Shared Care Guideline:

DAPSONE for the treatment of IMMUNOBULLOUS DISEASES, NEUTROPHILIC DERMATOSES and CUTANEOUS VASCULITIS

County Durham & Tees Valley Area Prescribing Committee

Drug	DAPSONE
Indications	• Immunobullous diseases e.g. dermatitis herpetifromis, bullous pemphigoid, linear IgA disease, and others • Neutrophilic dermatoses e.g. Sweet's syndrome, pyoderma gangrenosum, and others • Cutaneous vasculitis including urticarial vasculitis • Cutaneous lupus
Overview	Dapsone is structurally related to the sulphonamides and shares their antimicrobial action. It also has anti-inflammatory actions that account for much of its use in dermatological diseases.
Specialist's Responsibilities	**Initial investigations:** FBC, reticulocyte count, U&Es, eGFR, LFTs and glucose-6-phosphate dehydrogenase level (G6PD), urinalysis Assessment for any medical condition (e.g. cardiorespiratory) that might be exacerbated by a minor reduction in haemoglobin level **Initial regimen:** 50mg once daily is the usual starting dose then it can be gradually adjusted to 1-2mg/kg/day depending on response, tolerance and nature of condition treated **Clinical monitoring:** For adverse effects and usual disease management **Frequency:** Usually every 3 months once stabilisation phase is reached (unless instructed differently by the responsible clinician in certain high risk patients) **Safety monitoring:** FBC, reticulocytes, U&Es, LFTs weekly in the first month, fortnightly in the second month then monthly for 2 months; then every 3 months provided the stable phase of treatment regime achieved Urinalysis every 3 months (looking for haemolysed haemoglobin) Urgent FBC if patients develop symptoms suggestive of agranulocytosis **Prescribing duration:** Minimum of 3 months from hospital then transferred to GP **Prescribing details:** **Documentation:** Clinic letters and nurse-led monitoring clinic proformas
GP's Responsibilities	**Maintenance prescription:** 50mg -100mg daily in majority of patients (as advised at transfer) **Clinical monitoring:** For adverse effects and usual disease management **Safety monitoring:** FBC, reticulocytes, U&Es, LFTs and urinalysis every 3 months **Frequency:** Every 3 months (unless otherwise indicated by the treating clinician)

Duration of treatment: Long-term as recommended by specialist

Re-referral criteria: See table in Adverse Event Section

Documentation:

Adverse Events

Adverse events	Action
Haemoglobin drop of 1-2g/DL	Continue treatment, this is expected especially in the first few weeks of Dapsone introduction. Please check ferritin, B12 and folate to exclude other co-incidental causes.
Haemoglobin drop of >2g/DL	Withhold & discuss with specialist
Significant drop in neutrophil count: (especially < $1x10^9$/L)	Withhold & discuss with specialist
Derangement of LFTs: (ALT > twice of the upper normal limit)	Withhold & discuss with specialist
Derangement of renal function +/- proteinuria (If eGFR <30ml/min)	Withhold & discuss with specialist
Fever, mouth ulcers and sore throat	Withhold, check FBC and discuss with specialist
Methaemoglobin levels >20%	Withhold & discuss with specialist (secondary care input required to organise)
Methaemoglobin levels >30%	Withhold and discuss with specialist: (secondary care input required to organise) may require treatment with cimetidine 400mg tds or oxygen and methylene blue (in hospital)

Contra-indications Cautions Drug Interactions

Please refer to the BNF and/or SPC for information

Other Information

Adverse Effects

- **Haemolysis and haemolytic anaemia** are dose related and due to reduced erythrocyte survival. Mild haemolysis with a drop in Hb of 1-2g/DL occurs in most patients at a standard therapeutic dose.
- **Gastrointestinal adverse effects** such as anorexia, nausea and vomiting may occur. Hepatitis, jaundice, cholestasis and abnormal LFTs may also occur.
- **Methaemoglobinaemia** can lead to symptoms of headache, shortness of breath, lethargy and a bluish/brown discolouration to lips and fingertips. Methaemoglobinaemia does not always require treatment unless patients are symptomatic. If the level is >20% then dapsone should be discontinued; at a level of >30% the patient is likely to require cimetidine and methylene blue.
- **Agranulocytosis** is a rare side effect occurring in about 1 in 10000 prescriptions. It is usually gradual in onset occurring within 2-16 weeks of starting therapy, but may be sudden.
- **Dapsone hypersensitivity syndrome** is a serious side effects and usually takes the form of DRESS type reaction. It is estimated to occur in 1% of patients. The onset is usually within 4-6 weeks of starting therapy but may be delayed up to 6 months.
- **Severe cutaneous reactions** including toxic epidermal necrolysis and Stevens Johnson syndrome have also been reported.
- **Peripheral motor and sensory neuropathies** have been reported rarely. They are dose related and caused by axonal damage. Headache, insomnia, malaise and rarely

psychoses have been reported.
- **Renal adverse effects** include proteinuria and very rarely nephrotic syndrome.

Contraindications
Dapsone hypersensitivity, previous adverse reaction to sulphonamides, acute porphyria, severe ischaemic heart disease or pulmonary disease, severe anaemia (treat before starting dapsone), severe G6PD deficiency.

Cautions
Cardiac, peripheral vascular and pulmonary disease- particularly in the elderly who may not tolerate minor reductions in haemoglobin concentration.
Other conditions predisposing to haemolysis.
Dapsone can artefactually lower glycosolated haemoglobin (HBA1c) levels in patients with diabetes and impair disease monitoring.
Product contains lactose.

Essential patient information
Patients should be advised of the need to attend for regular monitoring and to seek urgent medical attention if affected by the following:
- Sore throat, mouth ulcers, purpura, bleeding- may indicate agranulocytosis/ bone marrow suppression
- Shortness of breath, angina, jaundice- may indicate significant haemolysis.

Pregnancy and fertility
Dapsone can cross the placenta and avoidance in pregnancy is preferred if possible (pregnancy category C in the US). Limited evidence form case series of its use in linear IgA disease and leprosy suggest that dapsone can be used on a selective basis and such decision should be left for the treating clinician after appropriate counselling of the patient. The greatest risk is in the last trimester when it may lead to neonatal haemolysis and methaemoglobinaemia. If dapsone is used then folic acid 5mg once daily should be given to the mother throughout pregnancy.
Dapsone can also reduce sperm count and motility in males.

Lactation
Dapsone is secreted in breast milk and absorbed by the infant with a risk of inducing haemolytic anaemia, hence avoid in lactation if possible.

Important drug interactions
Rifampicin and rifabutin: induces dapsone metabolism and enhances urinary excretion.
Cimetidine: inhibits formation of toxic hydroxylamine metabolites and increases the therapeutic/toxic ratio.
Trimethoprim and co-trimoxazole: decreases renal clearance of dapsone and increases the risk of toxicity.
Nitrofurantoin: use with caution due to increased risk of side-effects.
Antiepileptics: use with caution due to increased risk of side-effects.
Antimalarials (chloroquine, primaquine): use with caution due to increased risk of side-effects.
Folic acid antagonists (e.g. Methotrexate: increase in dapsone levels; increased risk of side effects.
Sulphonamides: increased risk of haemolysis.
Clozapine: contraindicated due to the risk of blood dyscrasias.
Saquinavir: contraindicated due to the risk of cardiac arrhythmias.
Probenecid: reduces renal clearance of dapsone and increases the risk of toxicity.

Contact Details

Name: Dermatology : Email stees.dermatologymonitoring@nhs.net or contact Monittel 01642 854722 or the Dermatologist responsible for the care of the patient

Trust Logo
Department of …….

GP name
GP address

Dear Dr …… **Date:**

Request for Shared Care of XXXXXX

Re: Patient's name DOB:
Address Hospital Number:

This patient has been prescribed **……** for the management of ……..

The patients' current dose is ……per day

The patient was commenced on this drug on ……..and has been stable on the current dose since ……

I would now like to ask you to take over the responsibility for prescribing this medication for this patient, as agreed by your CCGs and the Area Prescribing Committee.

The shared care document lists the monitoring requirements for this medication. Can I ask that any problems are reported back into secondary care.

The next blood monitoring is due on …… and should be continued in line with the shared care guideline.

In addition, the following patient specific monitoring is required for this patient

……
This is part of the shared care guideline approved by the Area Prescribing Committee, available at http://medicines.necsu.nhs.uk/guidelines/durham-darlington/.

The patient will remain under regular clinical review by his or her usual consultant/ specialist nurse as described in the shared care agreement.

Please send back the second part of this letter, within 28 days, so we know that we have your agreement to this arrangement. If you are not happy to accept this patient or have any concerns, then please contact my secretary as soon as practically possible

Yours sincerely

Consultant name
Contact details

GP Agreement

Patient's Name:
DOB:
Hospital No:

I agree to take over the prescribing and monitoring of XXXXXXXXX in line with the approved shared care document as found at http://medicines.necsu.nhs.uk/guidelines/durham-darlington/

Dose to be prescribed ……..

Dated ……/……/

Signed: …….

GP's Name:

GP contact details

Please return to Consultant's secretary. You may wish to keep a copy for your records.