Name of Shared Care Agreement:

AZATHIOPRINE/6-MERCAPTOPURINE: **Oral immunomodulating drugs for inflammatory bowel disease.**
Reference number: 01/2008

Shared care agreement has been developed appropriately	Signed: ***A Radley*** For Medicines Policy Group Date:
Shared care agreement meets the governance requirements of NHS Tayside	Signed: ***A Timoney*** For Area Drug and Therapeutics Committee Date:
Protocol has been reviewed by Primary Care Services and remuneration for monitoring requirements by GPs (if any) has been negotiated	Signed: ***A Russell*** For Primary Care services Date:

Where there is a substantial shift in expenditure from hospital prescribing to GP/ nurse prescribing as a result of this shared care protocol, each clinical group must discuss budgetary implications with the CHP lead pharmacists/ general managers.

Shared care agreement: AZATHIOPRINE/6-MERCAPTOPURINE

This agreement provides additional limited information necessary to help in the treatment of patients with inflammatory bowel disease that are prescribed these drugs. Significant prescribing issues are highlighted but the agreement should be used in conjunction with the ABPI summary of product characteristics where available:http://www.medicines.org.uk/

1. Therapeutic use & Background	Azathioprine and 6-mercaptopurine are antimetabolite drugs that interfere with nucleic acid synthesis. Azathioprine is extensively metabolised to mercaptopurine in vivo. Both are used as second line therapy for patients with steroid dependent ulcerative colitis or Crohn's Disease or where there are frequent relapses or severe disease. Mercaptopurine is an option where azathioprine has been beneficial but patients were unable to tolerate its side effects. The use of these drugs in inflammatory bowel disease is well established but currently unlicensed.
2. Indications for therapy	Treatment of adults with inflammatory bowel disease. Resistant or frequently relapsing cases of ulcerative colitis and Crohn's disease.
3. Typical Dosage Regimen	**Azathioprine:** the usual dosage range is 2 to 2.5 mg/kg body weight daily in one or two divided doses. **Mercaptopurine**: the usual dosage range is 1 to 1.5 mg/kg body weight per day in one or two divided doses. The dose should be adjusted by the specialist within these limits, depending on clinical response and haematological tolerance.
4. Administration	Drug therapy should be initiated and prescribed by the hospital consultant.
5. Annual cost of therapy	The annual cost of therapy depends on the dose the patient is receiving for the individual conditions: For example as a guide only: • Azathioprine 25mg daily for 28 days – £ 8.14 • Azathioprine 50mg daily for 28 days - £ 4.33 • Azathioprine 75mg daily for 28 days - £ 12.91 • Azathioprine 100mg daily for 28 days - £ 8.66 • Mercaptopurine 100mg daily for one month –£42.06 Costs as Drug Tariff April 2008 and MIMS May 2008. Costs may vary depending on pack size used for dispensing.
6. Adverse effects, precautions and contra-indications	**Contraindications** • Hypersensitivity to azathioprine or mercaptopurine. **Cautions** • Renal, hepatic impairment and elderly patients. The doses used in these patient groups should be at the lower end of the normal range and the haematological response should be carefully monitored**.**

	• Patients with documented pre- existing low levels of thiopurine methyltransferase (TPMT) • Vaccinations Vaccination with live vaccines (for example polio, rubella) is not recommended. • Pregnancy Both men and women taking either mercaptopurine or azathioprine who are considering starting a family should contact their consultant for further advice. If unplanned pregnancy occurs whilst taking mercaptopurine, the patient should be referred back to the hospital specialist for advice. • Breastfeeding Contact NHS Tayside medicines information unit for the most up to date information • Alcohol may be taken in moderation • Sunscreens and skin cancer-There is an increased risk of patients developing skin cancer. Follow the advice given in the patient information leaflet **Adverse effects** 1. General signs of malaise, dizziness, diarrhoea, rash, myalgia and arthralgia can occur infrequently. If severe, refer to the specialist 2. Nausea and vomiting. Giving a single dose at night or taking the tablets after food may improve nausea. If nausea remains troublesome, an anti-emetic can be tried, but if unsuccessful the dose will need to be reduced 3. Rash or mouth ulcers may respond to dose reduction, but stop if severe 4. Hypersensitivity reactions 5. Dose related bone marrow suppression. Patients should be advised to report immediately any signs or symptoms of bone marrow suppression e.g. infection, unexplained bleeding and bruising 6. Rarely azathioprine and 6-mercaptopurine may cause cholestatic hepatitis or pancreatitis. **If suspected, contact the specialist urgently.**
7. Common drug interactions	**Azathioprine and 6-mercaptopurine** • **Allopurinol** may enhance the effects of this drug and precipitate toxicity. If a patient is already taking allopurinol, it should be stopped and an alternative therapy prescribed. • **Antibacterials**- increased risk of toxicity with co-trimoxazole and trimethoprim • **Anticoagulants**-anticoagulant effect of warfarin is possibly reduced. Regular INR monitoring should be undertaken if both agents are used. • **Clozapine**- avoid concomitant use –increased risk of agranulocytosis • **Aminosalicylates** e.g**.** sulfasalazine, mesalazine may inhibit the TPMT enzyme and contribute to bone marrow toxicity. FBCs and LFTs should be monitored more closely after the introduction of these drugs by the specialist team

	• **ACE inhibitors**-There may be an increased risk of leucopenia with concomitant use of ACE inhibitors. **This list is not exhaustive.** Please use the current edition of the BNF, SPC and Stockley's Drug Interactions for up to date information about potential interactions when co-prescribing other drugs. Contact NHS Tayside medicines information unit (01382 34374) for further advice if needed.
8. Monitoring	• U&ES/LFTs/FBC should be checked weekly for the first 8 weeks and 2 weeks after any dose changes. • Thereafter monthly FBCs are recommended. • U&Es and LFTs should be checked every 8 weeks when on a stable dose. A rise in MCV is to be expected. If an isolated MCV rise, check for other causes (B12, TFT, folate and alcohol consumption). A high MCV is not an indication to stop treatment. Early use of antibiotics should be considered during periods of infection and the FBC checked. As a guide, GPs should **withhold treatment and contact the hospital specialist if:** • WCC< 4 X 10 g /litre • Neutrophils < 2 x 10 g/litre • Platelets < 150 x 10 g /litre • ALT > 2 times the upper limit of normal • The patient develops unexplained rash/ abnormal bruising • The patient develops oral ulceration or a sore throat
9. Pharmaceutical aspects	No special considerations
10. Secondary care contact information	Tayside IBD Service Department of Gastroenterology Ninewells Hospital & Medical School Dundee DD1 9SY Tel: ext 33118 Fax: 01382 425504 GI registrar: bleep 4482
11. Responsibilities of initiating consultant	• Select patients requiring azathioprine/ 6-mercaptoprine therapy • Discuss with the patient the risks and benefits of treatment • Refer patient to specialist nurse where appropriate (eg new patient) for advice on the treatment and monitoring requirements. • Provide patient/ carer with relevant patient information leaflets on use, side- effects and need for monitoring of medication • Ensure that patients understand the nature and complications of drug therapy and their role in reporting adverse effects promptly • Decide on the dose, frequency, duration of therapy and subsequent dosage adjustments. • Arrange shared care with the patient's GP • Provide shared care monitoring record booklet if used • Complete baseline tests FBC, LFTs, U&Es • Monitor response to treatment and the need to continue therapy • Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is

	reviewed • Notify GP if patient fails to attend for monitoring and advise GP on appropriate action • Provide any other advice or information for the GP if required
12. Responsibilities of primary care	• Prescribe azathioprine/6-mercaptopurine on the specialist's advice • Arrange and record ongoing monitoring as agreed with specialist • Identify and report adverse events to the specialist and the CSM • Ensure no drug interactions with other medicines • Ask the patient about oral ulceration/ sore throat, unexplained rash or unusual bruising at every consultation • Prompt referral to a specialist if there is a change in the patient's status • Stopping treatment in the case of a severe adverse event or as shared care agreement
13. Responsibilities of patients	• Consent to the shared care treatment • Must not exceed the recommended dose • Attend regular appointments with specialist centre and GP for blood tests • Report any side effects to the specialist or GP whilst taking these drugs
14. Supporting documentation	• Patient information leaflet for Azathioprine/6-Mercaptopurine • Patient information leaflet: Avoidance of Skin Cancer during treatment with Azathioprine/ 6-Mercaptopurine
15. Patient monitoring booklet	Not used.
16 GP letter	Attached below
17. Consultation	Tayside IBD service including specialist doctors, nurses and pharmacists. Tayside Medicines Governance Unit
Guideline date	July 2008
Guideline review date	July 2010

Shared Care Agreement Form

Consultant request

Dear Dr ***IMPORTANT: ACTION NEEDED**

Patient name:
CHI:
Diagnosis:

This patient is suitable for treatment with (*insert drug name*) for the treatment of

(insert indication)

This drug has been accepted for Shared Care according to the enclosed protocol (as agreed by ADTC and Primary Care services). I am therefore requesting your agreement to share the care of this patient.

Treatment was started on (*insert date started*) (*insert dose*)

If you are in agreement, please undertake monitoring and treatment from *(insert date*)
NB: date must be at least 1 month from initiation of treatment).

Baseline tests: *(insert information)*

Next review with this department: *(add date)*

You will be sent a written summary within 14 days. The medical staff of the department are available at all times to give you advice. The patient will not be discharged from out-patient follow-up while taking *(insert name of drug)*.

Please use the reply slip overleaf and return it as soon as possible.

Thank you.

Yours

Signature

Consultant name

GP Response

Dear Dr

Patient *(Insert Patients name)*

Identifier *(Insert Patient CHI/address)*

I have received your request for shared care of this patient who has been advised to start *(insert name of drug)*

A I am willing to undertake shared care for this patient as set out in the protocol

B I wish to discuss this request with you

C I am unable to undertake shared care of this patient.

GP signature Date

GP address/practice stamp