RE: RECOMMENDATION TO LIST RECTAL TACROLIMUS ON THE FORMULARIES OF WA PUBLIC HOSPITALS FOR USE IN INFLAMMATORY BOWEL DISEASE

The WA Drug Evaluation Panel (WADEP) recommends the listing of rectal tacrolimus ointment (extemporaneous preparation) for patients with resistant ulcerative colitis (UC) or Crohn’s disease (CD). Rectal tacrolimus may be prescribed by, or in consultation with a Gastroenterologist who has experience treating UC and CD. Prescribers should follow the attached algorithm which specifies the starting and stopping criteria for treatment for the following approved indications:
1. Resistant UC proctitis where active inflammation is limited to up to 25 cm from the anus
2. Resistant perianal Crohn’s disease
3. Cuffitis in patients with UC who have undergone proctocolectomy who have remaining affected rectal mucosa
4. Resistant pouchitis in patients who have undergone total colectomy

Inflammatory bowel disease (IBD) is a lifelong relapsing condition which can be difficult to manage. Patients will often require long-term systemic steroid treatment and surgical intervention and their quality of life may be significantly impacted from a young age. For patients with refractory pouchitis or cuffitis treatment options are limited and the last resort is permanent ileostomy. Oral tacrolimus has been shown as efficacious at high blood concentration levels however is also associated with an increased risk of adverse effects. Alternatively topical tacrolimus allows for high local mucosal concentrations with lower systemic absorption and therefore less risk of systemic side effects. Rectal tacrolimus provides patients with another topical option either in combination with or in trying to avoid systemic steroid and immunosuppression treatment.

WADEP considered two small cohort studies and one case series when evaluating the evidence for the use of rectal tacrolimus, all studies used rectal tacrolimus ointment in strengths between 0.3 – 1 mg/g in 3 gram doses twice daily. Rectal tacrolimus was found to effective at 8 weeks in 75% (6/8) of patients with refractory UC1, 87.5% (7/8) refractory oral and/or ulcerating perianal CD paediatric patients had responded to treatment at 6 weeks2 and at 12 weeks 75% (3/4) patients with perianal or ulcerating anal disease3. However the long-term evidence of remission, rates of relapse and need for surgical intervention is lacking.

Rectal tacrolimus is required to be extemporaneously prepared by a TGA licensed compounding facility. WADEP consider rectal tacrolimus cost-effective at a maximum cost of $800 for 60 doses (not including the applicator cost) and it is estimated that 25 – 30 patients will be eligible for treatment per annum across the state. WADEP consider rectal tacrolimus as novel with limited evidence at this point however understand the difficult position patients are in when their disease is refractory to all other treatment options. The Panel will review the listing with the emergence of further evidence.

Richard Wojnar-Horton
Chairman, WADEP

3 Hart AL, Plamondon S, Kamm MA. Topical Tacrolimus in the Treatment of Perianal Crohn’s Disease: Exploratory Randomised Controlled Trial. Inflamm Bowel Dis 2007; 13(3):245-53
Rectal Tacrolimus for Refractory Inflammatory Bowel Disease

**Rectal Tacrolimus**

0.5 mg/mL, 3 mL twice daily

Prescribers are encouraged to contact the hospital pharmacy department in advance to allow sufficient time to arrange supply.

**Remission or significant response**

1. Change to 1 mg/mL, 3 mL at night

   Attempt to wean down tacrolimus every 1 – 2 months:

   2. Reduce frequency to 0.5 mg/mL, 3 mL alternating with 5-ASA suppository at night

   3. Wean off tacrolimus as appropriate and maintain on 5-ASA suppositories

**Response**

Increase dose to 0.8 – 1 mg/mL, 3 mL twice daily

Review every 3 monthly

**No clinical or endoscopic response**

If no response by 12 weeks of treatment then rectal tacrolimus must be ceased.