Practical Immunosuppression Guidelines for Patients with Glomerulonephritis

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Many forms of glomerular disease are immune mediated and are therefore treated with immunosuppression. The particular regimen that is used may vary depending on the underlying condition, but many protocols are based on combination therapy using glucocorticoids and a second agent, which has historically often been cyclophosphamide. With the introduction of newer immunosuppressive agents, including biologics, these protocols have been modified for different conditions and, in only some cases, tested in randomised controlled trials. Certain protocols are based on oral therapies and can easily be delivered safely as outpatients; others require infusions which necessitate careful co-ordination of day case admissions and outpatient monitoring to allow early recognition of potential adverse events. Regardless of the actual regimen used, there are some general principles that apply to delivering a safe immunosuppressive service. In this chapter, we discuss practical issues surrounding immunosuppression in glomerular disease.

Protocol Constituents

Cyclophosphamide

The risks of cyclophosphamide are believed to be outweighed in severe life- or organ-threatening conditions; however, it is important to make patients aware of potential toxicities (see Appendix 1, e.g. of a cyclophosphamide consent sheet). Limiting the patient's total exposure is desirable, as adverse events are related to cumulative dose and there are significant increases in haematological and bladder malignancies once total exposure exceeds 36 g [1].

Cyclophosphamide may be used orally (at doses of 2–3 mg/kg), for example, in anti-GBM disease or intravenously as pulses every 2–3 weeks depending on the protocol, for example, in the Eurolupus regimen or the CYCLOPS vasculitis regimen.

There is ample evidence that pulsed intravenous treatment induces remission as rapidly in as many patients as daily oral therapy but exposes the patients to lower drug levels and thus is associated with fewer leucopenic episodes [2]. Long-term lower doses of cyclophosphamide are associated with higher relapse rates, in certain conditions [3, 4]. While the data are available to confirm benefit in SLE and ANCA-associated vasculitis (AAV), no direct comparisons have, or will likely to be, performed in anti-GBM disease. Therefore, many practitioners still utilise oral cyclophosphamide in anti-GBM disease based on established protocols.

With modern dosage regimens of cyclophosphamide, the incidence of haemorrhagic cystitis is low and the use of MESNA as a bladder protectant may be unnecessary [5]. In addition there may be reactions to the MESNA itself and thus some units have abandoned the routine use of MESNA. Encouraging oral input (assuming the patient is not oligo-anuric) to maintain a good urine output and reduce the concentration of bladder accumulating metabolites is useful.

Dose adjustments should be made based on age and renal function. A schema for dose reduction of pulsed intravenous cyclophosphamide as used in ANCA-associated vasculitis is shown in Table 23.1, while if daily oral treatment is used, the dose should be reduced by 25 % if >60 years and 50 % if >70 years.

Cyclophosphamide should be withheld if the total WCC is less than 4×10^9, and oral doses should be reduced by 50 mg if the white count is trending downwards, to avoid development of episodes of leucopenia. Weekly WCC checks are mandatory whilst on oral cyclophosphamide for the first month, twice weekly for the second month and monthly thereafter for the first year.

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Table 23.1 Intravenous cyclophosphamide regime used in systemic vasculitis demonstrating dose adjustment for both age and renal function

	Creatinine μmol/l	
Age (years)	<300	300–500
<60	15 mg/kg/pulse	12.5 mg/kg/pulse
60–70	12.5 mg/kg/pulse	10 mg/kg/pulse
>70	10 mg/kg/pulse	7.5 mg/kg/pulse

Taken from [2]
Patients with a nadir leucocyte count of $2–3 \times 10^9$/l had a dose reduction of 20 %. Dose reduced by 40 % in those who had a nadir leucocyte count of $1–2 \times 10^9$/l. Omit pulse if WBC nadir $<1 \times 10^9$/l and consider g-CSF administration and antibiotic prophylaxis

Table 23.2 Steroid reducing protocol. If pulsed methylprednisolone is given, starting dose of steroid could be reduced

Prednisolone (non-enteric-coated) protocol	Starting dose: 1 mg/kg daily orally (maximum 60 mg/day)
Week 1	60 mg/day
Week 2	45 mg/day
Week 3	30 mg/day
Week 4	25 mg/day
Week 5	20 mg/day
Thereafter steroid reductions depending on patient's response	2.5 mg dose reduction every 2 weeks
Month 3–4	10 mg/day

Pulsed therapy dosage should be adjusted depending on nadir WCC, checked 7–10 days after treatment. We ensure that a recent (within 1 week) blood test is available prior to delivering the next dose.

Prophylaxis for pneumocystis jiroveci with low-dose co-trimoxazole is required in CYP-treated patients. This can be delivered as 480 mg daily or 960 mg three times a week. In cases of co-trimoxazole allergy monthly nebulised pentamidine may be used instead. Anti-emetics, such as ondansetron 8 mg or granisetron 1–2 mg, should be given 30 min pre- and 12 h post-infusion.

Glucocorticoids

Steroids (glucocorticoids) have been the mainstay of treatment for nearly all immune-based diseases, and this is true of most glomerular diseases. The dose regimens used in glomerular diseases have been highly variable and mostly decided on empirically without any comparative trial data. There are two main ways of delivering steroids by intravenous bolus (using methylprednisolone or dexamethasone) or by daily or alternate-day oral medication (using prednisolone or methylprednisolone). These are clearly not mutually exclusive. Conventionally, in adult practice, steroids are taken daily and doses of 1 mg/kg, with a maximum starting dose of 60 mg, of prednisolone are commonly used to induce remission. The speed of taper and decision to wean completely or not are highly variable in clinical practice. One current strategy commonly used for weaning is shown in Table 23.2. If pulses of methylprednisolone are used, then it seems sensible to reduce the initial dose of oral prednisolone, to start at 30 mg/day although there are no available trial data to support this approach at present. Pulsed methylprednisolone has been delivered at doses of 250–1,000 mg/day over three consecutive days, again without ever comparing efficacy of differing doses. It is probably reasonable to limit pulses to a total of 1.5 g of methylprednisolone, as it is generally believed that much of the early morbidity following immunosuppression induction may relate to steroid usage. Pulsed steroid use may be a reasonable temporising measure if plasmapheresis is not immediately available, although the latter is preferable based on randomised trials, at least in management of systemic vasculitis and anti-GBM disease [6, 7].

Infection, Bone and Gastric Prophylaxis

Prevention of steroid side effects warrants prophylactic treatment with regard to gastric, bone and fungal complications. All patients on high-dose steroids should receive gastric protection with proton pump inhibitors or H2 antagonists. Bone protection with calcium D3 combination (1 g of calcium/day) and consideration for bisphosphonate use if renal function allows and if there is any pre-existing bone mineral density loss. Fungal prophylaxis may be in the form of nystatin suspension or low-dose fluconazole (but confirm no possible drug interaction with other immunosuppressants such as calcineurin inhibitors).

Plasmapheresis

Plasmapheresis removes a number of plasma proteins that may contribute to disease pathogenesis, including autoantibodies, immune complexes, complement components, clotting factors and microparticles derived from inflammatory or endothelial cells. There are two main ways of performing plasmapheresis, using a plasma filter or a centrifugal bowl. The advantage of the former is that it is easily performed by most dialysis nurses, but the filter may limit removal of larger molecules such as IgM; by contrast bowl centrifugation has the advantage of removing all plasma components but may be limited in availability in certain units. Further modifications of these techniques exist including the double-filtration plasmapheresis method (DFPP), which returns some of the smaller plasma molecules (such as albumin) to the patient, necessitating less replacement fluid; cryofiltration which is when the plasmapheresis is performed at lower

temperatures in an attempt to increase removal of immune complexes; and plasma absorption when specific affinity columns are used to allow greater removal of certain molecules such as immunoglobulin (using protein A columns).

Replacement fluid should be in the form of 4.5 % albumin, unless there is a bleeding tendency; a recent invasive procedure or the procedure is aimed at replacing a missing factor, such as in atypical HUS where an abnormal complement factor may be contributing to disease. In those oligo-anuric or anuric patients, the salt load from the 4.5 % albumin solution can be considerable, and increased fluid removal with subsequent dialysis may be necessary to prevent fluid overload.

The dose of plasmapheresis should be calculated based on plasma volume or body weight, and typically 1–1.5 plasma volumes are exchanged per session (generally 50–60 ml/kg). It is important to review the delivered dose that is achieved, as failure to respond may be due to inadequate plasma exchange.

Plasmapheresis has been shown to be of benefit in anti-GBM disease, when it is delivered for 14 exchanges or until the anti-GBM antibody is negative, and in patients with ANCA-associated vasculitis (AAV) and severe renal involvement (creatinine > 500 μmol/l) [6, 7]. It may be of benefit in less severe forms of AAV, and this is currently being tested in a randomised clinical trial (see www.vasculitis.org). There is no evidence for a benefit in SLE [8] or in other forms of rapidly progressive glomerulonephritis, but it is often used in such patients with renal deterioration in the hope that there may be some benefit (see RPGN below).

Fertility Sparing Measures and Pregnancies

Fertility impairment is related to use of cyclophosphamide and is in part related to the age of the patient and the pre-treatment sperm viability or ovarian function. It is therefore always best to sperm bank men of child-bearing age, prior to cyclophosphamide treatment, and discuss ovarian protection or egg harvesting in women. Practically, the induction therapy for egg harvesting is not suited to acutely ill patients who may need to start cyclophosphamide therapy urgently, and so a more favoured approach is the use of gonadotropin-releasing hormone (GnRH) analogues prior to the use of cyclophosphamide treatment, which may be appropriate in female patients up to the age of 40 years [9]. Use of Goserelin monthly (3.6 mg) or three monthly is generally adequate for induction of chemical menopause. There are no data however confirming that this approach results in a better proportion of patients with preserved fertility, but many practitioners use such an approach nonetheless.

In those planning a pregnancy, this should be ideally delayed for a period such as 6 months following the last dose of cyclophosphamide. The patient should also have had a period of disease remission for several months before planning a pregnancy. Certain maintenance immunosuppressives can be continued, while others need to be stopped or switched to more appropriate equivalents. Examples of drugs that can be or cannot be continued in pregnancy are shown in Table 23.3.

Table 23.3 Drug modifications in those planning pregnancy

Can be continued in pregnancy	Needs to be discontinued	Uncertain
Azathioprine	Mycophenolate mofetil/MPA	Rituximab
Steroids	Cyclophosphamide	
Tacrolimus or cyclosporin A	ACE inhibitors/ARB	
Hydroxychloroquine	Proton pump inhibitors	

Rituximab

This anti-CD20 monoclonal antibody, first introduced for treatment of lymphoma, is now extensively used in autoimmunity and in many forms of glomerular disease. It is administered as a slow intravenous infusion with steroid and antihistamine premedication (methylprednisolone 125 mg and chlorpheniramine). Infusion reactions are the most common adverse event. B-cell depletion is generally achieved after one dose but may be less efficacious if significant monoclonal is lost in the urine, in nephrotic states. B-cell numbers should be checked following administration. It may be administered as two infusions 2 weeks apart (each of 1g) or as a four-dose weekly regimen of 375 mg/m^2. Both appear to be equally efficacious in glomerular disease.

Secondary hypogammaglobulinaemia may result and the more severe this is, the more likely the patient will develop an infectious complication. IgG levels should be monitored in case levels are low and replacement immunoglobulin may be required. Rituximab is also currently being trialled as a maintenance therapy in two randomised vasculitis trials.

MMF and Azathioprine

MMF is extensively used as induction therapy in SLE and has been shown to be of equal efficacy in inducing remission in lupus nephritis as cyclophosphamide – with better tolerability in certain ethnic groups (such as African-Americans and Hispanics). Some centres advocate therapeutic drug monitoring, although many trials treated to a particular dose. Starting at a lower dose and increasing rapidly may allow for fewer gastrointestinal side effects.

Azathioprine requires no such dose adjustments, but TPMT levels should be checked prior to commencing therapy as this may allow dose adjustment in patients likely to suffer bone marrow toxicity, with low TPMT activity. Care should be taken if patients are on allopurinol as this increases azathioprine toxicity. Monitoring of liver function tests and a full blood count regularly will help prevent hepatitis and leucopenia. Azathioprine is infrequently used for induction therapy, but rather as a common maintenance agent. It is more effective than MMF in vasculitis maintenance, with significantly less time to relapse.

Protocols for Particular Glomerular Diseases

Rapidly Progressive Glomerulonephritis

Rapidly progressive glomerulonephritis (RPGN) is defined as sudden loss of renal function, with halving of GFR within 3 months. Prompt diagnosis and treatment is crucial to prevent irreversible loss of renal function. Histologically, RPGN is caused by a crescentic glomerulonephritis, which is due to severe glomerular injury, as a result of rupture of the glomerular capillary loop basement membrane. Crescentic glomerulonephritis is generally defined as having more than 50 % of glomeruli involved with crescents, which are identified by the presence of at least two layers of cells in Bowman's space.

RPGN can be commonly categorised into being caused by:

- Anti-glomerular basement membrane (GBM) disease
- Immune-complex glomerulonephritis
- Pauci-immune glomerulonephritis, associated with ANCA in most cases

The standard of care has long been steroids and cyclophosphamide, with trials in pauci-immune GN demonstrating that newer regimens using lower doses of cyclophosphamide delivered as intravenous pulses provide equal efficacy and fewer adverse events such as leucopenia. New trials in ANCA-associated vasculitis have demonstrated that induction therapy with rituximab is as effective as cyclophosphamide [10, 11], while studies in SLE have failed to demonstrate benefit of additional RTX therapy above standard treatment [12, 13]. Since there have been few randomised studies of treatment of other causes of RPGN, we are left to extrapolate protocols from these studies.

Anti-GBM Disease

Treatment should be initiated immediately in those in whom it is appropriate. Recommendations are to initiate daily plasma exchange for a total of 14 sessions or until the anti-GBM antibody has disappeared. Plasma exchange should be against human albumin solution, unless there has been a recent renal biopsy or active bleeding, and then it should be replaced in part (300–600 ml) with fresh frozen plasma (FFP) [14]. Long-term immunosuppression is not required due to the monophasic nature of the disease, with cyclophosphamide treatment recommended for 2–3 months and steroid for no more than 6–9 months (see Table 23.4).

Table 23.4 Treatment regime for anti-GBM disease [14]

Drug/treatment	Dose	Duration
Corticosteroids	1 mg/kg/day (max 60 mg/day)	6–9 months
Cyclophosphamide	Oral: 2–3 mg/kg Dose reduction in >55 years	2–3 months
Plasma exchange	Human albumin solution; 50 ml/kg max 4 l	At least 14 days or till anti-GBM antibody normalised
Prophylaxis	Nystatin or fluconazole	For duration of high-dose steroids
	Calcium D3	
	PPI or H2 antagonist	
	Septrin 480 mg daily or 960 mg three times a week	For duration of cyclophosphamide

Immune-Complex Glomerulonephritis

This describes the formation of immune deposits, which contain immunoglobulins, complement and other proteins within the glomerulus resulting in glomerular injury. There are several underlying causes of a RPGN with immune-complex deposition histologically.

IgA Nephropathy (IgAN)

While there are data demonstrating efficacy of immunosuppression with steroids in patients with IgAN with moderate proteinuria (1–3.5 g/day) and mild renal impairment (serum creatinine $\leq$1.5 mg/dl) [15], evidence is lacking for treatment of a crescentic IgAN. A rapidly progressive course with crescents has been treated with a regimen based on that for systemic vasculitis using combination steroids and cyclophosphamide. A small study of 12 patients with a crescentic, progressive disease treated with pulsed steroids and monthly cyclophosphamide resulted in a reduction in proliferative lesions and proteinuria and stabilisation in renal function [16]. In some young patients with crescentic IgA and a rapid renal decline, plasmapheresis has also been used with variable results.

Lupus Nephritis

Renal involvement frequently occurs in SLE, with proliferative lesions (class III and IV) having a poorer outcome, than mesangial lesions (class II). The treatment regimen can be considered in two parts: induction therapy and maintenance. However, there are limited published data on treating crescentic lupus nephritis or SLE causing a RPGN.

The old NIH high-dose pulsed cyclophosphamide (CYP) regimen [17] has for the most part been abandoned, and there are now two significant protocols to consider. The first

Table 23.5 Treatment in lupus nephritis (class III, IV)

Drug	Dose	Investigations	Caution
MMF	Titrate aiming to 3 g/day (induction) 2 g/day (maintenance)	WCC: stop if neutropenic	Teratogenic
Cyclophosphamide Eurolupus: outpatient infusions	500 mg IV every 2 weeks for 3 months	WCC: 10–14 days after last dose. Hold dose if WCC < 4	Mesna optional, dose 20 % of CYP dose Ovarian protection with GnRHa may be beneficial
Corticosteroids	60 mg/day: taper decreasing to ≤10 mg by 24 weeks		Gastric protection Bone protection
Azathioprine	2 mg/kg	TPMT (thiopurine methyltransferase) activity: low levels will require decreasing the dose FBC, LFTs: monitor after initiation of therapy	Can replace MMF as maintenance therapy if pregnancy being considered
Consider:			
Rituximab	1 g day 1 and 15	Peripheral B count (CD19) to assess depletion	Prevention of transfusion reaction give methylprednisolone 100 mg
Belimumab	Day 0, 14 and 28 then every 28 days		

is the Eurolupus protocol [18]. The Eurolupus trial consisted of predominantly Caucasian patients with proliferative lupus nephritis, including those patients with glomerular crescents, and compared low-dose CYP with standard high dose (NIH) CYP. This trial provided evidence for a short, low-dose course of intravenous cyclophosphamide (500 mg every 2 weeks for 3 months) followed by azathioprine (2–2.5 mg/kg/day) which was initiated 2 weeks after the last dose of CYP, as well as corticosteroids [18]. The dose of steroids was initially started at 1 mg/kg/day, with a gradual taper down to 5–7.5 mg after approximately 6 months of therapy.

The second is based on the use of mycophenolate mofetil (MMF) at a target dose of 3 g/day [19], in conjunction with prednisolone starting at 60 mg/day. Although a recent multicentre trial failed to demonstrate MMF *superiority* over intravenous cyclophosphamide (0.5–1 g/m^2 6 monthly pulses), the two drugs induced similar rates of remission and MMF treatment was associated with significantly fewer serious adverse events. In addition, differences in response to these immunosuppressants were found in different ethnic groups, with MMF proving more effective than cyclophosphamide in black and Hispanic patients [19].

After the completion of induction therapy, patients are prescribed maintenance treatment to reduce the risk of flares. This treatment should be continued for some time although exactly how long is debated. Similar to the induction treatment trials, there seems to be an ethnic variation in the response to treatment. In a predominantly Caucasian cohort, MMF (2 g/day) was not superior to azathioprine (2 mg/kg per day) with respect to renal flares, doubling of creatinine or infectious complications [20]. However, in the ALMS study, which included more of the high-risk black patients, MMF was superior to azathioprine at maintaining disease remission [21].

Various uncontrolled studies have demonstrated promising results with rituximab for patients with lupus nephritis [22] including those with refractory/relapsing disease [23]. However, a large multicentre, randomised trial (LUNAR), investigating the use of rituximab alongside steroids and MMF in proliferative lupus nephritis, failed to demonstrate additional impact of rituximab [13]. Currently, rituximab may be considered an option for those with refractory, relapsing disease or intolerant of first-line therapies. However, an anti-Blys (B-lymphocyte stimulator)monoclonal antibody, belimumab, has been shown to be effective in a recent SLE trial demonstrating improvements in a number of disease domains and has recently been licensed for treatment of SLE [24]. The treatment options are summarised in Table 23.5.

Postinfectious Glomerulonephritis (PIGN)

Infections can result in glomerulonephritis, with a variety of different histological manifestations. Bacteria such as *Staphylococcus aureus* and Streptococci as well as infective endocarditis are well recognised as underlying causes of an infection-related glomerulonephritis, which may manifest as a RPGN with crescentic or vasculitic lesions seen on renal biopsy. The association between staphylococcal infections and IgA rich PIGN is now well established. Antibiotic therapy is clearly crucial in these infectious diseases, while there may be a role for corticosteroids under certain circumstances. However, overall no correlation between steroid use and renal outcome has been demonstrated [25], so this issue remains controversial.

Pauci-Immune Glomerulonephritis

This describes the appearance on renal biopsy in which there is little or no glomerular staining of immunoglobulins, which most commonly is associated with anti-neutrophil cytoplasm antibody (ANCA), and represents the most likely cause of a RPGN in adults [26]. Like treatment of SLE, treatment of AAV consists of induction and maintenance. Renal function and age are important predictors of outcome. Cyclophosphamide has been part of the gold standard induction agent for many years, although its use at high doses for prolonged periods resulted in significant adverse effects. Treatment regimens have been refined over the years to reduce the total cumulative dose of cyclophosphamide. Numerous EUVAS (European Vasculitis Study Group) trials have investigated optimal regimens for different disease states. The CYCLOPS trial included patients with a serum creatinine <500 μmol/l and demonstrated that the combination of pulsed intravenous cyclophosphamide and oral steroids was as effective at inducing disease remission as an oral cyclophosphamide regimen but induced fewer episodes of leucopenia [2], although long-term follow-up has shown that this intravenous regime is associated with increased relapses [3]. Table 23.1 demonstrates the intravenous dosing regimen used in this study.

The MEPEX study investigated patients with more advanced renal failure (serum creatinine >500 μmol/l) and demonstrated the benefits of plasma exchange, alongside oral cyclophosphamide and corticosteroids in renal recovery at 3 months and 1 year [6]. There is now increasing use of intravenous cyclophosphamide in this group of patients with severe renal failure to reduce the incidence of leucopenia, with patients receiving 6–10 pulses of cyclophosphamide. The dose of steroids is usually started at 1 mg/kg, with tapering to a dose of 10–15 mg/day by 3 months and 5 mg by 1 year. Maintenance therapy consists of long-term immunosuppression following the period of induction therapy. The CYCAZAREM trial demonstrated that cyclophosphamide at 3–6 months could be safely substituted for azathioprine (2 mg/kg/day) [27], while a recent study demonstrated that MMF is not as effective as azathioprine in maintenance therapy [28], so should be reserved for patients who cannot tolerate azathioprine.

There is increasing use of rituximab in patients with AAV, with 2 randomised trials providing evidence that its use as induction therapy is equivalent to that of cyclophosphamide [10, 11]. The RAVE trial compared oral cyclophosphamide with rituximab, excluding those with severe renal failure (creatinine > 4 mg/dl), although patients with less severe renal disease were included [10] and demonstrated equivalence of RTX and CYP but superiority of RTX for those with relapsing disease. RITUXVAS included those with severe (dialysis dependent) renal involvement and demonstrated the rituximab regime not to be inferior [11]. Both the 375 mg/m^2 × 1/week for 4 weeks (regime in RAVE and RITUXIVAS) and 1 g repeated after 2 weeks appeared equally effective. Table 23.6 shows the treatment options in AAV.

Table 23.6 Induction and maintenance doses of immunosuppressive agents in ANCA-associated vasculitis

Therapy	Dose	Specific investigations that modify dose/therapy
Cyclophosphamide	MEPEX oral: 2–3 mg/kg	WCC: <4 withhold drug
	Age > 60 years 2 mg/kg	WCC: 4–5 reduce dose
		Prophylaxis as for anti-GBM disease
Rituximab	Either 375 mg/m^2 × 1/week for 4 weeks	Monitor CD19 count: adequate peripheral blood depletion $<0.005 \times 10^9$
	Or 1 g at day 1 and day 15	WCC: neutropenia reported following chronic use
		Monitor immunoglobulins
Azathioprine	1–2 mg/kg	TPMT (thiopurine methyltransferase) activity: low levels require decreasing the dose to 1 mg/kg
		FBC, LFTs: monitor after initiation of therapy
Mycophenolate mofetil	2 g/day	WCC: stop if neutropenic
		Reduce dose WCC < 4
Methotrexate	0.03 mg/kg/week	Check LFT, WCC alt weeks to begin with
		Annual CXR
	Starting at 10–15 mg/week	Procollagen III may be helpful in monitoring for liver damage
		Add folic acid 5 mg weekly taken 2 days after MTX

Appendix 1: Information for Renal Patients Receiving Cyclophosphamide Therapy

This information sheet describes cyclophosphamide, how it is administered and some of the side effects it may cause. Please ask a member of staff if you want information about other alternatives to treatment with cyclophosphamide or if you have any other questions.

How Is It Given?

Cyclophosphamide can be given by injection into a vein (intravenously) or as a tablet. Your doctor will agree with you as to which the best route is for you to receive the drug.

Tablets may have to be taken for a number of months; the intravenous infusion is generally given every 2–4 weeks. The length of the treatment will depend on your condition and response to treatment, but it generally lasts 3–4 months.

If you are receiving the intravenous infusion, you will attend the renal day ward (3 East). You will need to stay for up to 2 h, although generally it takes less time.

How Does Cyclophosphamide Work?

Cyclophosphamide works by depressing ('damping down') your immune system. The aim of the treatment is to reduce the inflammation that is causing the problem with your affected organs such as kidneys, lungs or nose.

What Are the Possible Side Effects?

Nausea and vomiting may occur if you take cyclophosphamide. This can be controlled by giving you anti-sickness (anti-emetic) tablets as needed.

Increased risk of infection is a result of the suppression of white blood cell production in your bone marrow. White blood cells help to fight infection. Your levels of white blood cells will be monitored. If you develop a temperature, fever or any signs of infection, please contact either the ward or your GP. You should also report any bruising/bleeding or excessive tiredness. You will be given an antibiotic tablet (or nebuliser if you cannot tolerate the tablets) to stop certain infections, but this will not prevent all infections.

Bladder irritation is a possible side effect if you are receiving intravenous cyclophosphamide. Symptoms include blood in the urine and symptoms of cystitis. You may be given a drug called mesna during the intravenous infusion that will help to prevent this occurring. If you notice any blood in your urine after discharge home, please contact the ward.

Hair thinning may occur. This is not permanent and will grow back after treatment.

Mouth sores may develop if you are taking the tablets, and you will be given a supply of mouth lozenges to help prevent this. Good oral and dental hygiene is important.

Contraception and fertility should be discussed with your doctor or nurse as cyclophosphamide may affect your ability to conceive or father a child. With a standard treatment course, the risk of this happening is relatively small. Women may find their periods altered and men may wish to discuss sperm banking.

Cyclophosphamide and Pregnancy

Cyclophosphamide may cause several different birth defects if it is either taken at the time of conception or during pregnancy. Be sure that you practice effective birth control with a barrier method of contraception while you are being treated with cyclophosphamide. Tell your doctor right away if you think you have become pregnant while taking cyclophosphamide.

If You Become Unwell While Being Treated with Cyclophosphamide

If you become unwell or develop a temperature above 37.5 °C, you must let your doctors know. Please contact your clinic consultant (through switchboard) or the renal day ward during working hours or the on-call renal registrar out of hours, who can be reached through switchboard.

If you require any further information or advice, please ask either your doctor or nurse.

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