GP PRESCRIBING INFORMATION: ADULT RENAL TRANSPLANT
HEY Hospitals NHS Trust Renal Unit

Introduction

The aim of this document is to provide General Practitioners with information to facilitate joint care of kidney transplant patients managed by the Renal Unit at Hull and East Yorkshire Hospitals NHS Trust. It is not intended to encourage or oblige GPs to take responsibility for monitoring or changing doses of patients' immunosuppression, but to work in collaboration with hospital physicians to ensure optimal patient care.

It is hoped that this document, together with clinic letters, will allow the patients' GP to have an integral role in his or her ongoing care. As a general rule this group of patients are well known to their GP. Given the frequency of follow-up immediately post transplantation it is unlikely that the patient will have much need to contact their GP over the first three months. By the end of this period the patient is likely to be on a stable immunosuppressive regime and on treatment for co-morbid conditions such as hypertension and hyperlipidaemia.

This document should be read in conjunction with the relevant shared care frameworks and the Hull and East Riding Prescribing Committee standards for shared care.

This guide is not exhaustive and specialist advice should be sought from the transplant team whenever needed (see below).

Out-patient follow-up

After an uncomplicated kidney transplant patients are discharged from Leeds after 5 days. Initially they are seen three times weekly at Hull Royal Infirmary. This is reduced to twice weekly one-month post transplantation and weekly after two months, providing clinical progress is satisfactory. After 3 months patients will be followed up by the renal team in their local hospital (Hull, Bridlington, Scunthorpe, Grimsby or Goole). The frequency of appointments is reduced progressively so that by 3 years post transplantation a patient will typically be seen approximately 3-4 times per year. Exceptions maybe made where clinically indicated.

At each clinic visit all patients have their weight and blood pressure measured, urine dip stick tested and blood sent for FBC, BCP and trough immunosuppressive drug levels, typically tacrolimus. Other tests are performed as clinically indicated.

Clinic letters will detail the current status of the patient, transplant and also inform GPs of any changes in the patient's medication so that they can update repeat prescriptions. A weekly Transplant MDT meeting discusses all transplant recipients seen that week, or those with clinical problems and GPs will be informed of any changes to patient therapy.

Immunosuppression drugs

The following is a guide to the local practice of immunosuppression together with additional information, which GPs may find useful. It should be used in conjunction with the Summary of Product Characteristics for each drug (available at www.medicines.org.uk).

All transplanted patients require long term immunosuppression to maintain graft function. The most commonly use drugs are calcineurin inhibitors, mainly tacrolimus (adoport) and anti-proliferative agents, mainly mycophenolate mofetil. Other immunosuppressants may be used depending on

clinical need. **Changes to immunosuppression medication should only be made by the renal transplant team.**

Immunosuppressants prescribed for patients following renal transplantation are initiated by the specialist team. It is planned that the transplant centre or specialist renal centre remains responsible for all follow-up and changes in therapy, and will prescribe all immunosuppression required post-transplant.

Until that agreement is reached, patients will be prescribed and dispensed their immunosuppression from HRI for the first three months. After this time and when patients are on a stable dose a request will be sent to the patient's GPs to continue to prescribe these agents. The transfer of prescribing responsibilities is facilitated by use of prescribing frameworks (www.hey.nhs.uk/herpc/amber).

Immunosuppressives (both innovator brands and branded generics) will be prescribed by brand and referred to by that brand in all correspondence in tertiary, secondary and primary care, and with all patients themselves.

Tacrolimus
Tacrolimus is the preferred calcineurin inhibitor after transplantation (it has superseded ciclosporine). **There is more than one formulation available but these cannot be used interchangeably**. Tacrolimus should be prescribed by brand, most commonly this will be Adoport (Prograf is the less commonly used alternative). These are both twice daily preparations; in some circumstances patients will be prescribed a once daily preparation (Envasus or Advagraf). Side effects include tremor, hypertension, diabetes and dyslipidaemia. Tacrolimus has a narrow therapeutic window, high levels can cause decreased kidney function and low levels increase the risk of rejection. Trough levels are used to titrate the dose (target 8-10 for the first 3 months the 5-8 thereafter). Tacrolimus is safe in pregnancy and breast feeding.

Mycophenolate Mofetil (MMF)
MMF is the preferred antiproliferative drug for renal transplant (it has superseded azathioprine). It does not need to be prescribed by brand. Occasionally patients are unable to tolerate this drug and may be switched to Mycophenolic acid (Myfortic), this is the active metabolite of MMF. It is possible to measure drug levels but the practicality and difficulties with interpretation are such that it is rarely done. Common side effects include diarrhoea and leucopoenia. Diarrhoea usually settles quite quickly without the need to stop or alter the dose of the drug. MMF and Myfortic are teratogenic and women of child bearing are informed of this and should be on contraception. If pregnancy is planned then this should be changed in advance of conception (90 days) to an alternative (usually azathioprine) under supervision of the transplant clinic. There is a theoretical risk to pregnancy for men taking this this drug and they are counselled about this.

Other immunosuppressant agents may be used depending on multiple factors including, the primary renal disease, risk of future rejection, an episode of rejection, cancer and infections. All changes will be made under the supervision of the transplant team.

Prednisolone. Most transplant recipients will be on a 'steroid free' regimen. However they are occasionally still needed, most commonly to treat and maintain patients after rejection. The side effects of long term steroid therapy are well known

Azathioprine. When possible MMF is used in preference to azathioprine, however azathioprine is safe in pregnancy whereas MMF is not. Common side effects include bone marrow suppression,

hepatotoxicity and skin changes. Co administration with allopurinol should be avoided due to bone marrow suppression.

Sirolimus. This is an mTOR inhibitor that is occasionally used in renal transplantation. It is a once daily drug which is monitored with trough levels (target 5-10). It is given with steroids. It is often used in patients who are unable to tolerate tacrolimus or have had recurrent skin cancers. Side effects are numerous and include, mouth ulcers, GI upset, oedema, raised lipids, proteinuria and infections. Sirolimus impairs wound healing and anything other than minor surgery necessitates a temporary switch to an alternative agent for the time of surgery (this does not include minor dentistry).

Adjunctive prescriptions

Co-trimoxazole 480mg OD is given for 6 months post-transplant for PCP prophylaxis in all patients (dapsone is often used if the patient is intolerant of co-trimoxazole).

Valganciclovir may be given as CMV prophylaxis. The decision to use, dose and the duration will depend on the patient's risk factors and creatinine clearance. This drug will be prescribed from the transplant clinic for the duration of its use.

Ranitidine is given to all transplant recipients for 1 month post-transplant if they are not already on antacid medication.

There are often large changes to patients' prescriptions after receiving a transplant. Leeds transplant unit will provide an up to date list of medication on discharge. Medications used in end stage kidney disease such as phosphate binders, diuretics, sodium bicarbonate and antihypertensives are often stopped.

Medications to avoid

There are multiple drugs which may need to be avoided altogether of have their posology altered depending on kidney function and other medications. The BNF and Renal Drug Handbook should be used as first reference. If needed a pharmacist or member of the renal team can be consulted (details below). Some commonly used drugs to avoid or alter the dose include:

All NSAIDS: Increased risk of AKI through multiple pathways.

All macrolide antibiotics (clarithromycin and erythromycin): Toxic elevation in tacrolimus levels and AKI.

Antifungals: Fluconazole, Itraconazole, Ketoconazole - toxic elevation in tacrolimus levels and AKI if needed will need consultation with transplant team first.

Nitrofurantoin: Is contraindicated in all kidney transplant patients.

Trimethoprim: Avoid if possible as interference with creatinine assay but can be used if no alternative (not if already on co-trimoxazole).

Allopurinol: Must not be used ii the patient is taking azathioprine - drug toxicity and blood dyscrasias.

Diltiazem: Toxic elevation in tacrolimus levels and AKI.

Suspected infection

Although immunosuppressed patients are at risk of opportunistic and rare pathogenic infections these are not common. Urinary tract and respiratory tract infections caused by common community acquired pathogens predominate. Normally these can be managed as would be done for non-transplant recipients. Sending appropriate samples for culture before starting antimicrobials is crucial to guide management; however treatment should not be delayed while waiting for results. If there is any concern about the nature, severity, management or effect on transplant function then

this should be discussed with the renal team (see below). If the patient requires urgent admission to hospital discussion with the renal team should not delay this process.

Malignancy

Reduced immunosurveillance in the transplant population results in an increased incidence of certain cancers including lymphomas and skin cancers. Lymphomas may occur surprisingly early following transplantation and most are due to EBV infection. Skin tumours occur most commonly on sun exposed skin. To reduce the risk of melanoma and non-melanoma skin cancers patients are advised to cover their skin from sun exposure. Sunscreen with a UVB SPF of at least 30 (preferably 50) should be applied to all exposed skin even in a British Summer. Higher SPF and UVA reflectors should be considered in patients travelling abroad. Patients should be strongly encouraged to take up all screening programmes for cancer that are applicable to their age and gender

Pregnancy and contraception

Fertility may return rapidly after transplantation (for men and women). With a well-functioning transplant pregnancy is often uncomplicated. We advise women to wait until they are at least 2 year post transplant with stable function before trying to conceive. During this time patients receive advice on contraception; this should be a non-oestrogen based method. Ideally we would like to know in advance of plans for conception (for men and women) so they can be counselled about any potential risks to their health, the transplant and the foetus. They will also need a medication review and may need to change the drugs they are on (such as MMF or ACE inhibitors).

Hormone replacement therapy and osteoporosis prevention

Generally we advise against the use of HRT in transplant patients because of the increased cancer risk.

Contacting Hull and East Yorkshire Nephrology Staff

Depending on the urgency and nature of the problem at hand there are several ways of contacting renal staff for advice:

1 On-call consultant available 24 hours/day via switch board for urgent problems only.
2 Transplant specialist nurses during office hours; typically reply that day.
3 E mail Advice and Guidance request via “choose and book”; typical reply with 24 hours.
4 Letter to a transplant consultant.

Document prepared by:

Dr Tom Jorna, Consultant Renal Physician
Aaron Acquaye, Renal Pharmacist
Prof Sunil Bhandari, Consultant Renal Physician
(Oct 2017, Review Oct 2020)

GP PRESCRIBING INFORMATION: ADULT RENAL TRANSPLANT
HEY Hospitals NHS Trust Renal Unit

Vaccination

Live attenuated vaccines must not be given to renal transplant patients. Kidney transplant recipients should receive influenza and pneumococcal vaccination unless there is a contraindication. Kidney transplant recipients should not receive the shingles vaccine.

SAFE VACCINES	CONTRAINDICATED
Pneumococcal	MMR
Hepatitis A	Polio [Live Oral]
Hepatitis B	Yellow Fever
Tetanus toxoid	Varicella
Haemophilus Influenza B	BCG
Meningococcus	Typhoid [Live Oral]
Polio [Killed]	
Diphtheria	
Pertussis	
Influenza	
Typhoid [Killed]	

Chickenpox exposure

Exposure to patients with varicella zoster (VZ) is a serious risk to those transplant patients who have not had chickenpox in childhood. Immunosuppressed patients who believe they have been exposed should be referred to the renal unit for assessment as to whether passive immunity with VZ immunoglobulin should be offered.