Tacrolimus Intravenous INFUSION for Adults

Who can administer

May be administered by registered competent doctor or nurse/midwife

Important information

- **Intravenous tacrolimus may ONLY be used in consultation with nephrology consultant or other consultant with expertise in organ transplantation - as the daily intravenous dose is very significantly less than the oral dose**
- **Not normally stocked in GUH**
- **Sublingual tacrolimus** (unlicensed) may be an option for short term use (a dose conversion will be necessary). **Its use MUST be discussed with the nephrology consultant on call via switch**
- See **monitoring** requirements below
- There are numerous **important interactions -** check current BNF
- **Non-PVC infusion devices and giving sets** required- see below
- **Consider intravenous to oral switch as soon as possible**; IV therapy should not normally exceed 7 days
- **Risk of anaphylaxis** due to polyoxyl castor oil - caution in patients who have previously received preparations containing polyoxyethylene castor oil (by IV route) and in patients with an allergic predisposition. Risk of anaphylaxis may be reduced by using a slow rate of infusion, or giving an antihistamine prior to tacrolimus infusion.
- Must have access to facilities for managing hypersensitivity reactions including **anaphylaxis**

Available preparations

Prograf 5mg per 1ml ampoule

Reconstitution

Already in solution

Draw up using a 5 micron filter needle

Dilute further prior to administration

Infusion fluids

Sodium Chloride 0.9% or Glucose 5%

Methods of intravenous administration

Continuous intravenous infusion (only) (administer using an electronically controlled infusion pump device)

- Dilute the required dose to a final concentration of 4 to 100 micrograms/ml. Final volume can be from 20ml to 500ml, given over 24 hours
- Incompatible with PVC. **Non-PVC infusion container** (e.g.Braun Ecoflac or Baxter Viaflo are suitable) and a **low adsorption giving set** (e.g. Baxter VMC9606, or Braun 8700110SP) must be used.

(available from pharmacy)
- **Alternatively** a syringe pump and a low adsorption administration set (e.g. Vygon Lectro-spiral 1155.80 or Braun Original Perfusor - Leitung PE 8723060) can be used and may be more suitable in fluid restricted patients.

Dose in adults

- For transplantation, various dosing regimens are used in specialist centres.
- Higher doses are used initially and maintenance treatment is adjusted according to response.
- Contact specialist centre for detailed guidance.

For use in patients normally on the ORAL formulation who require temporary IV use

- The daily intravenous dose is **very significantly less than the oral dose**
- Various conversion ratios have been suggested, depending on the type of transplant, the time after transplantation and various patient factors
- See SPC for details
- **Consultant specialist input and close monitoring of levels is required**

Hepatic impairment

- Dose reduction may be necessary in patients with severe hepatic impairment in order to maintain blood trough levels -under direction of transplant team

Monitoring

- **Observe patient** for at least 30 minutes after starting the infusion and at frequent intervals thereafter, including **neurological and visual status**
- Markedly **nephrotoxic**, monitor kidney function. Need to distinguish between rejection and tacrolimus induced nephrotoxicity if serum creatinine rises
- **Monitor** ECG, liver function, blood pressure, fasting blood glucose, serum potassium, magnesium, lipids, FBC, coagulation values, plasma protein values, neurological and visual status

Therapeutic drug monitoring recommended

- Monitor **whole blood trough** level. Take level from the arm that is not being infused
- During the early post-transplantation period - twice weekly
- Following dose adjustment
- Change of route
- Co-administration with interacting drug
- During episodes of altered bowel habits
- At regular intervals during maintenance therapy.
- Need to state dose regimen, time and date of last dose and of blood sample
- It is necessary to consider the clinical condition of the patient when interpreting whole blood levels

Suggested whole blood trough level (but specialist centres must be contacted)

Early post transplant

- Liver transplant: 5 to 20 ng/ml
- Kidney and heart transplant: 10 to 20 ng/ml

Maintenance therapy

- Liver, heart and kidney transplant: 5 to 15 ng/ml

Further information

- Irritant if **extravasation** occurs
- Consider ethanol content of injection (638mg/ml)
- Contraindicated if hypersensitive to macrolides
- **Vaccinations** may be less effective; avoid live attenuated vaccines
- If sublingual tacrolimus is being used as an alternative to oral tacrolimus, an initial dose of 50% of the oral dose is suggested (ie if a patient is on tacrolimus 1mg bd **PO**- then 0.5mg bd **sublingually** may be considered). Monitor tacrolimus levels and renal function if such an approach is used. This approach may only be done on the recommendation of a consultant nephrologist [ref 1,2]. Prograf immediate release capsules to be used for this purpose (unlicensed).

Storage

- Store below 25^{0}C, in the original package to protect from light.
- Due to the risks of oral to IV switch, and on the advice of nephrology **intravenous tacrolimus is NOT stocked in GUH**. For advice in patients unable to take oral tacrolimus seek an urgent nephrology opinion and refer to this document.

References

SPC 05/09/2024

1:Sublingual tacrolimus as an alternative to oral administration for solid organ transplant recipients. Pennington CA Park JM 2015 PubMed assessed online 3/10/2018 (full text article attached below)

2: Email communication with Nephrologists- Oct 2018, on file

Therapeutic classification

Macrolide immunosuppresssant