Tertiary/Quaternary Level Essential Drug List
Medication Review Summary

Medication Name: Tacrolimus **Date:** 18 April 2017

Indication:
Tacrolimus use as primary therapy in renal transplant recipients who have a high immunological risk and patients on ciclosporin therapy who experience steroid resistant biopsy proven acute transplant rejection.

Context:
The Calcineurin Inhibitors (CI) ciclosporin and tacrolimus are the mainstay of maintenance immunosuppression for renal allograft recipients to prevent acute allograft rejection, which reduces overall graft survival. Ciclosporin is used in both high and low immunological risk transplant recipients. The aim is to review the use of tacrolimus in recipients with high immunological risk and those who develop biopsy proven acute rejection while on ciclosporin.

Quality of evidence:
A meta-analysis and meta-regression of randomized trial data[i] was done in 2005 by Webster and colleagues. The review investigated tacrolimus versus ciclosporin as primary immunosuppression in renal transplant recipients. The analysis included 4201 randomized patients from 30 clinical trials.
The studies included in the meta-analysis were mostly small, with methods not well described, and overall the results are regarded as unreliable.

Clinical efficacy:
At one year, tacrolimus treated patients had less acute rejection (RR = 0.69, 95% CI 0.60 to 0.79) and less steroid resistant rejection (RR = 0.49, 95% CI 0.37 to 0.64) but more post-transplant diabetes mellitus (RR = 1.86, 95% CI 1.11 to 3.09). Treating 100 recipients at low risk (such as adult, well matched, first transplants) with tacrolimus instead of ciclosporin would avoid six cases of acute rejection; this rises to 17 cases when including recipients at high immunological risk (such as sensitized recipients of subsequent grafts, or children). Treating with tacrolimus however, would cause an extra five recipients to develop post-transplant diabetes mellitus.

Safety concerns:
Evidence from meta-regression suggests that targeting tacrolimus concentrations lower than 10 ng/ml will minimize graft loss and temper the increased risk of diabetes mellitus without increasing the risk of acute rejection.

Cost:

	Strength	Daily dose (70kg)	Total Dose	Cost per day	Cost per month
Tacrolimus	1mg or 5mg	0.1mg/kg/day	7mg	R 114.46	R 3 204.77
Ciclosporin	25 mg or 100 mg	5mg/kg/day	350 mg	R 52.80	R 1 478.22

Cost reference: HP04-2017 contract prices

Recommendation:
Tacrolimus is recommended for inclusion into the Tertiary/Quaternary Essential Medicine List. The indication is for primary therapy in high immunological risk renal allograft recipients and for recipients on ciclosporin who experience steroid resistant acute allograft rejection.

[i] Webster AC, et. al. Tacrolimus versus ciclosporin as primary immunosuppression for kidney transplant recipients: meta-analysis and meta-regression of randomized trial data. BMJ. 2005: 1-11.