

# Intravenous Cyclophosphamide for Renal Patients

## Protocol

### **1. Patients will have counselling and receive a patient information sheet from their nephrologist prior to their first infusion at Ambulatory Care.**

These issues will be covered:

- a. Haemorrhagic Cystitis, Haematuria.
- b. Malignancy which may occur over a prolonged latent period: TCC Bladder
- c. PCP Prophylaxis
- d. Mesna does not enhance the effectiveness of Cyclophosphamide in treating the autoimmune disease, but is designed to PROTECT the bladder and kidney from the recognised toxic metabolite that is liberated in the production of the active Cyclophosphamide-Mustard agent.
- e. Risks of Hypersensitivity to Mesna are seen more commonly in patients receiving this therapy for Autoimmune disease than for malignant disease.

### **2. Check UA, FBC, EUC prior to commencement of infusion (This may be done the week before).**

- i. UA: **de novo** microscopic haematuria may indicate cystitis or TCC. In most cases haematuria will be present as part of the underlying renal disease.
- ii. FBC: A cyclophosphamide dose reduction or omission may be required if leukopenic
- iii. EUC: Dose of cyclophosphamide may need to be adjusted according to renal function (decline or recovery).

### **3. Commence infusion in the morning, so that frequent voiding occurs and Cyclophosphamide metabolites do not rest in the bladder for prolonged periods.**

### **4. Contraindication to therapy**

- a. UTI, Sepsis, Hypersensitivity, Pregnancy, Lactation

### **5. Pre-infusion Therapy**

- a. 500mL Normal Saline over 1 hour

### **6. Antiemetic Protocol. Use all three, administered half hour prior to Cyclophosphamide infusion.**

- a. Lorazepam 0.5mg sublingual
- b. Ondansetron 8mg po
- c. Dexamethasone 4mg iv

### **7. Mesna:**

- a. The TOTAL dose of MESNA (in mg) is 60% of the Cyclophosphamide dose.
  - i. Commence Mesna a half hour before the Cyclophosphamide is given: minimises renal-urothelial injury.
- b. Administer 1/3 of Mesna dose intravenously in 100ml Normal Saline, over 30 minutes, commencing ½ hour prior to infusion of Cyclophosphamide.

- c. The remaining 2/3 Mesna dose should be given with the cyclophosphamide infusion. This combination will be made up by HODC pharmacy.

#### 8. **Cyclophosphamide Infusion**

- a. The dose will be determined by the treating Nephrologist or Renal Registrar, who will take into account
  - i. Prior leukopenia history
  - ii. Total cumulative dose
  - iii. Renal Function
- b. **The Cyclophosphamide and Mesna will be administered together** (both prepared in 500mL Normal Saline, given over 1 hour), which will be prepared by the Pharmacist.
  - i. This should be charted by the renal team at least 24 hours prior to the scheduled appointment. HODC pharmacy requires this amount of time to prepare the solution.
  - ii. Eg. For a 500mg dose of Cyclophosphamide with Mesna (Total Mesna dose is 300mg- this is 60% of the 500mg dose of cyclophosphamide), then Cyclophosphamide 500mg is administered with Mesna 200mg in 500mL Normal Saline over 1 hour.

#### 9. **Post Infusion**

- a. Normal Saline 500mL intravenously over 1 hour

#### 10. **Follow Up arrangements**

- a. Keep Hydrated. Void frequently.
- b. A fall in the WCC will be anticipated following this treatment. Patients should report fever, macroscopic haematuria, or other illness' to their local doctor or nephrologist.
- c. Patients should be reviewed by their nephrologist prior to subsequent cyclophosphamide dose to ensure dose appropriateness.
- d. Ensure a follow-up booking with the Nephrologist is arranged prior to the patient leaving Ambulatory Care.

An example of this protocol, for a patient receiving 500mg iv Cyclophosphamide

- STEP 1** 1 hour prior to Cyclophosphamide Infusion  
500mL N Saline q 1 hour IV
- STEP 2** Half hour Prior to Cyclophosphamide infusion
1. Lorazepam 0.5mg po
  2. Ondansetron 8mg po
  3. Dexamethasone 4 mg IV
  4. Mesna 100mg iv (1/3 dose of total Mesna) in 100mL Normal Saline given over ½ hour.
- STEP 3** Cyclophosphamide infusion  
Cyclophosphamide 500mg IV + Mesna 200mg (2/3 of dose) IV made up in the same 500mL Normal Saline over 1 hour
- STEP 4** Following Cyclophosphamide Infusion  
500mL N Saline q 1 hour

# Patient information sheet for renal patients undergoing Intravenous Cyclophosphamide therapy

**Your kidney specialist has considered your individual medical condition and recommended treatment with intravenous cyclophosphamide.**

Some of these conditions include Systemic Lupus Erythematosus, Lupus Nephritis, Wegener's Granulomatosis, Minimal change disease, and membranous nephropathy. Cyclophosphamide is also used in other medical conditions such as leukaemias, and solid cancers. It is a form of chemotherapy. This information sheet specifically refers to renal patients.

Cyclophosphamide has been available for decades in the successful cure and remission of these diseases. There are however potential risks and complications associated with cyclophosphamide:

**1. Haemorrhagic Cystitis:** This is an inflammation of the lining of the bladder. It may manifest as haematuria (blood in the urine), as passing clots of blood, and in severe but rare cases frank bleeding from the bladder, which may be fatal. The likelihood of passing blood is small, overt bleeding and death is extremely rare.

What we will do: We will give your infusion through a "drip" in the morning so that you will be able to urinate easily and comfortably. You should not retain urine in the bladder for long periods of time over the rest of the day. This will limit the risk of cystitis. We will also give you intravenous fluid hydration to assist you in voiding. You may be on a "fluid restriction" prescribed by your nephrologist, and we have taken this into consideration today.

What you can do: *If you develop burning or discomfort when you urinate, or see blood in your urine, you should contact your local doctor or kidney specialist. If the symptoms are severe you should go to your local hospital for assessment.*

**2. Transitional cell carcinoma (TCC):** this may occur many years (even 20 years) after cyclophosphamide treatment. This is a cancer in the bladder, but also occurs in the ureters, and part of the kidney. Smoking may further increase the risk of developing TCC. The rates of developing a TCC from the treatment have been reported at 2% (compared to the general population at 0.04%). The risk of TCC accumulates with time following treatment.

What we will do: We will give you a concurrent intravenous treatment with "Mesna" which is designed to limit toxicity to the bladder. In the future you may need to perform urine tests to screen for cancer cells in the urine. Some patients may need to see a urologist to investigate this further. Your kidney specialist will advise you on this.

What you can do: *You should not smoke cigarettes.*

**3. Infections:** Cyclophosphamide is a potent immune suppressing drug. It turns off cells that rapidly divide, such as the inflammatory cells involved in your kidney

disease. We expect a reduction in your white cells (the cells that fight infection) following treatment with cyclophosphamide.

You may be at risk of common bacterial and viral infections. Cyclophosphamide may also suppress the immunity and put you at risk of opportunistic infections. These are infections that would in normal circumstances not harm a person with intact immunity. One such infection is called Pneumocystitis (previously also called PCP). A prophylactic antibiotic may be necessary (such as “Bactrim”). The concurrent use of Prednisone may also increase the risk of both the common bacterial and viral infections and the opportunistic infections.

*If you develop fevers, chills, sweats or other symptoms of illness, you should contact your local doctor or kidney specialist. If you develop severe symptoms, you should go to your local hospital for assessment.*

**4. Infertility:** Cyclophosphamide has been associated with premature menopause in some women and if enough cyclophosphamide is given infertility rates increase. If this concerns you, you should discuss this with your kidney specialist. It may also cause infertility in men. Men may have the opportunity to sperm-bank prior to treatment.

**5. Nausea:** As with any medication, nausea may develop. Nausea has been associated with cyclophosphamide, and for some patients may be distressing, and limit your tolerance of this treatment.

What we will do: You will receive three anti-nausea medications just before the cyclophosphamide infusion. They will act in different ways to make you as comfortable as possible. One (dexamethasone) will be given intravenously, the other two (Lorazepam and Ondansetron) are oral tablets. Dexamethasone may increase the blood glucose level temporarily in some patients. If you have DIABETES your blood sugar may rise for about 24 hours but normally returns to baseline after this.

**You will receive a drug called Mesna during the infusion.**

Mesna may also be given in tablet form, however we believe it is more effective when given intravenously.

Mesna does not enhance the effectiveness of Cyclophosphamide in treating your condition, but is designed to PROTECT the bladder and kidney from developing cystitis, scarring, and TCC. The mesna will be given to you today in two parts: one intravenous injection through a ‘drip’ prior to your cyclophosphamide treatment, and the other with the cyclophosphamide treatment.

Some patients may develop a hypersensitivity (allergic) reaction to Mesna. The risk is small, it occurs slightly more frequently in patients with autoimmune diseases (such as nephritis). If you develop a hypersensitivity reaction, this can be treated in the ward before you go home.

You will spend about 4 hours in the ward to have this treatment. Please ensure you have another appointment with your kidney specialist arranged before your next cyclophosphamide infusion.