NORFOLK AND WAVENEY STP THERAPEUTICS ADVISORY GROUP (TAG)

SHARED CARE AGREEMENT

Shared care guidelines for use of Tacrolimus in Ulcerative Colitis
Monitoring level Amber Level 1 – Prescribe drug and perform higher level of monitoring, e.g. 6-monthly

Generic and Proprietary/Brand Name

Tacrolimus (please use generic preparations)

Indications for shared care

Maintenance and induction of remission in patients with ulcerative colitis who have failed to respond to or not tolerated thiopurines and/or methotrexate.

Specialist Prescribing and Monitoring Responsibilities – summary. Full details in main body of document	GP / Community Team - Primary Care Prescribing and Monitoring Responsibilities – summary. Full details in main body of document
• Review patient in clinic • Inform the patient of side effects and long term monitoring before initiating treatment. • Prescribe for at least three months until stable. • Inform the GP when tacrolimus is initiated. Write to the GP to request they take over prescribing. • Inform the patient/carers of the arrangements being made to share care with their GP, including information on who will be monitoring each aspect of therapy. • Inform the GP of the results taken at each clinic visit and action required • Weekly monitoring for 4 weeks, monthly monitoring for 3 months then 3-monthly monitoring indefinitely. Monitoring consists of the following: FBC, U&Es, LFTs, glucose, tacrolimus level.	• Prescribe tacrolimus once the patient has been stabilised and side effects have been excluded • If the GP has concerns over the prescribing of tacrolimus, they will contact the consultant gastroenterologist as soon as possible. • Identify adverse effects and treat or report to consultant • Alert gastroenterology unit to any identified non-compliance with immunosuppressants • Avoid drug interactions • Avoid live vaccines • If a patient presents with a likely infection an urgent FBC and urea & electrolytes should be taken (see section on Indication for referral back to specialist)

Patient Information

All patients will receive counselling and information regarding indications for treatment, potential side effects and need for monitoring from the IBD nurses prior to treatment initiation.

Specialist Contact Details

- Inflammatory Bowel Disease (IBD) helpline – Tel 01603 288403
- If Helpline not available then please contact IBD nurse directly via NNUH switchboard (01603 286 286) and request bleep 0493.
    - Dr. Mark Tremelling 01603 288612
    - Dr. Richard Tighe 01603 288230
    - Dr Simon Chan 01603 288534
    - Dr. Ian Beales 01603 288366
    - Prof. Alastair Watson 01603 288366

GENERAL PRINCIPLES FOR SHARED CARE PRESCRIBING

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- GPs are **invited** to participate. If GPs are not confident to undertake these roles, they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.
- **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable if they are unwilling to do so.**
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and when the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring.
- **The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.**

Background to Treatment
NICE recommend the addition of oral tacrolimus to oral prednisolone in out-patients and in-patients with mild to moderate ulcerative colitis who are steroid dependent despite adequate doses of alternative immunosuppressants. This is currently an unlicensed indication for the induction and maintenance of remission in ulcerative colitis.
Licensed use and agreed local off-label use
Tacrolimus is a potent immunosuppressant normally used in the prevention of solid organ rejection in transplant patients.
Criteria for Patient Selection
Out-patients and in-patients with mild to moderate ulcerative colitis which relapses on withdrawal of steroids despite optimised doses of alternative immunosuppressants, (normally azathioprine, mercaptopurine or methotrexate) or who are unable to tolerate these immunosuppressants.
Form and strength of preparation
500mcg, 1mg, 5mg capsules
Side Effects and Management
Link to BNF Link to SPC
Drug Interactions
Link to BNF Link to SPC
Cautions and Contraindications
Link to BNF Link to SPC
Initiation of therapy and ongoing dose regimen
Consultant Gastroenterologist. Treatment indication will be reviewed in out-patient clinic at least 4 monthly initially. If ineffective tacrolimus will be stopped. If effective and tolerated then treatment will normally continue for at least 12 months. **Initial dose** - 0.1mg/kg/day in two divided doses with subsequent doses guided by serum levels Maintenance dose - Tacrolimus dose adjusted to achieve a trough level of 5-10ng/ml

Duration of therapy / How the treatment will be reviewed and if appropriate, stopped

It is usual to administer the drug for a period of several months but the optimal duration of therapy is not known and will be decided on an individual basis for each patient by the patient's consultant gastroenterologist. In studies of ulcerative colitis, tacrolimus has been given for 12 months and occasionally longer.

Baseline assessment and ongoing monitoring – by Specialist

Weekly monitoring for 4 weeks, monthly monitoring for 3 months then 3-monthly monitoring indefinitely. Monitoring consists of the following: FBC, U&Es, LFTs, glucose, tacrolimus level.

- The tacrolimus dose will adjusted to achieve a trough level of 5-10ng/ml. The patient should be advised to attend for their blood test in the morning and to delay that morning's dose of tacrolimus until after the blood has been taken (must be a trough level). An EDTA sample (as for full blood count) is required.
- Initially FBC, U&Es, LFTs, glucose and tacrolimus levels will be done weekly for at least 4 weeks until a stable level is achieved. This is followed by monthly testing for 3 months.

Results and actions to be taken:

Monitoring	Indication for intervention	Intervention
WCC	Below 3.5 ($x10^9$/L) or neutrophil count less than 1.5 ($x10^9$/L)	**STOP** tacrolimus Monitor WCC weekly When within normal range if it has been effective recommence tacrolimus at lower dose (1/2 of previous dose) and build up to optimal dose as tolerated.
Creatinine	Above 130mmol/L	Reduce dose of tacrolimus by 1/3 Monitor creatinine weekly **If** creatinine continues to rise – **STOP** tacrolimus, arrange clinic review to assess other causes for possible raised creatinine and need for ongoing therapy.
Tacrolimus trough levels	<5ng/mL	Increase dose by 1/3. This necessitates reintroduction of weekly monitoring.
	>10ng/mL	Decrease dose by 1/3. This necessitates reintroduction of weekly monitoring.
Drug related side effects		Decrease dose by 1/3. This necessitates reintroduction of weekly monitoring.
Blood pressure	Systolic > 150mmHg	Decrease dose by 1/3. This necessitates reintroduction of weekly monitoring.

- To send a letter to the GP requesting shared care for a patient regarding continued prescribing of tacrolimus once a satisfactory initiation period has been achieved.
  - Diagnosis
  - Results of blood tests
  - Results of other appropriate investigations
  - Dose and name of treatment
  - Advice on dose alterations where appropriate

- Patients on tacrolimus will be reviewed in clinic at least every 4 months for the first year by a consultant or a specialist registrar or nurse specialist in discussion with a consultant.
- Annual cholesterol

GP / Community Team or other Primary Care monitoring responsibilities

- Identify adverse effects and treat or report to consultant gastroenterologist where appropriate
- If a patient presents with a likely infection an urgent FBC and urea & electrolytes should be taken (see section on Indication for referral back to specialist)
- Alert the specialist to any identified non-compliance with immunosuppressants

Consultant / Specialist prescribing responsibilities

- Review patient in clinic
- Inform the patient of side effects and long term monitoring before initiating treatment.
- Prescribe tacrolimus for at least three months until the immunosuppression regimen is stable.
- Inform the GP when tacrolimus is initiated. When the patient is near completing a satisfactory initiation period, the consultant gastroenterologist will write to the GP to request they take over prescribing.
- Inform the patient/carers of the arrangements being made to share care with their GP, including information on who will be monitoring each aspect of therapy.
- Inform the GP of the results taken at each clinic visit. Any action required will be taken by the consultant gastroenterologist and information on any changes to medication will be given in the accompanying letter.

GP prescribing responsibilities

- Prescribe tacrolimus once the patient has been stabilised on therapy and side effects have been excluded as far as possible by the hospital.
- If the GP has concerns over the prescribing of tacrolimus, they will contact the consultant gastroenterologist as soon as possible.
- Identify adverse effects and treat or report to consultant gastroenterologist where appropriate.
- Alert gastroenterology unit to any identified non-compliance with immunosuppressants
- Avoid drug interactions
- Avoid live vaccines

It is vital that doses are not changed without first consulting the gastroenterology physician.

Indications for referral back to Specialist

- Neutropenia (white cell count <3.5 * 109/L, neutrophils <1.5 * 109/L
- Significant decline in renal function (creatinine > 130mmol/L)
- Hypertension systolic bp > 150mmHg
- Concerns by GP or patient

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Document history:

Version	Date	Author / Editor	Status	Comment
1.0	January 2014	Dr Simon Chan, Registrar in Gastroenterology and Dr Mark Tremelling, Consultant Gastroenterologist, Norfolk and Norwich University NHS Trusts / Fiona Marshall TAG Lead Pharmacist	Draft proposal	For consideration by the TAG. Submitted with NNUH business application.
1.1	February 2014	As for 1.0 above	Current	Draft re-proposal post NNUH DTMMC meeting Feb 2014 - amended to reflect that responsibility for blood testing and monitoring remains with the specialist. Supported by the TAG March 2014 – published as Version 1.
2.0	August 2016 – March 2017	Dr S Chan and Dr M Tremelling / Fiona Marshall, TAG lead Pharmacist, NEL CSU	Draft	Updated into format of current shared care agreement template. Sent to the NNUH for review. No recommendations for change received. Supported by the TAG for continued use March 2017.
3.0	Aug 2021	Jen Carroll, TAG Lead Technician	FINAL	Discussed at August 2021 TAG meeting. Review dates extended for a year from meeting due to covid pressures
4.0	Feb 2024	Jen Carroll, TAG Lead Technician	FINAL	Existing SCA transferred to new template ready for publication on KNoW. For TAG review