng/ml.

Ciclosporin is given twice daily approximately 12 hours apart. Blood levels are taken pre-dose to determine the “trough” level. Doses are adjusted to reach target blood levels which vary depending on time after transplant and other immunosuppressive agents used.

Brand Prescribing: Ciclosporin will soon be available from several generic companies. It is vital that ciclosporin is prescribed by brand name. The only brand currently used in Manchester is Neoral.

Tacrolimus (Prograf and Advagraf)

Tacrolimus should be prescribed by brand name and in the vast majority of cases this will be Prograf. Treatment is initiated within 24 hours after completion of the kidney transplant surgery at a daily dose of 0.15-0.30mg/kg body weight given in two divided doses. Doses are gradually reduced to maintain blood trough levels of 5-13ng/ml

Prograf (Standard release tacrolimus) is given twice daily approximately 12 hours apart. This is the product of choice at CMFT and SRFT.

Advagraf (Tacrolimus MR) is given once daily and is used in a subgroup of patients who are at high-risk of adherence problems.

Brand prescribing: Prograf and Advagraf are not equivalent and can not be interchanged without increased monitoring and input from the transplant team. Due to significant numbers of prescribing and dispensing errors we ask that you be particularly vigilant in prescribing the correct tacrolimus preparation.

Blood levels are taken pre-dose to determine the “trough” level. Doses are adjusted to reach target blood levels which vary depending on time after transplant and other immunosuppressive agents used. tacrolimus has a longer half-life than ciclosporin and changes in the dose may take several
days to be reflected in the blood levels. Maintenance doses are based on blood trough levels and clinical assessments of rejection and tolerability. Mycophenolate mofetil (Cellcept) and mycophenolate sodium (Myfortic)

Mycophenolic acid (MPA) is the active metabolite of both mycophenolate preparations. Most patients will be prescribed mycophenolate mofetil but may be switched to mycophenolate sodium if gastrointestinal side-effects are problematic. Oral mycophenolate is initiated within 72 hours following transplantation. The recommended dose in renal transplant adult patients is 1g twice daily for mycophenolate mofetil and 720mg twice daily for mycophenolate sodium and these doses are equivalent in terms of MPA content. If gastrointestinal side-effects are a problem mycophenolate doses may be split (see table four) or in some cases switched to azathioprine.

Dose adjustments will be made by the transplant team, and are based on drug tolerability, clinical signs and symptoms and tissue biopsies.

**Brand prescribing:** Mycophenolate mofetil will soon be available from generic companies. It is important that mycophenolate is prescribed by brand name until assessments can be made about the suitability of different generics. Brands currently used in Manchester are Cellcept (mycophenolate mofetil) and Myfortic (mycophenolate sodium).
Sirolimus

**Initial Therapy** (2 to 3 months post transplantation) – loading dose of 6mg orally, administered as soon as possible after transplantation. This is followed by 2mg once daily. The sirolimus dose should be individualised to maintain target blood trough levels.

**Maintenance Therapy** – as the ciclosporin is progressively discontinued over 4 to 8 weeks, the sirolimus dose will require adjustment to reach the new target blood trough levels. Sirolimus dose adjustment is required because:

i) ciclosporin inhibits the metabolism of sirolimus, so sirolimus levels will reduce as the ciclosporin is discontinued

ii) as the ciclosporin is discontinued, a slightly higher target blood trough level is required to maintain the level of immunosuppression

Maintenance therapy should be based on blood trough levels, clinical signs and symptoms and tissue biopsies. Trough drug levels are usually maintained 5-10ng/ml.

Dose alterations should be made only on the advice of a senior doctor from the Transplant Team
5 Regimen Management

5.1 Referral of patients

No shared care prescribing until the immunosuppressive regimen is stable. Most patients will be stabilised on a final immunosuppression regime within three months of renal transplantation. Prescribing remains within the hospital until a patient is stable and the GP has agreed to accept responsibility for shared care.

5.2 Referral criteria

- The GP has agreed to prescribe the required medication for the patient and has read a copy of this shared care guideline.
- The patient has been stabilised on a maintenance regime
- The patient has been dispensed a further two week supply of medication and reminder cards updated with the maintenance doses.
- The patient has been supplied with information about their immunosuppression therapy (see section 10)
- The GP has a full referral letter giving details of clinical history and relevant therapy.
- The GP may ask the Transplant Consultant to take back prescribing responsibility if the patient’s condition becomes unstable.

5.3 Responsibilities

**Transplant Team**

- Initiate treatment and adjust dosage to achieve appropriate therapeutic levels*
- Monitoring the progress of the patient, their response to treatment and graft function*
- Performing any required drug levels (therapeutic drug monitoring)/ full blood counts relating to immunosuppression in line with clinic visits (see below)*
- Initiate any dose changes, including supply of additional medication needed until the next GP appointment*

*Communicate any of the above to the GP

- Evaluation of adverse effects reported by the GP or patient
- The supply of immunosuppressants for the first 3 months post-transplantation or until graft function and immunosuppression regime has stabilised
- The supply of immunosuppressants for 3 months following initiation of new immunosuppressant agents
- Provision of patient medication leaflet and record card detailing current immunosuppression regime
• Encouraging the patient to present medication record cards at all hospital and GP appointments.
• Send a letter to the GP with a copy of SCP inviting shared care for the patient
• Provision of access to back-up support facilities, including consultant opinion, extended outpatient service for urgent clinic appointments, and pharmacist advice.
• Annual review of the patient including cancer (skin) screening and kidney function testing. See Appendix 1 for details of the annual review.
• Non-attendance at the clinic will be followed up by the clinic staff. The GP will be contacted if non-attendance remains a problem

**General Practitioner**
• Monitoring continued well-being of patient
• Monitoring the patients blood pressure every three months and refer back the Transplant Team at the base hospital if consistently above 130/90mmHg
• Adverse drug reaction and drug interaction monitoring
• Prescribing maintenance immunosuppression. Prescribing by brand name where appropriate.
• Be aware of the adverse drug reactions and drug interactions with immunosuppressive therapy, and report any evidence of these to the Transplant Team.
• Be aware of the increased incidence of skin and other cancers in patients receiving long-term immunosuppressive therapy and ensure female patients receive their cervical smear test at the GP practice each year
• Encourage the patient to carry an up to date medication record card, encourage compliance and recommend not to use OTC medications without seeking medical advice
• Inform the Transplant Team at the base hospital of any patient consultations or changes made to drug therapy
• Report any lack of communication about dosage and progress to the Transplant Team at the base hospital
6 Summary of cautions, contraindications, side-effects and drug interactions

See the summary of product characteristics (SPC) of each drug for full details \(^{(2)}\)

6.1 Cautions

All immunosuppressants cause increased susceptibility to infection and increased risk of neoplasia. Patients should be advised to use high factor sun block (SPF25 or above) during the months April to October and on sunny days / holidays including skiing holidays. UV rays are strongest between April and October so protection should be worn even when cloudy.

Ciclosporin and tacrolimus can cause dose dependent rises in serum creatinine which may require dose reduction once rejection is ruled out. Renal function must therefore be monitored closely. Ciclosporin and tacrolimus can also cause irreversible damage in the longer term (chronic allograft nephropathy). Disturbances in biochemical parameters can also occur including hyperkalaemia and hypomagnesaemia.

Mycophenolate and sirolimus can cause blood dyscrasias secondary to bone marrow suppression including anaemia, thrombocytopenia and neutropenia. Blood tests will be checked at each clinic visit (see 4.3) unless alternative arrangements have been arranged.

It is also necessary to monitor liver function as all immunosuppressants in this protocol can cause abnormal liver function tests.

6.2 Contra-indications

Tacrolimus is contra-indicated in patients allergic to macrolides including erythromycin. Neutropenia is a relative contra-indication to mycophenolate and sirolimus. Also see 6.3. Ciclosporin has some additional contra-indications:

- in psoriatic and atopic dermatitis patients with abnormal renal function, uncontrolled hypertension, uncontrolled infections or any kind of malignancy other than that of the skin
- in rheumatoid arthritis patients with abnormal renal function, uncontrolled hypertension, uncontrolled infections or any kind of malignancy.
- ciclosporin should not be used to treat rheumatoid arthritis in patients under the age of 18 years.
- ciclosporin is contraindicated in nephrotic syndrome patients with uncontrolled hypertension, uncontrolled infections, or any kind of malignancy.
- Concomitant use of tacrolimus is specifically contraindicated.
- Concomitant use of rosuvastatin is specifically contraindicated
6.3 **Pregnancy and Breast-feeding**
The effectiveness of oral contraceptives may be reduced so additional barrier methods are advised. Tacrolimus, mycophenolate and sirolimus are contraindicated in pregnancy. Effective contraception must be used during treatment with mycophenolate and sirolimus and for 12 weeks afterwards.

Female transplant patients who are intending to or may possibly become pregnant or wish to breastfeed should be referred to the TT as a full risk/benefit analysis of their immunosuppression and/or contraceptive regimes can then be carried out.

6.4 **Side-effects**
A full list of side-effects of each drug can be found in the Summary of Product Characteristics / Data Sheet (2). Many of the side-effects are reversible and respond to dose adjustment. See 6.5 for a list of common side-effects and their management.

6.5 **Management of Adverse Events by the General Practitioner**

In general, for mild side-effects symptomatic relief should be offered. For more severe or persistent side-effects the patient should be referred back to the specialist centre.
### Ciclosporin

**Table Two: Ciclosporin Side-effects - GP Management**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burning sensation in hands and feet</td>
<td>May occur early in treatment, and should subside. Possibly indicates ciclosporin toxicity. If it persists – refer to TT</td>
</tr>
<tr>
<td>Nausea &amp; vomiting, diarrhoea</td>
<td>Continue medications if possible. If necessary – refer to TT</td>
</tr>
<tr>
<td>Abnormal bruising</td>
<td>Refer to TT</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Treat with appropriate antihypertensives. Refer to TT</td>
</tr>
<tr>
<td>Tremor</td>
<td>May indicate ciclosporin toxicity. Refer to TT</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>May be treated with an appropriate statin or other lipid-lowering agents. Increased risk of muscle toxicity – counsel patient.</td>
</tr>
<tr>
<td>Muscle cramps and myalgia</td>
<td>Refer to TT</td>
</tr>
<tr>
<td>Headache</td>
<td>Treat with appropriate analgesics (paracetamol). Refer to TT if necessary.</td>
</tr>
<tr>
<td>Hypertrichosis</td>
<td>May require cessation of therapy and substitution with Tacrolimus. Refer to TT</td>
</tr>
<tr>
<td>Gum hypertrophy</td>
<td>May require cessation of therapy and substitution with Tacrolimus. Refer to TT. May be enhanced by use of calcium channel blockers</td>
</tr>
</tbody>
</table>

### Tacrolimus

**Table Three: Tacrolimus side-effects – GP management**

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea &amp; vomiting, diarrhoea</td>
<td>Continue medications if possible. If necessary – refer to TT</td>
</tr>
<tr>
<td>Hyperglycaemia, diabetes</td>
<td>Inform TT – possible adverse effect of tacrolimus</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>May be treated with an appropriate statin or other lipid-lowering agents. Increased risk of muscle toxicity – counsel patient.</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Treat with appropriate antihypertensives. Refer to TT</td>
</tr>
<tr>
<td>Tremor or Paraesthesia</td>
<td>May indicate tacrolimus toxicity. Refer to TT</td>
</tr>
<tr>
<td>Headache</td>
<td>Treat with appropriate analgesics (paracetamol). Refer to TT if necessary.</td>
</tr>
</tbody>
</table>
Mycophenolate mofetil (Cellcept®) and Mycophenolate sodium (Myfortic®)

Both drugs are metabolised to the mycophenolic acid, and their indications, side-effects, and management are near-identical. Myfortic is an enteric coated formulation and may benefit patients who have intolerance of the gastrointestinal side effects of Cellcept.

Table Four: Mycophenolate side-effects – GP management

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opportunistic infections</td>
<td>Treat with appropriate anti-infective agent. Inform TT</td>
</tr>
<tr>
<td>Indication of bone marrow suppression</td>
<td>Refer to TT</td>
</tr>
</tbody>
</table>
| Gastrointestinal symptoms – nausea, vomiting, diarrhea, abdominal pain | It is standard practice in cases of severe GI intolerance to divide the total daily dose into smaller, more frequent doses;-
Example
If patient is taking Cellcept 1g bd, it is reasonable to change this to 500mg qds.
Example
If patient is taking Myfortic 720mg bid, it is reasonable to change to 360mg qds.
Total daily dose should not be reduced.
If in doubt refer to TT                                    |

Sirolimus

Table Five: Sirolimus side-effects: GP management

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia, thrombocytopenia</td>
<td>Refer to TT – possible side effect of sirolimus</td>
</tr>
<tr>
<td>Abdominal Pain, diarrhea</td>
<td>Continue medications if possible. If necessary – refer to TT</td>
</tr>
<tr>
<td>Hypercholesterolaemia, hypertriglyceridaemia</td>
<td>May be treated by the addition of standard agents such as statins, or increase in dose of existing statins. If in doubt contact TT.</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>Refer to TT</td>
</tr>
</tbody>
</table>

6.6 Drug Interactions

Ciclosporin, tacrolimus and sirolimus

Drugs and other agents may affect plasma concentrations of ciclosporin through competitive inhibition or induction of the hepatic enzymes involved in the metabolism of ciclosporin, in particular cytochrome P450. These drugs are detailed in the table below.
Concomitant nephrotoxic drugs should be avoided where possible including NSAIDs, aminoglycosides, amphotericin, ciprofloxacin, colchicine, cotrimoxazole (treatment doses) and melphalan. Trimethoprim should be avoided as it may interfere with creatinine measurements. Other drug interactions include possible reduced effectiveness of vaccinations and reduced efficacy of oral contraceptives (barrier methods of contraception should be used in addition).

Table Six: Drug interactions - ciclosporin, tacrolimus, and sirolimus

<table>
<thead>
<tr>
<th>Immunosuppressant</th>
<th>Drugs that increase therapeutic levels</th>
<th>Drugs that decrease therapeutic levels</th>
<th>Drugs which may increase other toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ciclosporin</strong></td>
<td>Allopurinol</td>
<td>Barbiturates</td>
<td>Increased risk myopathy:</td>
</tr>
<tr>
<td></td>
<td>Amiodarone</td>
<td></td>
<td>- Statins</td>
</tr>
<tr>
<td></td>
<td>Chloroquine</td>
<td></td>
<td>- Fibrates</td>
</tr>
<tr>
<td></td>
<td>Cimetidine</td>
<td></td>
<td>Increased diclofenac bioavailability</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
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<tr>
<td></td>
<td>Diltiazem</td>
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<tr>
<td></td>
<td>Doxycycline</td>
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<td></td>
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<tr>
<td></td>
<td>Erythromycin</td>
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<td></td>
<td>Fluconazole</td>
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<td></td>
<td>Ketoconazole</td>
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<td></td>
<td>Itraconazole</td>
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<td></td>
<td>Nicardipine</td>
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<td></td>
<td>Oral contraception</td>
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<td></td>
<td>Protease inhibitors</td>
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<td></td>
<td>Verapamil</td>
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<td></td>
<td>Grapefruit juice</td>
<td></td>
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<tr>
<td><strong>Tacrolimus</strong></td>
<td>Cimetidine</td>
<td>Barbiturates</td>
<td>Increased risk of hyperkalaemia:</td>
</tr>
<tr>
<td></td>
<td>Clarithromycin</td>
<td></td>
<td>- ACE inhibitors</td>
</tr>
<tr>
<td></td>
<td>Clotrimazole</td>
<td></td>
<td>- Amiloride</td>
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<tr>
<td></td>
<td>Diltiazem</td>
<td></td>
<td>- Spironolactone</td>
</tr>
<tr>
<td></td>
<td>Doxycycline</td>
<td></td>
<td>Increased hyperglycaemia:</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td></td>
<td>- Steroids</td>
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<td></td>
<td>Fluconazole</td>
<td></td>
<td>Increased phenytoin levels</td>
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<td></td>
<td>Ketoconazole</td>
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<td></td>
<td>Itraconazole</td>
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<td>Nicardipine</td>
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<td></td>
<td>Nifedipine</td>
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<td>Omeprazole</td>
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<td></td>
<td>Protease inhibitors</td>
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<td></td>
<td>Verapamil</td>
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<td></td>
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<tr>
<td></td>
<td>Grapefruit juice</td>
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<td></td>
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<tr>
<td><strong>Sirolimus</strong></td>
<td>Clarithromycin</td>
<td>Carbamazepine</td>
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<td></td>
<td>Cimetidine</td>
<td>Phenobarbital</td>
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<tr>
<td></td>
<td>Ciclosporin</td>
<td>Phenytoin</td>
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<td></td>
<td>Diltiazem</td>
<td>Primidone</td>
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<tr>
<td></td>
<td>Erythromycin</td>
<td>Rifampicin</td>
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<td></td>
<td>Fluconazole</td>
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<tr>
<td></td>
<td>Ketoconazole</td>
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</tr>
<tr>
<td></td>
<td>Itraconazole</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Verapamil</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grapefruit juice</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Mycophenolate mofetil and mycophenolate sodium

## Table Seven: Drug interactions - Mycophenolate

<table>
<thead>
<tr>
<th>Drugs that increase therapeutic levels</th>
<th>Drugs that decrease therapeutic levels</th>
<th>Drugs which may increase other toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aciclovir</td>
<td>Antacids: aluminium or magnesium</td>
<td>Increase risk of bone marrow suppression with other immunosuppressants</td>
</tr>
<tr>
<td>Probenicid</td>
<td>Cholestyramine</td>
<td></td>
</tr>
</tbody>
</table>

If azathioprine is used as part of the immunosuppressive regimen, **DO NOT** use allopurinol as there is a significant risk of severe, and potentially life-threatening marrow suppression and leucopenia.
7 Back-up care available to GP from Hospital, including emergency contact procedures and help line numbers, for the Greater Manchester Area;

- All Renal Transplant Consultants are contactable via the Trust switchboard: 0161 276 1234
- Transplant Unit at Manchester Royal Infirmary: 0161 276 5106
- Renal Pharmacist: 0161 701 4327

Contacts for more detailed info, including out of hours

<table>
<thead>
<tr>
<th>Name</th>
<th>Base</th>
<th>Contact number</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMFT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SpR on call for transplantation</td>
<td>CMFT</td>
<td>0161-276 1234 (bleep via switch)</td>
</tr>
<tr>
<td>Renal Outpatient Department (Sister)</td>
<td>CMFT</td>
<td>0161-276 8721</td>
</tr>
<tr>
<td>Direct line to Renal Transplant Unit</td>
<td>CMFT</td>
<td>0161-276 4402</td>
</tr>
<tr>
<td>Renal Pharmacist</td>
<td>CMFT</td>
<td>0161-701 4327</td>
</tr>
<tr>
<td>SRFT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transplant Nursing Team</td>
<td>SRFT</td>
<td>0161 206 1295 or long range pager (07623 620320)</td>
</tr>
<tr>
<td>Renal Medical Baton Bleep Holder</td>
<td>SRFT</td>
<td>0161 206 7373 switch board and ask to bleep</td>
</tr>
<tr>
<td>Renal Pharmacists</td>
<td>SRFT</td>
<td>0161 206 4207</td>
</tr>
<tr>
<td>Out of hours – on-call renal registrar</td>
<td>SRFT</td>
<td>0161 206 7373 bleep via switch</td>
</tr>
</tbody>
</table>

8 Statement of agreement

- Shared care is an agreement between the GP and the Consultant. This form is a request by the consultant to share the suggested care pathway of your patient. If you are unable to agree to the sharing of care and initiating the suggested medication, please make this known to the consultant within 14 days, ideally stating the nature of your concern.

9 Written information provided to the patient

- Patient information booklet entitled “Medication Advice for Patients with a Kidney or Pancreas Transplant”. Available from the Renal Transplant Unit.
- Patient information leaflet provided as package insert
10 Supporting References

3. The Royal Liverpool and Broadgreen University Hospitals NHS Trust – Safe Prescribing Guidelines for ciclosporin, mycophenolate, tacrolimus and sirolimus following renal transplantation.
Appendix 1. Transplant Annual Review (CMFT)

Every transplant patient receiving follow up care at the MRI will be offered a Transplant Annual Review.

The patient will always see an Advanced Nurse Practitioner and may also see a Consultant Nephrologist, Transplant Registrar (SpR), or Consultant Transplant Surgeon according to clinical necessity.

Investigations on that clinic visit:
Routine blood screens: full blood count, renal screen, liver screen.
Fasting lipid screen
Parathyroid Hormone (PTH)
Fasting blood sugar
24 hour urine for protein and sodium excretion
Body Mass Index measurement

Advanced Nurse Practitioner responsibilities:

- Cardiovascular health check: blood pressure, cholesterol, BMI (advise to see dietitian if necessary), advise to stop smoking / seek cessation advice), advise on exercise activity, alcohol intake, diet (refer to dietician if necessary).
- Record history of infections in the past 12 months.  Check patient is up to date with vaccines (influenza & pneumococcal) and refer to GP if necessary.
- Record signs and symptoms of current or recent morbidity including lumps or swellings, persistent indigestion, persistent cough or hoarseness, altered bowel habits, unexplained weight / appetite loss, abnormal bleeding, anogenital lesions.  Refer to SpR / Consultant if necessary.
- Dental health – advise to see dentist every six months for examination, clean and polish.
- Female health: encourage breast self-examination and mammograms as per national guidance, establish if any problems menstruating and refer to GP if necessary, advise on appropriate contraception (coil not recommended due to risk of infection), advise annual cervical smears via GP, refer problems relating to infertility, urinary and sexual health to GP or specialist
- Male health: encourage testicular self examination; refer problems with urinary and sexual health to GP or specialist.
- Diabetes mellitus: identification of abnormal blood sugars, confirmation of diabetes and follow up care in existing patients.  Advise annual eye test and regular foot examination by a chiropodist.
- Record accurate list of prescribed and over the counter medications and assess patient adherence.  Refer to Pharmacist if necessary. Inform GP of up-to-date list of medications.
- Advise to attend Transplant Dermatology Clinic for skin care advice and full skin examination.
• Identification of current health problems potential problems to be addressed by the transplant doctor and referral made if necessary.
• Nurse Practitioner referrals, for example, dietitian, clinical psychologist, dental hospital, dermatologist, urology NP, pelvic floor NP, obstetrician for pre-conceptual advice, anaemia co-ordinator.

**Medical Staff responsibilities:**
• Addressing identified current health problems
• Reviewing medical and transplant associated problems from the previous year
• Routine renal and immunosuppression review
• Referrals where appropriate
Appendix 2. Transplant Clinics at Salford Royal NHS Foundation trust (SRFT)

There are two medical transplant clinics held at Hope Hospital, per week. These are on Tuesdays and Thursdays.

Standard investigations at these clinics are:

- FBC, ferritin and iron studies
- Profile including LFTs
- Random blood sugar
- Lipid screen
- Immunosuppressive level
- PTH – 6 monthly
- MSSU for MC&S
- Urine protein/creatinine ratio
- Hepatitis B&C

All these results will be checked by the Transplant specialist nursing team, who will discuss with a Consultant Nephrologist at a post clinic meeting.

A nurse led clinic is also held on a Tuesday and Thursday. The nursing team will see patients who are perhaps changing their medications or requiring additional review for current problems. Blood and urine samples taken will depend on individual assessment of the patient. Patients are triaged for medical review as appropriate.

Anniversary Clinic

Each year the patient will be sent an appointment to attend for a separate review by the transplant specialist nursing team. This is for purposes of health promotion, prevention and early intervention, aiming to promote quality of life and increase longevity of transplant.

Particular areas included in this review are:

- Issues regarding medication, such as non concordance and side effects
- If experiencing UTI’s, how often and management plan
- Assessment of health risks:
  - BMI
  - BP
  - Smoking habits
  - Alcohol consumption
  - Exercise profile
  - Diabetic status and follow up care
  - Cardiovascular events
- Cancer prevention and early detection
Skin care
Smear advice (annual)
Breast care
Testicular/prostate care
Cancer screening questions
- General care
  - Diet and fluid intake
  - Reproductive and sexual health
  - Oral/dental care
  - Mobility in relation to joint discomfort and/or gout
- Social and psychological effects
  - Demands on self care
  - Sleep pattern
  - Coping skills and general mood
- Transplant progress over previous 5 years
  - Assessed in relation to creatinine/eGFR/UPCR trends from previous 5 years. Aim to pick up deteriorating grafts which may have gone undetected
  - Relevant results from previous 12 months
    - Blood glucose
    - HbA1c – if diabetic
    - Cholesterol
    - PTH
    - FBC
    - Ferritin

Actions including those required by the patient to change lifestyle, referrals to other services and follow up are made between the Transplant nurse specialist and patient. Post clinic letters are sent primarily to the patient and a copy to General practitioner.

Annual dermatology clinic

Transplant patients are sent a dermatology appointment to see one of our Dermatology Consultants every year. It is important that patients follow skin care advise but also that they attend this review.

Please note that access to this appointment is via nurse led anniversary review as described above.