# Specialised Medicines Service Guideline ~ Dapsone for the treatment of dermatitis herpetiformis and other dermatoses in adults

**This guideline highlights significant prescribing issues. Not all prescribing information and potential adverse effects are listed. Please refer to the BNF and individual product SPCs for full prescribing data.**

**Specialist:** Please complete letter at the end of this document and send together with the shared care guideline to the GP.

**GP:** Please indicate whether you wish to share patient's care by completing letter at the end of this document and return to specialist.

GPs are invited to participate. If a GP is not confident to undertake these roles, then 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.

**The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.**

## Introduction and aims of treatment

Dapsone is an antibacterial medicine belonging to the sulfonamide class of antibiotics. The mechanism of action is probably via the inhibition of folic acid synthesis in susceptible organisms. It acts as an anti-inflammatory drug and has been used successfully as a treatment for several skin conditions such as dermatitis herpetiformis, pyoderma gangrenosum, Sweet's syndrome and vasculitis for many years. It may also be used for other inflammatory skin conditions, where other treatments are ineffective.

**This guideline covers the use of dapsone within the licensed indications of treatment of dermatitis herpetiformis and other dermatoses, in adults.**

Dapsone is licensed for a number of other indications; these are outside the scope of this guideline.

## Specialist responsibilities

- Assess the patient, establish a diagnosis and the need for treatment with dapsone
- Discuss with the patient (and/or carer) the benefits, side effects (and when and how to seek medical advice), potential for drug interactions, frequency of dosing and monitoring requirements of dapsone treatment; provide relevant supporting information in writing. Ensure the patient understands that treatment may be stopped if they do not attend for monitoring & treatment review
- Undertake baseline tests (see "Monitoring", below)
- Prescribe dapsone and stabilise the patient on a therapeutic dose. Prescribing and monitoring will remain in secondary care until the patient is stable and GP agrees to share care (**minimum two months** – see "Monitoring", below)
- Ask the GP in writing whether they are willing to participate in the sharing of care for a particular patient. Include all relevant test results (GPs may not have access to these results in primary care)
- Advise GP (in writing) of any dose changes required, highlighting where necessary the need for increased frequency of monitoring and the duration thereof (see "Monitoring", below)
- If increased frequency of monitoring is required (in primary or secondary care), communicate this to the patient
- Continue to review the patient at agreed specified intervals (including response to treatment and need to continue therapy), sending a written summary to the GP whenever the patient is reviewed, including the current dose to be prescribed and any relevant test results
- Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required
- Provide any other advice or information for the GP if required.

# General practitioner responsibilities

- Ensure a timely reply is sent to specialist in response to request for shared care

If GP has agreed to share care:

- Prescribe dapsone in accordance with these guidelines, and on the advice of a specialist
- Ensure the patient understands when and how to seek medical advice regarding side effects (see below)
- Undertake ongoing monitoring as specified. Review and act on results or reported side-effects as described in monitoring section below
- Ensure that the results of monitoring are recorded in the patient's notes
- Follow specialist advice on any changes in treatment
- Report adverse events to specialist, and to MHRA via yellow card scheme
- Stop treatment/amend dose in the case of a severe adverse event or as per prescribing guideline
- Report and seek advice from specialist on any aspect of patient care which is of concern to GP.

# Monitoring

**Baseline assessment & ongoing monitoring to be completed by specialist service provider:**

| **Monitoring** | **Frequency** |
|---|---|
| Glucose-6-phosphate dehydrogenase (G6PD) deficiency | Baseline |
| Urea, electrolytes and creatinine<br>LFTs<br>FBC<br>Reticulocyte count | Baseline; then weekly for 1 month; then again 1 month later |

**Monitoring (and action to be taken) during treatment to be completed by the GP:**

| **Monitoring** | **Frequency** |
|---|---|
| LFTs<br>FBC<br>Reticulocyte count (This is not reported in standard FBC results; and **must be specifically requested**) | Monthly for two months, then<br>Every three months<br>(more frequently following dose increase e.g. weekly for 1 month, then monthly for 3 months, then every three months) |

| Test results | Action to be taken |
|---|---|
| LFTs >2 times the upper limit of reference range, **OR** below 2 times the upper limit of reference range but >3 fold rise | **If results meet specified criteria, stop treatment and seek specialist advice.**<br>If small rise in values, early next test. |
| Bilirubin >3 times the upper limit of reference range | **Consider haemolytic anaemia -** seek specialist advice |
| WCC <3.5 x $10^9$/L | **If results meet specified criteria, stop treatment and seek specialist advice.**<br>In addition to absolute values, a rapid fall or consistent downward trend should prompt caution and extra vigilance – consider early re-test and/or seek specialist advice.<br>If isolated MCV rise, check for other causes (B12, folate, thyroid function and alcohol consumption). If results are normal, seek specialist advice. |
| Neutrophils <2.0 x $10^9$/L | |
| Haemoglobin decrease >20g/L from baseline | |
| Platelets <150 x $10^9$/L | |
| MCV >105fl<br>*(In West Devon, the threshold for action is **>108fl** due to local reference range differences, however if blood samples are not being analysed by Derriford Hospital lab, confirm MCV threshold for action with specialist)* | |
| Reticulocyte count | If there is a steady rise in reticulocyte count (even if within normal limits) accompanied by a decrease in haemoglobin and/or signs or symptoms suggestive of anaemia, **seek specialist advice.** |

**Additional action to be taken by GP if the patient reports any of the following adverse effects:**

| **Symptoms** (See also adverse effects section) | **Action to be taken** |
|---|---|
| *Methaemoglobinaemia*<br>(shortness of breath, headache, fatigue, dizziness, blueish skin or lips, chest pain or palpitations) | Stop dapsone immediately and seek immediate admission. |
| *Dapsone syndrome*<br>(rash, fever and eosinophilia – see adverse effects, below) | Stop dapsone immediately and seek specialist advice about urgent admission; consider immediate admission if warranted. |
| *Cutaneous hypersensitivity reactions*<br>(Stevens-Johnson syndrome, toxic epidermal necrolysis etc. see adverse effects, below) | |
| Any of the following: mouth ulcers or bleeding gums, sore throat, fever, epistaxis, unexpected bruising or bleeding, unexplained illness or infection | See patient within 24 hours of contacting the practice for urgent FBC and LFT. Signpost patient to alternative provider if this is not possible e.g. weekend/bank holiday |

# Patient responsibilities

- Tell the GP or specialist if they have any concerns or do not understand any aspect of treatment
- Attend specialist, GP, practice nurse and blood test appointments
- Understand that treatment may be stopped if they do not attend for monitoring & treatment review
- Take (or support administration of) medication as directed by the prescriber
- MUST **urgently** report any of the following to their GP and/or specialist (if out of hours, seek alternate medical advice e.g. NHS 111):
    - Shortness of breath, headache, fatigue, dizziness, blueish skin or lips, chest pain or palpitations

    - Rash, fever, malaise
    - Mouth ulcers or bleeding gums, sore throat, nose bleeds, unexpected bruising or bleeding, unexplained illness or infection
- Report any other side effects to the doctor or nurse
- Talk to their doctor as soon as possible if they become pregnant or are planning a pregnancy
- Tell their community pharmacist that they are being treated with dapsone when buying any over-the-counter medicine
- Store their medicines safely and securely, and dispose of any unused medication appropriately

# Supporting Information

Please refer to individual product SPCs for full prescribing data; these can be accessed at www.medicines.org.uk.

### Dosage and administration

Patient specific dosage guidance will be provided to the GP by the specialist.

Usually initially 50mg orally daily, gradually increased to 300mg daily if required. Once lesions have begun to subside, the dose should be reduced to a minimum as soon as possible, usually 25-50mg daily, which may be continued for a number of years.

### Contraindications and precautions

Refer to BNF and individual product SPCs for dapsone

Contraindicated in people with hypersensitivity to sulfonamides, sulfones, or any of the excipients; severe anaemia, porphyria; or severe G6PD deficiency.

Dapsone products contain lactose, and should not be used in people with rare hereditary problems of galactose intolerance, the LAPP lactose deficiency, or glucose-galactose malabsorption.

Dapsone be used with caution in patients with cardiac or pulmonary disease; and in patients with anaemia; severe anaemia should be treated before starting dapsone.

### Pregnancy and lactation

Refer to BNF and individual product SPCs for dapsone

Dapsone has been used safely in pregnancy however neonatal haemolysis and methaemoglobinaemia has been reported in the third trimester. If dapsone is necessary, folic acid supplementation (5mg daily) should be prescribed to the mother prior to conception and throughout pregnancy.

Dapsone diffuses into breast milk and there has been a report of haemolytic anaemia in a breast fed infant. Risks to the infant are thought to be very small unless the infant is G6PD deficient. Seek specialist advice.

### Adverse effects

Refer to BNF and individual product SPCs for dapsone and “Monitoring” section, above.

Dose-related haemolysis and methaemoglobinaemia are the most frequently reported adverse events.

Rash, photosensitivity, and pruritis may develop.

Serious cutaneous hypersensitivity reactions occur rarely and include maculopapular rash, exfoliative dermatitis, toxic epidermal necrolysis, and Stevens-Johnson syndrome. **Discontinue dapsone immediately and seek specialist advice about urgent admission; consider immediate admission if warranted**

“Dapsone syndrome” may occur after 3-6 weeks therapy; symptoms include rash, which is always present, fever and eosinophilia. If this occurs, **discontinue dapsone immediately and seek specialist advice about urgent admission; consider immediate admission if warranted** (may progress to exfoliative

dermatitis, hepatitis, hypoalbuminaemia, psychosis, and death). Most patients require steroid therapy for several weeks.

Peripheral neuropathy with motor loss has been reported. Other adverse effects occur infrequently and include anorexia, headache, hepatitis, jaundice, changes in liver function tests, insomnia, nausea, psychosis, tachycardia, and vomiting.

### Drug interactions

This list is not exhaustive; for additional information, and further interactions, consult the BNF and individual product SPCs.

The following drug interactions are classified in the online version of the BNF as **severe** (the result may be a life-threatening event or have a permanent detrimental effect).

- **Trimethoprim** increases exposure to dapsone, and exposure to trimethoprim is increased by dapsone (may increase the risk of haematological reactions)

There is also a ***theoretical*** increased risk of methaemoglobinaemia with the following medicines; **concomitant use of these medicines need <u>not</u> be routinely avoided**; however, patients should be reminded to report any signs or symptoms of methaemoglobinaemia (see page 3).

- Aminosalicylic acid, chloroquine, co-trimoxazole, fosphenytoin, glyceryl trinitrate, isosorbide dinitrate, isosorbide mononitrate, nitrofurantoin, paracetamol, phenobarbital, phenytoin, topical prilocaine, primaquine, primidone, sodium nitroprusside, sulfadiazine, sulfadoxine, and sulfamethoxazole (all predicted to increase the risk of methaemoglobinaemia when given with dapsone).

The following drug interactions are classified in the online version of the BNF as **moderate** (the result could cause considerable distress or partially incapacitate a patient; they are unlikely to be life-threatening or result in long-term effects). These two predicted interactions are based on formal study data (including those for other drugs with the same mechanism):

- **Rifabutin** and **rifampicin** decrease the exposure to dapsone

In addition, the SPC notes that excretion of dapsone is reduced and plasma concentrations are increased by concurrent administration of **probenecid**

## Advice and support

| **Contact details** |
| --- |
| For advice and support, GPs can contact the consultant with whom they have agreed to share care, via the consultant's secretary (details will be provided to the GP by the specialist when requesting the sharing of care).<br>The on-call dermatology registrar can also be contacted via the individual trusts' switchboards:<br>Northern Devon Healthcare NHS Trust: 01271 322577<br>Royal Devon and Exeter NHS Foundation Trust: 01392 411611 |

Date ratified: October 2019

## References

Current BNF can be accessed at: bnf.nice.org.uk

Individual product SPCs for full prescribing data can be accessed at: www.medicines.org.uk

Wakeline, S.H., Maibach, H.I. and Archer, C.B. eds., 2015. *Handbook of systemic drug treatment in dermatology*. Second edition. Boca Raton, FL: CRC Press

# Shared Care Agreement Letter - Consultant Request

| | |
|---|---|
| **To:** | **Dr:** |
| | **Practice Address:** |
| **Patient Name:** | |
| **NHS Number:** | |
| **Date of birth:** | |
| **Address:** | |

**Diagnosed condition: ……**

I recommend treatment with the following drug: ……

At the following dosage: ……..……

I request your agreement to continue the care of this patient according to the Specialised Medicines Service Guidelines for this drug. The patient has been initiated on treatment and stabilised in accordance with the appropriate Specialised Medicines Service Guidelines.

The results of any relevant baseline tests and any additional supportive information (target range, date of last blood test etc.) are included below:

| |
|---|
| |

**Principles:**
GPs are invited to participate, but **if the GP is not confident to undertake these roles then they are under no obligation to do so.** If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

**Remember: the doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.**

| | | |
|---|---|---|
| **Signed:** | | **Date:** |
| **Consultant name:** | | |
| **Telephone number:** | | |
| **Email address** | | |

**Please sign below and return promptly.** Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

**GP Response**

**I agree / do not agree* to share the care of this patient in accordance with the Specialised Medicines Guideline.**

**Signed: …….. Date: …….**

**GP name: ……** *Delete as appropriate.

**Patient agreement**

**I understand and agree to my responsibilities as described above.**

**Signed: …….. Date: …….**

**Name:**