# RENAL TRANSPLANT: IMMEDIATE MANAGEMENT - SCH

## PRACTICE GUIDELINE ©

## DOCUMENT SUMMARY/KEY POINTS

- The purpose of this protocol is to provide guidance for the admission and medical management of children who are undergoing kidney transplantation for medical and nursing staff.
- Variations from this guideline may be required for individual patients but this should only occur under consultant supervision.

## CHANGE SUMMARY

- Review of document.
- Drug dosages for basilixmab and valganciclovir changed.
- Target level for tacrolimus adjusted.

## READ ACKNOWLEDGEMENT

This practice guideline is relevant to the following staff:

- Medical and surgical junior staff involved in the care of kidney transplant recipients
- Medical and surgical senior staff involved in the care of kidney transplant recipients
- Nursing staff in C1S and CICU involved in the care of kidney transplant recipients
- Pharmacy staff involved in the care of kidney transplant recipients





| | | |
|---|---|---|
| **Approved by:** | SCHN Policy, Procedure and Guideline Committee | |
| **Date Effective:** | 1st May 2021 | **Review Period**: 3 years |
| **Team Leader:** | Clinical Nurse Specialist | **Area/Dept**: Renal SCH |

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# Background

Kidney transplantation is the preferred mode of renal replacement therapy in children, providing both improved quality of life and survival for children with end stage kidney disease (ESKD). [1]

The two major programs for kidney transplantation are the living related/unrelated kidney donation and deceased donor program. Living related/unelated kidney donation can be done pre-emptively, however children can only be wait listed for deceased donor kidney transplant whilst on dialysis. Living related/unrelated kidney transplantation is scheduled electively.

The purpose of this protocol is to provide guidance for the admission and medical management of children who are undergoing kidney transplantation for medical and nursing and pharmacy staff.

# Pre-Operative Admission & Workup

Business Hours: Direct ward admission C1S.

After Hours: Through emergency department or direct to ward if bed available
After hours registrar/SOS will be responsible for admission.

## Checklist of investigations and orders

Table 1 summarises the investigations and orders required on admission.

The consultant nephrologist will contact the transplant surgical consultant directly.

The following people are also to be notified by the admitting medical officer regarding the kidney transplant:

- Anaesthetic Registrar on call through switch.
- Request postoperative CICU bed by contacting CICU Team leader and CICU fellow.

The transplant surgeon will notify the renal transplant fellow at Prince of Wales through switchboard. Surgical team is responsible for consent and notification of theatres.

The medical officer clerking admission will liaise with the nephrologist on call to determine:

- Whether dialysis is required preoperatively.
- If the patient is medically well for kidney transplantation.
- Which of the patient's regular medications will be required preoperatively.
- The rate and type of IV fluids to be administered whilst fasting.
- The dose and timing of the initial pre-operative immunosuppression and medications. Many medications will require ordering from pharmacy in advance.
- Whether the child requires isolation bed due to known previous multi-resistant organism isolation.
- When a patient is listed for transplant, the renal team will have organised an individual plan for the patient as to immunosuppression and any additional investigations.

***Table 1: Pre-operative investigations to be performed on admission to SCH***

| *Investigations* | | *Comments* |
|---|---|---|
| *Bloods + IVC* | ***FBE*** | ***Send bloods urgently*** |
| | ***UEC/CMP/LFTs/BSL*** | |
| | ***Coagulation*** | |
| | ***Group and hold*** | |
| | ***X- match two units*** | |
| | ***Hepatitis B/C/HIV serology*** | |
| | ***EBV/CMV/Herpes/Varicella IgG*** | |
| *ECG* | | |
| *CXR* | | |
| *Microbiology* | ***MRSA screen swabs*** | ***Also swab any open wounds*** |
| | ***Gastrostomy site swab*** | |
| | ***CVL exit site swab*** | |
| | ***PD catheter exit site swab*** | |
| | ***PD fluid culture*** | ***Drain and cap PD catheter. Send fluid for MCS*** |
| | ***MSU*** | |
| | ***Viral throat swab or NPA (COVID-19 swab if appropriate)*** | |
| *Weight & height* | | ***Dry weight if on dialysis*** |

## Initial perioperative medications

All decisions regarding transplant immunosuppression are to be discussed with the nephrologist on call.

Table 2 denotes the medications which are required to be charted and administered prior and during the transplant operation.

***Table 2: Perioperative medications for kidney transplantation***

| Drug | Dose and Route | Timing | Comments |
|---|---|---|---|
| **Mycophenolate mofetil*** | 400mg/m$^2$ PO<br>Max dose 1000mg | Given prior to theatre | Continued 12 hourly<br>Use cytotoxic precautions |
| **Tacrolimus*** | 0.15mg/kg PO<br>Max dose 5mg | Given prior to theatre | May be withheld with deceased donor<br>Use cytotoxic precautions |
| **Corticosteroids** | Prednisone 2mg/kg (max 120mg) PO | Given prior to theatre | Continued daily |
| | Methylprednisolone 10mg/kg IV<br>Max dose 500mg | Given intra-operatively immediately prior to release of aortic clamp | |
| **Basiliximab**** | < 35kg 10mg IV<br><br>> 35 kg 20mg IV (adult dose) | Given intra-operatively | Infusion 50 mL 5% glucose or 0.9% sodium chloride over 30 mins<br>**After hours: available in the after-hours medication room via AHNM.** |
| **Antibiotics** | Piperacillin-tazobactam (Tazocin®) 100mg/kg(of piperacillin component)<br>Max dose 4 g of piperacillin component | Given-intraoperatively | Stat dose for surgical prophylaxis |

*See appendix regarding tablet strength: round to appropriate dose
**Thymoglobulin, a T cell depleting anti body, is an alternative induction agent which is used in selected patients. If required, dosing and administration is provided in Appendix A

## Anaesthetic Guidelines

- All children will require a multi-lumen central venous line inserted for CVP monitoring and fluids.
- An arterial line is typically inserted to monitor SBP and MAP
- A high intravascular volume and an adult blood pressure should be targeted intra-operatively due to the complication of thrombosis in paediatric transplant recipients. Assessment of intravascular volume can be achieved through direct visualisation of the IVC and also inferred from the CVP.
- Aggressive fluid replacement is generally required to achieve the high intravascular volume (generally CVP of 15mmgHg in infants and CVP of 12 mmHg in older children) at the time of vascular anastomosis and re-perfusion.
- mL:mL replacement of urine output should commence intra-operatively and continue through recovery as the risk of thrombosis is greatest immediately post-transplant.

# Immediate post-operative CICU management

- Day of transplant is referred to as Day 0.
- Handover of patient at the bedside from anaesthetics/surgeons should occur with CICU medical nursing staff and nephrology team present.
- Post operatively renal transplant patients are managed in CICU jointly with the Nephrology team.
- Patients should be nursed in a single room with protective precautions, unless contact precautions are required for the individual patient. Cytotoxic precautions should be used when giving cytotoxic medications, and handling body fluids.

The risk of graft thrombosis is greatest immediately post-operatively.

Aggressive fluid replacement is required for the first 24 - 48 hours

The Nephrology team in collaboration with the CICU team will set BP, CVP and UO targets at handover in CICU and at least daily on ward round.

Notify Nephrologist immediately if there is sudden fall in urine output below target.

## Fluid Management

- Note urine output target includes native urine output.
- Fluid replacement consists of two IV lines of the following:

**IV line 1: Insensible losses:** 400mL/$m^2$ /day of 0.45% sodium chloride + 5% glucose

**IV line 2: Urine replacement:** mL:mL replacement of previous hour urine output.

**Fluid options:** 0.9% sodium chloride, 0.45% sodium chloride and Plasmalyte

- Glucose free solutions are typically required for urine replacement due to high BSLs.
- 0.45% sodium chloride will need to be ordered in advance.
- Additional fluid bolus are commonly required to meet BP, CVP and UO targets. Patients may require inotropic support for blood pressure if fluids required is excessive.
- This fluid regime is generally continued for the first 48 hours and then a constant IV fluid rate can be used.

## Investigations and Observations

- FBE/UEC/CMP/glucose/VBG should be sent on arrival in CICU and every 6 hours thereafter.
- Tacrolimus trough levels should be measured each morning. The morning dose should be administered after blood has been collected. Levels are used to guide subsequent dosing as they are not available until late afternoon.
- Urinalysis should be performed daily.
- Strict fluid balance.
- Routine CICU observations.
- Renal transplant USS should be arranged within the first 24 hours of arrival in CICU. If the child arrives back to CICU within working hours this will be performed on the same day, otherwise the next morning. If there are clinical concerns about graft function at which time the SCH Radiology should be contacted urgently through switchboard.

## Post-operative Immunosuppression & Medications[2]

***Table 3: Postoperative immunosuppression and medications***

| Drug | Medication | Dosing | Comments |
|---|---|---|---|
| **Corticosteroids** | Methylprednisolone | 2mg/kg IV daily | Day 1 & Day 2<br>Day 4 prednisolone dose given as IV methylprednisolone as premedication for basiliximab along with promethazine |
| | Prednisolone PO | Wt < 20 kg: 2 mg/kg daily<br>Wt > 20kg: 1.5mg/kg daily | From Day 3: Weaning regimen see Page 13 |
| **Induction agent** | **Basiliximab*** | < 35kg: 10mg IV<br>>35kg: 20mg IV | Second dose Day 4<br>Infusion 50mL 5% glucose or 0.9% |

| | | | |
|---|---|---|---|
| | | | sodium chloride over 30 mins<br><br>Give IV methylprednisolone (omit oral prednisone) and promethazine 0.5mg /kg (maximum dose 25mg) as pre-med. |
| **Anti-proliferatives** | Mycophenolate mofetil IV or PO | 400mg/m$^2$ PO BD (max dose 1000 mg)<br><br>Trough levels on Day 7 and 14.<br><br>To be collected and dose given immediately post<br><br>Trough target > 1.4 mg/L | Commence Day 0<br><br>Give at 0800 & 2000<br><br>Switch to oral when tolerating fluids<br><br>IV mycophenolate (teratogenic) is to be ordered from Pharmacy (Mon-Fri)<br><br>**Please give pharmacy 48 hours' notice for live donor transplants.**<br><br>May need to be reconstituted for deceased donor transplants using cytotoxic precautions<br><br>Use cytotoxic precautions |
| **Calcineurin inhibitors** | Tacrolimus PO | 0.15mg/kg PO BD<br><br>Titrate to daily trough levels– give dose immediately post level. Aim for tacrolimus levels of 8-12 nanog/mL for the first month. Target changes with maintenance dosages, see Page 14. | Commence Day 0 unless delayed graft function. Give at 0800 & 2000<br><br>Use cytotoxic precautions for suspension |

| | | | |
|---|---|---|---|
| **Anti-infectives** | Ganciclovir IV | Initial dose assume CrCl 10-25mL/min/1.73m$^2$ 0.625 mg/kg/day | Commence Day 0 then switched to PO valganciclovir when tolerating fluids<br><br>Not given if donor and recipient CMV & EBV negative<br><br>Dose to be recalculated and sterile pharmacy to be informed by 1000 next am<br><br>Cytotoxic medication |
| | Trimethoprim-sulfamethoxazole PO | ≥ 50kg: 160 mg (trimethoprim component) tablet Mon/Wed/Fri<br><br>< 50 kg: 5mg/kg (trimethoprim component) Mon/Wed/Fri (Maximum 160 mg) | For PJP prophylaxis |
| | Nystatin PO | 1 mL QID | Fungal prophylaxis |
| **Other medications** | Pantoprazole | 1 mg /kg daily | |
| | Heparin | | As determined by the transplant surgeon and consultant nephrologist |

## General postoperative ward care

Patients should be nursed in a single room with protective precautions, unless contact precautions are required for the individual patient. Cytotoxic precautions should be used when giving cytotoxic medications, and handling body fluids.

### Observations and monitoring fluid status

- Patient should be weighed daily prior to breakfast.
- Fluid regimen and target daily fluid balance will be determined daily by nephrology team.
- Strict fluid balance should be kept and calculated as per medical team orders.
- On return to the ward, patients fluid balance is be assessed by evening and overnight medical cover for the first 48 hours.

- Routine observations. TPR, BP and Oxygen Saturations 4th hourly, or more frequently as required.

## Medications and investigations

- Daily bloods are performed for the first month post-transplant.
- Tacrolimus is given immediately post blood tests: levels are used to guide subsequent dosing as they are not available until late afternoon.
- Daily urinalysis to be attended.

## Wound and Drain Care

- Wound care to be attended as directed by transplant surgical team.
- Removal of drain to be determined by the transplant surgical team.

## Indwelling catheter

- IDC is to remain in situ as per transplant surgical team (typically 5-7days) and is not to be removed without discussion with the transplant surgical team or urology team if involved.
- If the IDC becomes blocked or is accidently removed, **following discussion with transplant surgical team** or urology team it is to be replaced immediately by nursing staff.
- Oxybutynin may be used to relieve bladder pain and spasms induced by IDC or polyuria.

## Ureteric Stents

- Double J stent routinely inserted at time of transplant and removed 3-4 weeks post-transplant. Liaise with Urology team to arrange date for removal before patient is discharged.
- If recurrent UTI or macroscopic haematuria, stent can be removed earlier on consultation with Urology and transplant surgical team.

## Dialysis and vascular access

- Non-tunnelled CVLs should receive standard care as per CVAD guideline: these are removed as soon as possible, typically post Day 4 basiliximab. They can be used for blood sampling.
- Non-tunnelled and tunned haemodialysis lines are sometimes required for plasmapharesis – these are NOT to be used for blood sampling unless directed by the Nephrology team.

## Mobilisation

- Referral to physiotherapy should be considered on return to the ward for chest physiotherapy.
- The patient should be encouraged to sit in a chair out of bed on day 2 and early ambulation should be encouraged.

## Feeds and Diet

- Transplant surgical team will determine upgrade in oral intake.

- Children who have previously required supplemental feeds pre transplant will often require feeds in the immediate post-transplant period. Often these can be transitioned to standard infant and paediatric formula.
- Early review by dietician is essential to encourage healthy habits and minimise post-transplant weight gain.

## Potential medical and surgical complications

***Table 4: Summary medical and surgical complications immediately post kidney transplant***

| | |
|---|---|
| **Graft thrombosis**<br><br>**EMERGENCY** | Highest risk first 48 hours post-transplant<br>Presents with sudden decrease in urine output<br>Flush IDC to see if it blocked using sterile technique<br>**Needs urgent return to theatre and USS to confirm diagnosis – notify nephrology and transplant surgical team IMMEDIATELY** |
| **Sepsis**<br><br>**INFORM NEPHROLOGY TEAM IF T > 38C** | Common sources include chest infection, CVL infection and urosepsis<br>Culture MSU, blood peripheral and CVL, PD and drains. Consider CXR<br>**Discuss with Nephrology and ID re antibiotics:** Typically IV piperacillin/tazobactam and consider antifungal cover |
| **Rejection** | Rejection is often subclinical with an elevated creatinine the primary presentation<br>Hyperacute rejection is uncommon today as tissue typing techniques have improved significantly. This presents with fever, tender graft and raised creatinine |
| **Wound infection** | Ensure any organisms grown from pre-op swabs are covered |
| **Bowel obstruction** | Higher risk with intra-abdominal transplants |
| **Lymphocoele** | Often conservatively managed, sometimes requires marsupialisation |
| **Ureteric anastomosis dehiscence** | Presents with abdominal distension and urinary ascites. Check ascites fluid creatinine<br>Acute management is for reinsertion of IDC and likely to require surgical correction |
| **Decrease in urine output** | Flush IDC to see if it blocked<br>Review fluid balance and discuss with Nephology Team regarding management |

## Common fluid and electrolyte problems encountered post operatively

- **Hyperglycaemia:** Due to the large volume of fluid replacement and use of corticosteroids at induction, transient hyperglycaemia is often seen immediately post transplant. It can be prevented by the use of glucose free fluids for urine replacement. However, a small number do develop new onset diabetes after transplantation (NODAT).
- **Acidosis:** Quite common as there may be a significant amount of lactic acid released into the circulation with reperfusion of the lower extremity. Acidosis typically self-resolves without intervention. Persistent acidosis with bicarbonate of less than 15 can be managed by switching to Plasmalyte or Hartmanns and or addition of bicarbonate to IV fluids.

  **Dosing PO:** sodium bicarbonate 1mmol/kg/**dose BD**

  **Dosing IV:** Add sodium bicarbonate 2mmol/kg/**DAY** to compatible fluids.
- **Phosphate:** large amounts of phosphorous may be excreted by the new kidney. Oral dosing is preferred.

  **Dosing PO:** Starting dose 1mmol/kg/**DAY**

  Phosphate Sandoz® effervescent tablets contain 16mmol phosphate per tablet

  **Dosing IV:** sodium or potassium dihydrogen phosphate

  0.15 to 0.3 mmol/kg/**dose** given over 4-6 hours

  Ideally to be given at slower rate of 0.06mmol/kg/hour

  Max rate is 0.2mmol/kg/hour with cardiac monitoring

  Do not exceed 10mmol/hr
- **Magnesium:** If magnesium is less than 0.5mmol/L and IV replacement is required give magnesium sulfate. Note that hypotension is a potential complication. Ongoing oral replacement with oral magnesium may be required.

  **Dosing PO:** 0.1 to 0.8 mmol/kg/**dose** daily to QID

  Available as Bio-Logical Magnesium Complex 50 mg/mL (2.06mmol/mL) oral solution (magnesium citrate/magnesium amino acid chelate/magnesium chloride)& Magmin/Mag-Sup® (magnesium aspartate) 1.55mmol per tablet

  **Dosing IV:** Magnesium sulfate 0.1 to 0.2 mmol/kg/**dose** over 60 mins (maximum dose 10 mmol)

  Max rate is 0.5 mmol/kg/hour

  Note: IV magnesium sulfate vial is supplied as magnesium sulfate heptahydrate 50% (2mmol in 1mL)

# Immunosuppression and Medications – ongoing dosing and side effects

Information from the following section is summarised from the Australian Medicines Handbook, and supplemented from other sources as referenced. Renal dosing of anti-infectives is as per Australian Therapeutic Guidelines: antibiotic.

## Corticosteroids

**Prednisolone:** oral liquid 5mg/mL, tablets 1mg, 5mg and 25mg
**Dosing:** daily at 0800 (with food)

| | Wt <20 kg | Wt >20 kg | Max. dose |
|---|---|---|---|
| Days 3-7 | 2 mg/kg | 1.5 mg/kg | 80 mg |
| Days 7-14 | 1.5 mg/kg | 1 mg/kg | 60 mg |
| Days 15-21 | 1 mg/kg | 0.75 mg/kg | 45 mg |
| Days 22-28 | 0.7 mg/kg | 0.5 mg/kg | 40 mg |
| Wk 5 | 0.6 mg/kg | 0.4 mg/kg | 35 mg |
| Wk 6 | 0.5 mg/kg | 0.3 mg/kg | 25 mg |
| Wk 7-8 | 0.4mg/kg | 0.25 mg/kg | 20 mg |
| Month 3 | 0.3 mg/kg | 0.2 mg/kg | 15 mg |
| Month 4 | 0.2 mg/kg | 0.15-0.2 mg/kg | 10 mg |

This regimen may be personalised for higher risk recipients.

Alternate day dosing is possible after 5 months.

## Calcineurin Inhibitors

Inhibits calcium-calmodulin-calcineurin complex, inhibition of calcium dependent pathway of T cell activation. Tacrolimus is the preferred agent due to lower rates of acute rejection, however ciclosporin (cyclosporin) is sometimes used as an alternative. Please see Appendix A for dosing and levels of ciclosporin.

***Tacrolimus (FK 506)***

**Tacrolimus:** 1 mg/mL suspension from SCH pharmacy only (locally compounded product). Only short acting preparation- Prograf® (**not** Advagraf®) to be used in the immediate post-transplant period.
Capsules 0.5mg, 1 mg and 5 mg.
**Dosing:** 0.15 mg/kg BD at 0800 and 2000

Doses adjusted to maintain the following levels post-transplant.

An extended release (XR) form of tacrolimus is available – this is not used immediately post-transplant.

## Target levels (12 hour trough):

| | |
|---|---|
| 1st month | 8-12 nanog/mL |
| 2-6 months | 6 -10 nanog/mL |
| 6-12 months | 5-8 nanog/mL |
| >12 months | 5-7 nanog/mL |

Lower levels are to be targeted if there is delayed graft function: generally 5-8 nanog/mL until function has improved.

Tacrolimus target levels are also often personalised depending on the immunological characteristics of the transplant. Levels <5 can be associated with greater development of anti-HLA antibodies. Consider non-adherence if high tacrolimus level variability.

Levels are done at daily Monday-Friday and Sunday at SEALS. Levels may be performed on Saturday if negotiated with Head of Division of Medical Services and the laboratory informed.

Tacrolimus can be given as an IV infusion: starting dose is 0.03 mg/kg/DAY or one third of the current ORAL dose. Adjust dose to levels of 10-15 nanograms/mL as referenced POW East Coast Transplant protocol. Dose range 0.01 to 0.06 mg/kg/DAY.

**Side Effects**

Hypomagnasemia, hypophosphataemia, hyperkalaemia

Hypercholesterolaemia, deranged LFTs

Nephrotoxicity - acute reversible and chronic irreversible

Neurotoxicity – tremor, headaches, higher risk of PRES

New Onset Diabetes after Transplantation (NODAT)

Thrombotic microangiopathy

High levels are also seen commonly with diarrhoea

## Drug interactions

- Both tacrolimus and ciclosporin (cyclosporin) are substrates of CYP3A4/5 and thus there are many clinically significant drug interactions.
- Drug interactions can be checked using MIMs or the drug interactions tool in Micromedex through CIAP.
- Common interactions include: anticonvulsants (inducers), antifungal agents – azoles (inhibitors) and macrolide antibiotics (inhibitors).

## Antiproliferatives

Most patients will start on mycophenolate mofetil as part of routine triple immunosuppression due to lower rates of acute rejection. Azathioprine is sometimes used as an alternative, particularly if there is GI intolerance. Please see Appendix A regarding dosing of azathioprine

### *Mycophenolate mofetil*

Mycophenolate mofetil: suspension 50mg/ml & 250mg capsules and 500mg tablets

**Dosing:** with tacrolimus: 400mg/m$^2$ (max 1000 mg) BD

With ciclosporin (cyclosporin) or sirolimus 600 mg/m$^2$ (max 1000 mg) BD

There is considerable inter-individual variability in mycophenolate pharmacokinetics. There is some evidence to suggest that mycophenolate AUC > 30mg x h/L are associated with lower rates of acute rejection, which correspond to trough levels of 1.4mg/L. [3]

**Side Effects:** GI – diarrhoea, vomiting

Haematological - pancytopaenia

There is an alternative form of mycophenolate available: mycophenolate sodium (mycophenolic acid) (Myfortic). Dosing is **not equivalent**

| |
|---|
| In adults 250mg mycophenolate mofetil (Cellcept®) is equivalent to 180 mg mycophenolate sodium (Myfortic®). |

Mycophenolate sodium (Myfortic®) is enteric coated and may be of benefit if GI side effects are severe. It does not come in a liquid formulation. The same therapeutic drug monitoring levels as mycophenolate mofetil apply.

## Anti-infectives

### *CMV prophylaxis*

CMV is one of the most common infections seen post transplantation. Patients most at risk are CMV negative, receiving a kidney from a CMV positive donor. In addition, those patients who are CMV positive are at risk of CMV reactivation disease once immunosuppression is commenced. Prophylaxis is given for five months post-transplant. Prophylaxis is also given following treatment of rejection with thymoglobulin or plasmaphoresis for five months.

This calculator is based on the modified Schwartz formula:

$$\text{Child: eGFR (mL/min/1.73m}^2\text{)} = \frac{36.5 \times \text{height (cm)}}{\text{serum creatinine (micromol/L)}}$$

### *Intravenous ganciclovir prophylaxis[4]*

Ganciclovir is given post-operatively on Day 0. It needs to be pre-ordered from the sterile pharmacy as it is a cytotoxic medication. For the first dose on Day 0 assume CrCl 10-25 ml/min/1.73m2.

| | | |
|---|---|---|
| **Dosing:** | CrCl > 70mL/min/1.73m$^2$ | 5 mg/kg/day |
| | CrCl 50 – 69 mL/min/1.73m$^2$ | 2.5 mg/kg/day |
| | CrCl 25 - 49 mL/min/1.73m$^2$ | 1.25 mg/kg/day |
| | CrCl 10 - 25 mL/min/1.73m$^2$ | 0.625 mg/kg/day |
| | CrCl < 10 mL/min/1.73m$^2$ | 0.625 mg/kg three times per week |

***Oral valganciclovir***

Valganciclovir: Liquid 50mg/mL and 450mg tablets

**Dosing:** mg (once daily) = body weight [kg] x (0.07 x GFR [mL/min] + k);

Where k = 5 for GFR ≤ 30 mL/min,

k = 10 for GFR > 30 mL/min and weight > 30 kg, and

k = 15 for GFR > 30 mL/min and weight ≤ 30 kg.

Note: CrCl as above (modified Schwartz) is equal to GFR in above formula.

**Monitoring:**

- Trough level 7 days after commencing valganciclovir. (Serum 1.5 mL, paediatric tube OK)
- Levels attended Monday to Friday (Queensland Pathology 07 3646 0028).
- Routine monitoring of full blood count.
- Dosage to be adjusted according to level and WCC.

**Side Effects:** Haematological – marrow suppression common. May need to reduce dose.

***Pneumocystis Jiroveci (carinii) Pneumonia (PJP)***

Pneumocystis can be a fatal respiratory illness in immunosuppressed patients.

Pneumocystis infection can be prevented by trimethoprim/sulfamethoxazole and is continued whilst on immunosuppression. It has been shown that a higher dose three times a week is as effective as a smaller daily dose.

Trimethoprim/Sulfamethoxazole (Septrin®, Resprim®)

- Note: Doses and products refer to trimethoprim component
- Available as 8mg/mL trimethoprim suspension and 160mg trimethoprim tablets

| | | |
|---|---|---|
| **Dosing:** | ≥50 kg | 160 mg (of the trimethoprim component) (1 double strength tablet) Mon/Wed/Fri |
| | <50 kg | 5mg/kg (of the trimethoprim component) Mon/Wed/Fri (Max 160 mg) |

**Side Effects:** If the patient is unable to take trimethoprim/sulfamethoxazole because of allergy or G6PD deficiency, then intravenous pentamidine or dapsone are alternatives.

## Antibiotic prophylaxis for Urinary Tract Infections

If there is a history of urinary tract infections or ureteric stent is in situ trimethoprim/sulfamethoxazole 2 mg/kg can be given Tues/Thurs/Sat/Sun.

# Follow up post discharge

On discharge from hospital patients will be seen daily in clinic for four weeks post transplant. Summary of frequency of visits, immunosuppression dosing, viral PCR surveillance and other investigations are presented in Appendix B.

## Investigation of graft dysfunction post-transplant

Acute rejection is most worrying cause of an acute creatinine rise post transplant. However, the following should also be considered and or excluded:

- Dehydration, especially with inter current illness
- UTI
- Obstruction
- BK nephropathy
- Recurrent disease
- Vascular insufficiency such as renal artery stenosis

## School attendance

Children may attend school one month after receiving their renal transplant.

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# Appendix A

## Other Immunosuppresants

***Ciclosporin (cyclosporin)***

Liquid 100mg/mL or capsule 10mg, 25mg, 50mg and 100mg

**Dosing** 14mg /kg/day in two divided doses

**Target levels for 2 hour peak:**

| | |
|---|---|
| 1st 4 weeks | 1200-1400 microg/L |
| months 1-3 | 900-1200 microg/L |
| months 4-6 | 750-900 microg/L |
| months 7-12 | 600-750 microg/L |
| > 12 months | 450-600 microg/L |

Ciclosporin (cyclosporin) is also subject to the same drug interactions as tacrolimus

**Side effects** **As per tacrolimus**

*Hirstutism and gingival hyperplasia more common*

***Azathioprine***

- Treat as cytotoxic agent. Azathioprine converts to active 6-mercaptopurine which is cytotoxic.
- 25mg and 50mg tablets
- Also available as IV formulation

**Dosing:** 1-2mg/kg/DAY

**Side Effects:**

- Myelosuppression: check thyopurine methyltransferase (TPMT) activity. 1 in 300 will have low/non detectable TPMT activity and are risk of severe myelosuppression. Avoid or reduce dose to 10%.
- GI – diarrhoea/nausea/mouth ulceration and oesophagitis, less common than with mycophenolate
- Hepatitis: Hepatic sinusoidal obstruction syndrome, hypersensitivity syndrome

**Precautions:** allopurinol and febuxostat reduce azathioprine metabolism, increasing risk of marrow toxicity

***Sirolimus***

mTOR inhibitors bind to the same intracellular protein as tacrolimus but the protein drug complex blocks mTOR kinase, inhibiting cytokine induced T and B cell proliferation.

Liquid 1mg/mL or tablets 0.5mg, 1mg and 2mg

**Indication:** Documented evidence of toxicity on renal biopsy

Not used immediately post-transplant due to increased risk of graft thrombosis, poor wound healing and increased rates of acute rejection.

**Side Effects:** Impaired wound healing and lymphocoele

High lipids and diabetes

Mouth ulcers, interstitial lung disease, pericardial and pleural effusion

**Dosing:** > 40 kg loading dose 6 mg Day 1 then maintenance 2mg daily

< 40 kg loading dose 3mg/$m^2$ Day 1 then maintenance 1mg/$m^2$/day

**Monitoring:** Without CNI < 6 months 10-14 microg/L

6-10 months 8-10 microg/L

>12 months 4-8 microg/L

### *Antithymocyte globulins (ATG)*

Polyclonal purified horse or rabbit antibodies against human lymphocytes that deplete T lymphocytes in the circulation. They are used as an alternative to IL-2 monoclonal antibodies as induction therapy and also to treat moderate to severe rejection. The following information is from product information on MIMs.

Currently we use thymoglobulin which is rabbit derived. The horse derived thyloglobulin has different dosing.

**Thymoglobulin:** Rabbit polyclonal ATG

25mg vials

**Dosing**

- Induction therapy for kidney transplantation:
  - 1-1.5 mg/kg/day as prophylaxis for 5 - 7 days (maximum individual dose 150mg, maximum cumulative dose 13.5 mg/kg).
  - In obese patients dose according to ideal body weight.
  - Some sources suggest targeting lymphocyte count 0.1 to 0.2.
- Induction therapy in setting of delayed graft function (DGF) to minimise calcineurin inhibitors (CNI):
  - 1-2mg/kg/day typically for 2-3 days.
- Rejection
  - 1.5mg/kg/day for 5-7 days (maximum individual dose 150mg, maximum cumulative dose 21mg/kg).
- Dose Adjustments:

  Lymphocytes < 0.05 Withhold dose

| | |
|---|---|
| Total WCC 2.0 - 3.0 | Reduce dose by 50% |
| Total WCC < 2.0 | Withhold dose and consider discontinuation of therapy |
| Platelets 50 – 75: | Reduce dose by 50% |

Platelets < 50 Withhold dose and consider discontinuation of therapy.

Prophylactic valganciclovir, trimethoprim/sulfamethoxazole (**Septrin®/Resprim®**) and nystatin should be recommenced following administration of a course of ATG for six months.

## Premedications

- Paracetamol 20mg/kg Oral (maximum dose 1000mg).
- Promethazine 0.5mg /kg Oral (maximum dose 25mg).
- Hydrocortisone 2mg/kg IV (maximum dose 100mg).

***Administration***

There is a high incidence of drug reactions. Reactions include both anaphylaxis and cytokine release syndrome. Resuscitation equipment should be readily available.

ATG is diluted in 0.9% sodium chloride and is administered with a 0.22 micron in line filter. First dose is given over 6 hours then subsequent doses are given over 4 hours.

It is not compatible with glucose containing solutions.

# Appendix B

POST TRANSPLANT FOLLOW – UP.
Site of kidney:
Donor kidney source:
Number HLA mismatches:
Pre-transplant DSA (Date):
Post-transplant DSA (Date):
Date of Transplant:
Transplant number:

**JJ stent removal**
Date booked:
Stent removed:

Name:
MRN:
Date of Birth:

Cause of ESRD:

**Guide to Immunosuppression and Valgancyclovir doses and required levels from day of transplant.**

| **Daily Prednisolone dose** | | | | | ***1 Tacrolimus Levels*** | ***2 Sirolimus levels LCMS – Seals**** | ***3 Mycophenolate doses*** | ***4 Duration of Valgancyclovir prophylaxis*** |
|---|---|---|---|---|---|---|---|---|
| Day 3 to 7 | | 2 mg/kg | 1.5 mg/kg | 80 mg | **0 - 2 months:** 8-12 nanog/mL<br>**>2-6 months:** 6-10nanog/mL<br>**> 6-12 months:** 5-8nanog/mL<br>**> 12 months:** 5-7 nanog/mL | **Without CNI**<br>**< 6 months** 10-14 microg/L<br>**6-12 months:** 8-10 microg/L<br>**> 12 months:** | **1. With tacrolimus:** 400 mg/m2/dose bd to 600mg/m$^2$<br>**2. With cyclosporin or sirolimus:** 600 mg/m$^2$/dose bd<br>MPA trough target: 1.4 mg/L minimum | **CMV +ve to CMV -ve:** 5 months<br>**CMV +ve/-ve to CMV +ve:** 5 mths<br>**EBV +ve to EBV –ve:** 12 months<br>**Dose in mg once daily** = body weight [kg] x (0.07 x GFR [mL/min] + k); where k = 5 for GFR ≤ 30 mL/min, k = 10 for GFR > 30 mL/min and weight > 30 kg and k = 15 for GFR > 30 mL/min and weight ≤ 30 kg.<br>**Cr Cl = 36.5 x ht(cm)/serum creat**<br>**Consider further course following treatment for acute rejection.** |
| Day 8 | | 1.5 | 1 mg/kg | 60 mg | | | | |
| Day 15 | | 1 mg/kg | 0.75 mg/kg | 45 mg | | | | |
| Day 22 to | | 0.7 | 0.5 mg/kg | 40 mg | | | | |
| Wk 5 | | 0.6 | 0.4 mg/kg | 35 mg | | | | |
| Wk 6 | | 0.5 | 0.3 mg/kg | 25 mg | | | | |
| Wk 7 & 8 | | 0.4 | 0.25 mg/kg | 20 mg | | | | |
| Month 3 | | 0.3 | 0.2 mg/kg | 15 mg | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Month 4<br><br>onwards | | 0.2<br><br>mg/kg | 0.15-0.2<br><br>mg/kg | 10 mg | | 4-8<br>microg/L | | |

The prednisolone taper will generally be slower for retransplants, transplants with a high PRA or any other high risk situation. If graft function is stable and there is still growth potential (and not multiple previous rejection episodes) then alternate day prednisone should be considered after 5 months.

**Follow-up clinic visits and routine blood tests required from date of transplant – see following page for viral tests:**

| | | |
|---|---|---|
| Week 1 to 4 | Clinic daily | Daily EUC, CMP, second daily immunosuppressant drug level, twice weekly FBC, weekly LFT<br>**EBV PCR Day 7 post-transplant and MPA trough levels on Day 7 and 14** |
| Week 5 & 6 | Clinic every 2nd day | Second daily EUC, CMP, immunosuppressant drug level, twice weekly FBC, weekly LFT |
| Week 7 & 8 | Clinic twice a week | Twice weekly EUC, CMP, immunosuppressant drug level, weekly FBC, LFT and PTH once only |
| Week 9 & 10 | clinic weekly | Weekly EUC, CMP immunosuppressant drug level, FBC. monthly LFT |
| Week 11 to 16 | clinic every 2 weeks | Second weekly EUC, CMP, immunosuppressant drug level**,** FBC, monthly LFT, |
| 4 to12 months | clinic every 4 weeks | Monthly EUC, CMP, immunosuppressant drug level, FBC, LFT. |
| >12 months | Clinic 4-6 weekly | Monthly EUC, CMP, immunosuppressant drug level, FBC, LFT. |