North of Tyne
Area Prescribing Committee

Immunosuppression for children with Nephrotic Syndrome

March 2014
(Review date May 2016)

This guidance has been prepared and approved for use in Newcastle, North Tyneside and Northumberland. It gives details of the responsibilities of GPs and specialist services in shared care arrangements and is intended to provide sufficient information to enable GPs to prescribe this treatment within the shared care arrangement. Further information on this shared care guideline can be obtained from:

<table>
<thead>
<tr>
<th>PCO Pharmaceutical Advisers</th>
<th>Newcastle North Tyneside Northumberland Care Trust North East Commissioning Support (NECS)</th>
<th>T 0191 217 2858 or 0191 217 2533</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matthew Lowery, Formulary and Audit Pharmacist</td>
<td>Newcastle Upon Tyne Hospitals NHS Foundation Trust</td>
<td>T 0191 2231386 F 0191 2231385 <a href="mailto:Matthew.Lowery@nuth.nhs.uk">Matthew.Lowery@nuth.nhs.uk</a></td>
</tr>
</tbody>
</table>

An electronic version of this document can also be viewed / downloaded from the North of Tyne Area Prescribing Committee’s Website http://www.northoftyneapc.nhs.uk

Approved on behalf of the

<table>
<thead>
<tr>
<th>Name</th>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr M Wright</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. Campbell</td>
<td></td>
<td>11/3/14</td>
</tr>
</tbody>
</table>

North of Tyne Medicines Guidelines and Use Group
North of Tyne Area Prescribing Committee
Newcastle North and East CCG, Newcastle West CCG, Gateshead CCG, North Tyneside CCG, Northumberland CCG
Contents

Introduction 3
Immunosuppression protocol 5
Prophylactic treatment 7
Shared care guidelines 8
  Ciclosporin 8
  Tacrolimus 10
  Mycophenolate Mofetil 12
  Prednisolone 14
Contacts 16
A. Introduction to paediatric nephrotic syndrome

Nephrotic syndrome in children is often a chronic, remitting disease with a large disease burden. Depending on age of presentation and histology type around 20% will fail to respond to steroids alone. Of steroid sensitive children, up to 80% will relapse, with 35-50% relapsing frequently or become steroid dependent. Second, third or fourth line steroid sparing agents are often required to avoid the adverse effects of steroids. This condition often results in frequent hospital admissions to manage relapses and intensive immunosuppression therapy to maintain remission. The amount of immunosuppression required is often in excess of that required for transplantation.

Patients who fail to respond to steroids have a worse prognosis with a high incidence of progressing to chronic renal failure or requiring nephrectomy to reduce the harm of nephrosis.

The Paediatric Nephrology Department at the Great North Children’s Hospital in Newcastle provides a tertiary nephrotic syndrome service to children and adolescents in the Northern region. It is one of 13 UK tertiary paediatric nephrology centres. At any time, we manage >100 patients requiring treatment in excess of steroids treatment alone.

The service provides dedicated nephrotic nurses for management and coordination of care, access to 24 hour telephone contact and open access for relapses and any medical issues to our unit. We also coordinate open access and admission to local general paediatric units in the event of patients being unwell. A consultant paediatric nephrologist and renal nurse are always on service to support this specialist service.

Nephrotic patient clinic

Patients can be referred directly by primary or secondary care. Our service provides:

- Diagnostic service including appropriate histology and genetic analysis
- Holistic education of families to aid self management
- Management of relapses and complications of nephrotic syndrome
  - Thrombosis risk
  - Intravascular volume depletion
  - Long term cardiovascular risk
- Monitoring and modification of immunosuppressive therapy to reduce relapses
- Prevention and management of complications of treatment:
  - Infection
  - Growth and obesity
  - Steroid side effects
  - Nephrotoxicity
- Shared care with other specialists for those with co-morbidities
- Compliance with medication and follow up care
- Psychosocial issues are well supported with our dedicated team of specialist nurses, renal psychologists, play therapists and social worker
- Dietetic support
- Access to partake in local and national research studies

There are regular specialised nurse led clinics held in Newcastle, Middlesbrough, North Tees, Carlisle and Bishop Auckland. Education about this chronic condition is critical to avoid complications. This may include visits to home, school, nursery and to other care givers (eg grandparents).

Patients undergoing relapses can often be managed with rapid access day unit reviews and frequent telephone support. This reduces the burden of prolonged in-patient stays.
What happens at follow up appointments?

The majority of our patients will have steroid sensitive nephrotic syndrome. In the long term, the majority of these patients will grow out of their condition and stop or have fewer relapses. However, the patient journey is often long. Most children present before the age of 5 and will not out grow their condition until well into adolescence. The long term goal of treatment is to reduce the frequency of relapses with immunosuppression while minimising drug side effects. Some will require multidiscipline support for transition to adult services.

Steroids are the mainstay of treatment during relapses, to minimise steroid side effects, a variety of steroid sparing agents are available. Each has their unique spectrum of possible adverse and late effects.

At follow up clinics patients can expect:

- Measurement of growth and blood pressure
- To see a specialist paediatric nephrotic nurse +/- paediatric nephrologist
- Review of medications
- Monitoring for late effects (e.g. steroid induced cataracts or obesity)
- Measurement of appropriate blood parameters as necessary, e.g. serum creatinine, electrolytes, LFT, FBC, and trough levels of ciclosporin or tacrolimus
- To access psychosocial support that can impact on treatment compliance or quality of life
- To access specialist renal dietetic support to improve compliance with dietary restrictions associated with relapse and to provide advice to minimise weight complications associated with steroid treatment

To minimise time off school or travel, the nephrotic nurses may arrange for blood tests to be performed locally either at the local hospital or at the GP practice. The paediatric renal team will retrieve and review these results in a timely manner.

Following the clinic visit or blood tests:

- Blood results will be reviewed by the team
- Any abnormal results requiring action, or treatment changes, will be communicated to the patient by telephone, letter, or at a new appointment
- Following significant issues or significant changes to medication, a letter will be sent to the patient's GP, local paediatrician and parents

Shared care of nephrotic patients

All patients are followed in the nephrotic service until off medication and relapse free (for a period of time – average three years) or until transition to adult nephrology around age 16-18. The nephrotic service will monitor and adjust immunosuppressive treatment. We will initiate prophylaxis against opportunistic infection, and any treatments for the prevention of late effects such as cardiovascular diseases. Our current guidelines are listed below, and specific responsibilities enumerated in the guideline for each immunosuppressive drug.

Patients will continue to receive primary care from their own GP. Specific Primary Care responsibilities are listed in the guideline for each immunosuppressive drug.

Please note that:

- The paediatric renal team can be contacted at any time for advice (see ‘Contacts’ page 21)
- There are many important drug interactions with immunosuppressive medications, listed in the guideline for each drug
- Abrupt withdrawal or changes to immunosuppressive treatment may lead to nephrotic relapse
B. Treatment Protocol

Treatment of initial presentation

Steroids are the mainstay of treatment for the initial presentation and any subsequent relapses. Current evidence suggests longer initial course of steroids are superior to shorter duration course to reduce incidence of subsequent relapses.

Prednisolone 60mg/m$^2$ daily for 6 weeks (max 80mg) then
Prednisolone 40mg/m$^2$ alternate days (max 60mg) for a further 6 weeks

Then stop with active monitoring for relapse.

The following are also required at presentation and during each relapse:

1. PHENOXYMETHYL-PENICILLIN

This should be given as prophylaxis against pneumococcal infection.

Give:
- 1 - 5 years of age: 125mg bd
- > 5 years: 250mg bd

Stop when urine protein free for 3 days

2. RANITIDINE

Ranitidine should be given for the full 12 weeks of steroid treatment in order to reduce gastric symptoms. It is not always necessary during treatment for a relapse.

Give 2mg/kg per dose bd (maximum dose = 150mg bd). It is available in both tablet (150mg) and syrup form (75mg/ 5ml). Round to nearest ml or tablet.

3. LOW SALT DIET

This is employed to help prevent excess thirst and fluid retention. Stop when the urine is protein free for 3 consecutive days. (Fluid restriction is only considered if a child continues to gain weight despite a low salt diet and is clinically euvoalaemic, children will be admitted to hospital if this is required). Our renal dietician will offer support.

Treatment of relapses

Duration of steroid treatment is different from treatment of an initial presentation.

Prednisolone 60mg/m$^2$ daily (max 80mg) until proteinuria free for 3 days then
Prednisolone 40mg/m$^2$ alternate days (max 60mg) for a further 4 weeks

then stop, or revert to previous maintenance steroid dose as directed by nephrotic team. Occasionally a longer duration of steroid treatment is given for a relapse depending on clinical need.
Individualised protocol for every patient

For patients who frequently relapse or become steroid dependent, individualised immunosuppression plans are drawn up based on their clinical status, compliance with treatment, infection history, histology findings (if appropriate) and on the best available evidence.

<table>
<thead>
<tr>
<th>First line</th>
<th>Maintenance alternate day prednisolone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid sparing agents</td>
<td>Levamisole</td>
</tr>
<tr>
<td></td>
<td>Intravenous cyclophosphamide (given in hospital for 6 months)</td>
</tr>
<tr>
<td></td>
<td>Tacrolimus or ciclosporin</td>
</tr>
<tr>
<td></td>
<td>Mycophenolate Mofetil (MMF)</td>
</tr>
</tbody>
</table>

Maintenance alternate day prednisolone

The dose required for this maintenance regimen varies enormously. The aim is to keep the child on the lowest dose of maintenance steroids that keeps them relapse free. Alternative day prescribing reduces adverse steroid events.

Doses up to 0.5mg/kg alternate day can be used however, if the maintenance dose needed exceeds 0.5mg/kg on alternate days, steroid side effects are likely. We would usually introduce a 2nd line steroid sparing agent.

Drug dosing and monitoring

Initial doses and recommended monitoring for each drug are shown in the shared care guideline. The required dose of tacrolimus or ciclosporin varies substantially from patient to patient, and is determined by measurement of whole blood drug levels performed immediately before a dose (that is, a ‘trough’ level. Target drug levels are aimed to balance adequate immunosuppression with minimising side effects (particularly nephrotoxicity).

The target levels for tacrolimus is 5-7ng/l and for ciclosporin is 100 - 150 µg/L but maybe individualised, depending on clinical needs. Doses are adjusted in the nephrotic clinic.

Patients on tacrolimus or ciclosporin will have regular creatinine checked and the need for renal biopsy to monitor for nephrotoxicity, is reviewed every 5 years.

There are many important drug interactions with all immunosuppressants. The most important are listed in the shared care guideline for each drug, great care is needed when prescribing for these patients. Other information is available in the BNF or BNFC.

Please contact us before prescribing new medication as we may need to arrange for additional monitoring of blood levels.
C. Prophylactic Treatment

1. Anti-microbial prophylaxis

Patients on multiple immunosuppression are at increased risk of infection. Please contact us straight away if there is chickenpox contact or infection as treatment may be required.

Most of the excess risk is related to opportunistic infection with fungi (Candida spp, Pneumocystis jirovecii), viruses (CMV, VZV and other herpes viruses) and occasionally TB.

Immunosuppressive treatment does not seem to dramatically increase the risk of common bacterial infections, although when patients develop such infections they are more severe.

Pneumocystis jirovecii. Patients on the following medication receive **co-trimoxazole** 12mg/kg once daily max 960mg. Please round to nearest tablet (480mg or 960mg) or ml (240mg/5ml or 480mg/5ml).

- IV cyclophosphamide - during 6 month course and for further 2 months
- Mycophenolate mofetil and tacrolimus
- Mycophenolate mofetil and ciclosporin

Once stable and off prednisolone, selected patients reduce co-trimoxazole prophylaxis to three times per week.

2. Immunisation.

Patients on immunosuppressive treatment should NOT receive any live vaccines.

Examples of live vaccines include oral polio vaccine (OPV), BCG, Yellow Fever and the MMR vaccine.

All nephrotic recipients should receive the annual **Influenza vaccine**.

**Pneumococcal vaccine** should be given.

- **Under 5yrs** If not involved in infant immunisation program, one dose of 13-valent conjugate vaccine followed by second dose of 23-valent polysaccharide pneumococcal vaccine after 2nd birthday but not within 2 months of first dose.
- **5yrs and over** If not involved in infant immunisation program, one dose of 23-valent polysaccharide pneumococcal vaccine if not previously received
Ciclosporin shared care guideline

Introduction

Ciclosporin and the newer drug tacrolimus are inhibitors of the enzyme calcineurin. Calcineurin inhibition suppresses T lymphocyte activation (thought to be a key component in the pathogenesis of nephrotic syndrome), but also the T cell response to infection. Inhibition of T cell activity particularly predisposes to TB, viral infection (especially the herpes viruses such as VZV, EBV and CMV), and fungal infections (*Pneumocystis jirovecii* is the most important in the UK). Generic preparations of ciclosporin are available. There is significant variation in bioavailability between brands. Always prescribe using the brand name.

The renal team use the brand Neoral®.

Responsibilities of Nephrology Team

- Assessment of the patient as suitable for this treatment
- Provision of information regarding immunosuppression, especially the risks and side effects, before commencing medication
- Indefinite follow-up of the patient and monitoring of immunosuppressive treatment while on treatment for nephrotic syndrome
- Consideration of prophylaxis against opportunistic infection
- Provide 24 hour telephone advice and access to paediatric care for any medical concerns or infections
- Request participation in a shared care arrangement from the patient’s GP when the patient’s treatment has been stabilised and a shared care arrangement is clinically appropriate
- Communication regarding management plan with GP
- Inform the GP if the patient fails to attend monitoring appointments

Responsibilities of GP

- To contact the paediatric renal team to confirm that he/she is happy to accept the shared care arrangement within 28 days of receiving the request
- Communication with the paediatric renal team should the patient relapse or develop intercurrent illness
- Prescription of ciclosporin medication by brand
- Avoid all live vaccines

Responsibilities of Patient and family

- Compliance with urine checking for relapse, prescribed medications, dietary advice and regular clinic attendance
- To contact the paediatric renal team should they relapse, become unwell or be in contact with infectious diseases such as chickenpox
### Ciclosporin

<table>
<thead>
<tr>
<th>Indication</th>
<th>Immunosuppressive therapy to prevent relapse of nephrotic syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulations and strengths available</td>
<td>Neoral® Microemulsion soft gel capsules 10, 25, 50 and 100mg or as a liquid at 100mg/ml</td>
</tr>
<tr>
<td>Cost (for 28 days treatment – March 2010)</td>
<td>50mg bd £67.96 150mg bd £196.96 300mg bd £387.01 100mg bd £129.00 200mg bd £258.01 Liquid 100mg/ml £103.55</td>
</tr>
<tr>
<td>Dose</td>
<td>Maintenance dose determined by trough (pre-dose) measurement of whole blood ciclosporin level. Target level usually 100-150 µg/L but can be modified depending on clinical needs</td>
</tr>
<tr>
<td>Usual Dose Range</td>
<td>50mg bd up to 300mg bd</td>
</tr>
<tr>
<td>Likely duration of treatment</td>
<td>As long as treatment is considered appropriate by specialist</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Known hypersensitivity to ciclosporin</td>
</tr>
<tr>
<td>Warnings</td>
<td>Breast feeding is contraindicated. May be used during planned pregnancy under specialist advice. <strong>Avoid all live vaccines</strong></td>
</tr>
<tr>
<td>Side Effects (Full list in BNF)</td>
<td>Nephrotoxicity, hyperkalaemia Metabolic: hypertension, hyperlipidaemia and hyperuricaemia Cosmetic: hirsuitism, gingival hypertrophy Neurological: tremor, dysesthesia, rarely peripheral neuropathy Increased susceptibility to infection Increased risk of malignancy</td>
</tr>
<tr>
<td>Common drug interactions (Full list in BNF)</td>
<td><strong>Ciclosporin metabolism is inhibited (and toxicity enhanced) by:</strong> Macrolide antibiotics (e.g. erythromycin, clarithromycin &amp; azithromycin) Azole antifungal drugs (e.g. fluconazole, itraconazole, clotrimazole) Calcium antagonists (e.g. diltiazem, verapamil &amp; lercanidipine – less so other dihydropyridine drugs) Grapefruit juice <strong>Ciclosporin metabolism is induced (and efficacy reduced) by:</strong> Anticonvulsants (carbamazepine, phenytoin &amp; phenobarbitone) Some antibiotics (rifampicin &amp; rifabutin) <strong>Nephrotoxicity enhanced by all NSAIDs</strong></td>
</tr>
<tr>
<td>Monitoring</td>
<td>FBC, U&amp;E, LFT, ciclosporin trough levels monitored every 3 months and glycosuria and BP in nephrotic clinic. Need for renal biopsy reviewed every 5 years or earlier if clinically indicated</td>
</tr>
</tbody>
</table>
Tacrolimus shared care guideline

Introduction

Tacrolimus (Prograf®), like ciclosporin, is a calcineurin inhibitor. It probably has similar efficacy to ciclosporin for preventing relapses. Tacrolimus lacks the cosmetic side effects of ciclosporin, and may cause less hypertension and hyperlipidaemia. Both drugs can be nephrotoxic so surveillance monitoring by biopsy is required. Generic preparations of tacrolimus are available. There is significant variation in bioavailability between brands. Always prescribe using the brand name. This also avoids confusion between twice daily (Prograf®) and once daily preparations.

Liquid preparations: Dose changes are frequent after starting and during acute diarrhoeal episodes. Changes of doses are usually communicated to the parents by phone after drug levels are available from the laboratory. To avoid harm, it is essential that the concentration and formulation of liquid preparations never change. Patients will be on 1mg/ml preparations to minimise errors. This must also be prepared by a specials manufacturer using an identical formulation to that supplied by the hospital. This formulation must be made with tacrolimus powder suspended in 50:50 Oraplus and Orasweet SF. The hospital purchases this product from Newcastle Specials. (Contact information at end of document)

Responsibilities of Nephrology Team

- Assessment of the patient as suitable for this treatment
- Provision of information regarding immunosuppression, especially the risks and side effects, before commencing medication
- Indefinite follow-up of the patient and monitoring of immunosuppressive treatment while on treatment for nephrotic syndrome
- Consideration of prophylaxis against opportunistic infection
- Provide 24 hour telephone advice and access to paediatric care for any medical concerns or infections
- Request participation in a shared care arrangement from the patient’s GP when the patient’s treatment has been stabilised and a shared care arrangement is clinically appropriate
- Communication regarding management plan with GP
- Inform the GP if the patients fails to attend monitoring appointments

Responsibilities of GP

- To contact the paediatric renal team to confirm that he/she is happy to accept the shared care arrangement within 28 days of receiving the request
- Communication with the paediatric renal team should the patient relapse or develop intercurrent illness
- Prescription of tacrolimus medication by brand
- Avoid all live vaccines

Responsibilities of Patient and family

- Compliance with urine checking for relapse, prescribed medications, dietary advice and regular clinic attendance
- To contact the paediatric renal team should they relapse, become unwell or be in contact with infectious diseases such as chickenpox
Tacrolimus

<table>
<thead>
<tr>
<th>Indication</th>
<th>Immunosuppressive therapy to prevent relapse of nephrotic syndrome</th>
</tr>
</thead>
</table>
| Formulation and strengths available | Prograf® Capsules 0.5mg, 1mg & 5mg  
Advagraf® prolonged release capsules, 0.5mg, 1mg, 3mg, 5mg (only for use where specifically approved)  
Liquid 1mg/ml |
| Cost – Prograf® (for 28 days treatment – March 2010) | 0.5mg bd £39.30  
1mg bd £89.91  
5mg bd £332.16  
10mg bd £664.33  
Liquid 1mg/ml (60ml bottle) £50 (varies depending on which specials manufacturer is used) |
| Dose | Initiation in hospital. Maintenance dose determined by trough (pre-dose) measurement of whole blood tacrolimus level. Target level usually 5-7ng/L but may be modified depending on clinical needs |
| Usual Dose Range | 0.5mg bd up to 10mg bd |
| Likely duration of treatment | As long as treatment is considered appropriate by specialist |
| Contraindications | Known hypersensitivity to tacrolimus |
| Warnings | Breast feeding is contraindicated. May be used during planned pregnancy under specialist advice.  
Avoid all live vaccines |
| Side Effects (Full list in BNF) | Nephrotoxicity, hyperkalaemia  
Metabolic: hypertension, hyperlipidaemia, hyperuricaemia & diabetes  
Cosmetic: alopecia  
Neurological: tremor, dysaesthesia, rarely peripheral neuropathy  
Increased susceptibility to infection  
Increased risk of malignancy  
Rarely hypertrophic cardiomyopathy (only reported in children) |
| Common drug Interactions (Full list in BNF) | Tacrolimus metabolism is inhibited (and toxicity enhanced) by:  
Macrolide antibiotics (e.g. erthromycin, clarithromycin & azithromycin)  
Azole antifungal drugs (e.g. fluconazole, itraconazole, clotrimazole)  
Calcium antagonists (e.g. diltiazem, verapamil & lercanidipine – less so other dihydropyridine drugs)  
Grapefruit juice  
Tacrolimus metabolism is induced (and efficacy reduced) by:  
Anticonvulsants (carbamazepine, phenytoin & phenobarbitone)  
Some antibiotics (rifampicin & rifabutin)  
St Johns Wort  
Nephrotoxicity enhanced by all NSAIDs |
| Monitoring | FBC, U&E, LFT, tacrolimus trough levels monitored every 3 months and glycosuria and BP in nephrotic clinic. Need for renal biopsy reviewed every 5 years or earlier if clinically indicated |
Mycophenolate mofetil (MMF) shared care guideline

Introduction

MMF blocks both T and B lymphocyte proliferation by inhibiting purine nucleotide synthesis. Most cell types can synthesise purines using either a de novo or a scavenger pathway. In contrast, rapidly proliferating lymphocytes rely on the scavenger pathway. MMF inhibits the rate limiting enzyme of this pathway (inosine monophosphate dehydrogenase - IMPDH), and for this reason is a relatively specific immunosuppressive drug. Other bone marrow-derived cells can be susceptible to MMF, and anaemia, neutropaenia and thrombocytopaenia are possible side effects.

MMF is a pro-drug, and rapidly metabolised to the active compound mycophenolic acid (MPA) in the liver. MPA is excreted in bile, and undergoes entero-hepatic recirculation. As a result, the concentration of MPA in the intestinal lumen is high. This accounts for diarrhoea, which is the other important side effect of MMF. Generic preparations of MMF (Cellcept®) are available.

Responsibilities of Nephrology Team

- Assessment of the patient as suitable for this treatment
- Provision of information regarding immunosuppression, especially the risks and side effects, before commencing medication
- Indefinite follow-up of the patient and monitoring of immunosuppressive treatment while on treatment for nephrotic syndrome
- Consideration of prophylaxis against opportunistic infection
- Provide 24 hour telephone advice and access to paediatric care for any medical concerns or infections
- Request participation in a shared care arrangement from the patient’s GP when the patient’s treatment has been stabilised and a shared care arrangement is clinically appropriate
- Communication regarding management plan with GP
- Inform the GP if the patient fails to attend monitoring appointments

Responsibilities of GP

- To contact the paediatric renal team to confirm that he/she is happy to accept the shared care arrangement within 28 days of receiving the request
- Communication with the paediatric renal team should the patient relapse or develop intercurrent illness
- Prescription of mycophenolate mofetil medication
- Avoid all live vaccines

Responsibilities of Patient and family

- Compliance with urine checking for relapse, prescribed medications, dietary advice and regular clinic attendance
- To contact the paediatric renal team should they relapse, become unwell or be in contact with infectious diseases such as chickenpox
### Mycophenolate Mofetil (MMF)

<table>
<thead>
<tr>
<th>Indication</th>
<th>Immunosuppressive therapy to prevent relapse of nephrotic syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulation and strengths available</td>
<td>250mg capsules &amp; 500mg tablets or oral suspension (1000mg / 5ml)</td>
</tr>
</tbody>
</table>
| Cost (for 28 days treatment – March 2010)) | **Cellcept**
- 250mg bd £46.06
- 500mg bd £92.13
- 1g per 5ml powder for oral suspension (175ml) £115.16

**Arzip**
- 250mg bd £32.24
- 1g bd £128.96
- 1.5mg bd £193 |
| Dose                     | Initiation in hospital. Dose usually 600mg/m$^2$ bd but may be reduced depending on side effects. Occasionally total daily dose is divided to 4x/day to manage abdominal side effects |
| Usual Dose Range         | 500 to 2000mg daily in divided doses |
| Likely duration of treatment | As long as treatment is considered appropriate by specialist |
| Contraindications        | Known hypersensitivity to mycophenolic acid. Pregnancy and breast feeding |
| Warnings                 | Active gastro-intestinal disease. Side effects may be more common in children and the elderly **Avoid all live vaccines** If found to be pregnant, switch to alternative medication |
| Side Effects (Full list in BNF) | Myelosuppression  
- Gastro-intestinal toxicity, particularly diarrhoea  
- Increased susceptibility to infection  
- Increased risk of malignancy |
| Common drug Interactions (Full list in BNF) | Antacids and colestyramine reduce MMF absorption  
- Aciclovir & valganciclovir may increase risk of myelosuppression; plasma levels of aciclovir and valganciclovir increased by MMF |
| Monitoring               | FBC, weekly for three weeks after starting then 6monthly, and BP in nephrotic clinic. |
Prednisolone shared care guideline

Introduction

Corticosteroids are the mainstay of treatment for nephrotic syndrome. They act to inhibit the immune system at multiple levels. High doses are required to treat relapses.

The side effects of high dose long term corticosteroid use are well known (see below) and are the cause of potential morbidity in the long term. Our management strategy aims to reduce the frequency of relapses so minimising cumulative corticosteroid exposure. Side effects are monitored in the nephrotic clinics.

Responsibilities of Nephrology Team

- Assessment of the patient as suitable for this treatment
- Provision of information regarding immunosuppression, especially the risks and side effects, before commencing medication
- Indefinite follow-up of the patient and monitoring of immunosuppressive treatment while on treatment for nephrotic syndrome
- Consideration of prophylaxis against opportunistic infection
- Provide 24 hour telephone advice and access to paediatric care for any medical concerns or infections
- Request participation in a shared care arrangement from the patient’s GP when the patient’s treatment has been stabilised and a shared care arrangement is clinically appropriate
- Communication regarding management plan with GP
- Inform the GP if the patients fails to attend monitoring appointments

Responsibilities of GP

- To contact the paediatric renal team to confirm that he/she is happy to accept the shared care arrangement within 28 days of receiving the request
- Communication with the paediatric renal team should the patient relapse or develop intercurrent illness
- Prescription of medication
- Avoid all live vaccines

Responsibilities of Patient and family

- Compliance with urine checking for relapse, prescribed medications, dietary advice and regular clinic attendance
- To contact the paediatric renal team should they relapse, become unwell or be in contact with infectious diseases such as chickenpox
## Prednisolone

<table>
<thead>
<tr>
<th><strong>Indication</strong></th>
<th>Immunosuppressive therapy to treat and prevent relapse of nephrotic syndrome</th>
</tr>
</thead>
</table>
| **Formulations and strengths available** | 1mg, 5mg & 25mg tablets (plain or enteric coated)  
5mg soluble tablets |
| **Cost (for 28 days treatment – Oct 2006)** | 5mg daily £1.10  
10mg daily £2.20  
15mg daily £3.30  
20mg daily £4.40 |
| **Dose Range** | 2.5mg alternate day to 80mg daily depending on treatment regime and disease course (see pages 5-7) |
| **Likely duration of treatment** | As long as treatment is considered appropriate by specialist |
| **Contraindications** | Known hypersensitivity to prednisolone |
| **Warnings** | Prolonged treatment with corticosteroids leads to adrenal suppression.  
Abrupt withdrawal of prednisolone in patients on long-term treatment can lead to a hypo-adrenal crisis, and precipitate an episode of acute rejection.  
**Avoid all live vaccines** |
| **Side Effects** | Metabolic: hypertension, hyperlipidaemia, diabetes, weight gain  
Musculoskeletal: osteoporosis and avascular necrosis  
Increased risk of peptic ulceration  
Skin thinning and easy bruising  
Increased susceptibility to infection  
Increased risk of malignancy  
Cataracts |
| **Drug Interactions** | Prednisolone and other corticosteroids are metabolised by multiple pathways, principally in the liver. Although drugs that either induce or inhibit these pathways will influence steroid metabolism, the prednisolone dose is not usually adjusted. |
| **Monitoring** | Glyscouria, eyes and BP in Nephrotic Clinic |
E. Contacts

1. Urgent advice and referrals

Phone advice is available during office hours from the Paediatric nephrotic specialist nurse on 0191 2829599 and 0191 2829844.

There is always an on-service Consultant Paediatric Nephrologist responsible for all acute referrals and in-patient nephrology. The on-call Consultant can be contacted via the Hospital Switchboard (0191 233 6161).

There is always a Paediatric renal specialist nurse on-call day or night, contactable via switchboard.

2. Contact numbers

| Paediatric nephrotic nurse specialists | 0191 282 9599 |
| Paediatric nephrology ward (Ward 1A)    | 0191 282 6001 |
| Departmental secretaries                | 0191 282 0323 |
| Paediatric Nephrology Fax number        | 0191 282 0077 |
| Pharmacy (Medicine Information)         | 0191 282 5398 |

Guideline written by:

Dr. Vincent Tse           Consultant Paediatric Nephrologist
Karen Maddison            Paediatric Pharmacist
Denise Chisholm           Specialist Paediatric Nephrotic Nurse

Draft version 1
Date of acceptance:       Review date: