Tertiary/Quaternary Level Essential Drug List
Medication Review Summary

Medication Name: anti-thymocyte globulin **Date:** 20 June 2017

Indication:
Induction therapy for prophylaxis against acute rejection in high-risk renal transplant recipients.

Context:
Induction therapy in the transplant setting is an intense prophylactic treatment strategy intended to lower the risk of acute rejection in the early post-transplant period. Current treatment protocols consist of lymphocyte depleting agents, including anti-thymocyte globulin (ATG) and interleukin 2 receptor antagonists (IL2-RAs).

ATG (ATG) is a polyclonal gamma immunoglobulin generated in animals by inoculation with human thymocytes. The final product contains cytotoxic antibodies directed against a number of antigens including those expressed on human T lymphocytes. T-lymphocyte depletion is believed to be the primary mechanism leading to ATG's immunosuppressive activity.

Recommendations pertaining to interleukin-2 receptor antagonists such as basiliximab are contained in separate documentation wherein basixilimab has been recommended for use in the prevention of acute rejection in low risk renal transplant patients. In that review, data reflected benefit of ATG over IL2RAs at certain time points. As kidneys suitable for transplantation are a scarce resource there is need to ensure that all reasonably measures are taken to secure the best possible clinical outcome in post-transplant patients.

Quality of evidence:
No new randomized controlled trials, systematic review or meta-analyses were identified after the 2010 Cochrane review by Webster and colleagues. Although this paper set out to review the efficacy of IL2RAs in this indication, the review has also yielded valuable information pertaining to the benefit of ATG and has been used as the basis of this recommendation.

Clinical efficacy:
Webster *et al* (2010) reported that when IL2-RAs and ATG were compared (18 studies, 1844 patients), there was no difference in graft loss at any time point, or for acute rejection diagnosed clinically. ATG therapy, however, reduced biopsy-proven acute rejection at one year (8 studies: RR 1.30 95% CI 1.01 to 1.67).

Safety concerns:
For patients receiving ATG, malignancy was reported to be increased at 1 year (7 studies: RR 0.25 95% CI 0.07 to 0.87) while CMV infection at time during the first year was also elevated (13 studies: RR 0.68 95% CI 0.50 to 0.93). It is important to review these safety concerns in terms of the absolute number of patients affected. For malignancy, 2 of 537 patients in the IL2RA group and 11 of 530 patients in the ATG were affected. For CMV infection, 149 of 864 patients receiving an IL2RA were affected compared with 184 of 783 patients in the ATG group. However, the Committee agrees that the benefit outweighs these risks. In particular, the risk of CMV can be mitigated by the judicious use of prophylactic valganciclovir.

Further considerations: COST

	Strength	Dose*	Cost	Total dose	Cost per course
Basiliximab	20mg/vial	20mg IV on day 0 and day 4	R 10 397.11**	40mg	R 20 794.22
ATG (Equine)	100mg/vial	Total dose 9mg/kg	R 3 671.00**	630mg (700mg)	R 25 697.00

*Dose based on GSH dosing protocols (based on 70kg) **Cost based on GSH buy out price March 2017

Recommendation:
ATG should be included on the Tertiary/Quaternary Essential Medicines List as induction therapy for high-risk renal transplantation recipients.