Cambridgeshire & Peterborough Integrated Care System

NHS Cambridgeshire & Peterborough

Shared Care Guideline

Dapsone – Dermatitis Herpetiformis and other Dermatoses

Executive Summary

- Dapsone is licensed for use in dermatitis herpetiformis; and is also used in a number of other dermatoses. Other indications where dapsone is used are highlighted as Red on the AC formulary but are beyond the scope of this document. There is no locally agreed off-label use.
- Usual starting dose is 50mg/day. Maximum dose is 300mg/day. Typical maintenance dose is 25-200mg/day.
- Common side-effects are headache; lethargy; and mild haemolysis.
- Serious side-effects include severe haemolysis; agranulocytosis; methaemoglobinaemia; dapsone hypersensitivity syndrome; neuropathy; and hepatitis.
- Contra-indications include G6PD deficiency, severe anaemia, porphyria and hypersensitivity to sulfonamides.
- Regular monitoring of FBC, Reticulocyte count, U&E and LFT is required.

This shared care framework aims to provide clarity on the responsibilities of all professionals involved in commissioning and prescribing across primary, secondary and tertiary care. Sharing of care depends on communication between the specialist, GP and the patient or their parent/carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use. In that way, we ensure patients receive high quality care – and in making the best use of clinical time and NHS resources in all care.

1. Scope

Prescribing and Monitoring of Dapsone by General Practitioners to adult patients (>16 years).

2. Aim

To provide advice on safe prescribing and monitoring of Dapsone in dermatology patients.

3. Introduction

Dapsone is a sulfone antibacterial and antiprotozoal agent with additional anti-inflammatory properties. Its dermatological **licensed indication** is for dermatitis herpetiformis; and **unlicensed indications** are the following dermatoses: Linear IgA disease; subcorneal pustular dermatosis; hidradenitis suppurativa; vasculitis; pyoderma gangrenosum; severe acneiform eruption; erythema elevatum diutinum; bullous pemphigoid; pemphigus; lupus; granuloma faciale; and Sweet's syndrome.

Related medications include sulfapyridine and sulphamethoxypyridazine, which are sometimes used in cases of dapsone intolerance, but their use is out of the scope of this guideline.

4. Abbreviations

- FBC Full blood count
- WCC White cell count
- Hb Haemoglobin
- MCV Mean corpuscular volume
- LFT Liver function test
- U&E Urea and Electrolytes

5. Dose and Administration

- Dapsone is available in 50mg and 100mg tablets.
- The typical starting dose is 50mg once daily; increased by 50mg/day at 2 weekly intervals, if required, until the condition is controlled.
- The maximum dose is 300mg daily.
- Once the condition is controlled, decrease daily dose slowly to lowest dose for maintenance. This is usually 25-50mg daily, which can often be continued for a number of years. Maintenance dosage can often be reduced in patients receiving a gluten-free diet.
- Dapsone is not indicated in the pediatric patient for dermatitis herpetiformis.
- Dose Adjustments: No dose adjustments are necessary for patients with renal impairment. If the patient is on hemodialysis, dosing should be after dialysis, with consideration for a supplemental dose if the subsequent maintenance dose is not due immediately after dialysis. Peritoneal dialysis requires no dose adjustment and no supplemental dose. Hepatic dosing has no specific recommendations, but caution is advised. Dose should be reduced in the elderly.
- Termination of treatment will be the responsibility of the specialist.

6. Adverse Effects

Adverse effects are dose related. For a comprehensive list consult the BNF or Summary of Product Characteristics.

Note that dapsone may cause photosensitivity; use of sunbeds should be avoided, when outdoors protective clothing worn and use of sunscreen SPF 50 is recommended.

Common

Stomach upset (take Dapsone with food or milk if this occurs); anorexia; nausea; vomiting; headache; lethargy; mild haemolysis; methaemoglobinaemia; sulphaemoglobinaemia.

Infrequent

Depression; rash; moderate/severe haemolysis; hepatitis; motor/sensory neuropathy.

Rare

Agranulocytosis; hypoalbuminaemia; insomnia; psychosis; nephrotic syndrome; reduced fertility.

Serious Adverse Effects

- **Dapsone hypersensitivity syndrome** (incidence is 1 in 100; onset is typically 3-6 weeks after starting dapsone; initial symptoms include pruritus, fever, dermatitis and eosinophilia).
- **Haemolytic Anaemia** (raised reticulocyte count, bilirubin & possible drop in haemoglobin); Haemolysis can occur any point between 48 hours to 4 weeks from treatment initiation. At a dose of 100-150mg, 80% of patients will experience a fall in Hb by 1g/dl; 10% of patients will experience a fall in Hb by 2g/dl. Note that patients with a reticulocytosis are more prone to gallstones; may need additional folate supplements; and Hba1c monitoring is unreliable.
- **Methaemoglobinaemia** (Peak methaemoglobin levels usually occur two weeks after starting dapsone or after increasing the dose. Methaemoglobin levels are difficult to interpret in a nonoverdose situation as tolerance varies between individuals, and signs and symptoms may therefore be more appropriate for monitoring. However, in general: >15% methaemoglobin is associated with central cyanosis; >30% with dyspnoea, dizziness, and headache; and >60% is associated with coma).
- **Agranulocytosis** (incidence is 1 in 300; risk is dose-independent).
- **Hepatitis** (abnormal LFTs- AST or ALT>100 U/l).
- **Neuropathy** (rare at doses less than 300mg/day).
- **SJS / TEN**.

7. Cautions

- Dapsone should be used with caution in patients with cardiac, pulmonary, cerebrovascular, or peripheral vascular disease.
- Dapsone should be used with caution in anaemia. Severe anaemia should be treated before starting Dapsone.
- Dapsone should be used with caution in patients with methaemoglobin reductase deficiency, or with haemoglobin M.
- Dapsone should be used with caution in patients who are exposed to agents capable of causing haemolysis; or conditions associated with haemolysis such as certain infections.
- Refer to the current BNF and SMPC for information regarding pregnancy and lactation. Dapsone is not known to be teratogenic but there is a risk of haemolysis at birth and in breastfed infants.
- Product contains lactose.

8. Contraindications

- Known hypersensitivity to sulphonamides, sulphones, or any of the excipients.
- Severe / symptomatic anaemia.
- Porphyria.
- (Severe) Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency
- Dapsone contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

9. Interactions

For a comprehensive list consult the BNF or Summary of Product Characteristics. Seek advice from the initiating specialist if there are any concerns about interactions.

- Antiepileptics (fosphenytoin, phenytoin, phenobarbital, primidone) – use with caution due to increased risk of side-effects.
- Antimalarials (chloroquine, primaquine) – use with caution due to increased risk of side-effects.
- Clozapine – contraindicated due to the risk of blood dyscrasias.
- Cimetidine – may increase dapsone levels without increasing haemolysis, and given concomitantly may reduce the initial risk of methaemoglobinaemia.
- Folic acid antagonists (e.g. Methotrexate) - increase in Dapsone levels; increased risk of sideeffects.
- Nitrofurantoin – use with caution due to increased risk of side-effects.
- Saquinavir - contraindicated due to the risk of cardiac arrhythmias.
- Probenecid – contraindicated due to increase in Dapsone levels and increased risk of sideeffects.
- Rifampicin and rifabutin– use with caution due to decrease in Dapsone levels.
- Sulphonamides – increased risk of haemolysis.
- Trimethoprim and co-trimoxazole– use with caution due to increase in Dapsone levels, increased risk of side-effects. Be alert for evidence of increased dapsone toxicity (methaemoglobinaemia).

Further information about dose and administration, adverse affects, cautions, contraindications and interactions can be found in the current BNF and Summary of Product Characteristics for Dapsone 50 mg Tablets.

10. Monitoring Standards & Actions to take in the event of abnormal test results/symptoms

Monitoring:

Pre-treatment

- FBC including differential WCC, MCV, Reticulocyte count
- Creatinine, U&E
- LFT
- Urinalysis
- G6PD (particularly in patients of Middle and Far Eastern origin)

Patients should be advised to how to recognise signs of blood disorders and if present to seek medical attention. These signs are: breathlessness, fever, sore throat, mouth ulcers, rash, bruising/bleeding, light-headedness, or any other signs of infection.

Maintenance

- FBC including differential WCC, MCV:

Weekly for 1 month after a stable dose is reached / from initiation,
Then every 2 weeks until week 12,
Then every 3 – 4 months.

Please note FBC should be monitored more closely in patients with HIV disease.

- Reticulocyte count as needed.

- LFTs and U&Es every month for 3 – 4 months.
- Methemoglobin level as clinically indicated.
- Ask at intervals re: paraesthesiae, sensation loss, and weakness.
- Note that the use of glycosylated haemoglobin (HbA1c) to monitor diabetes mellitus can be unreliable on dapsone due to the risk of haemolysis and the formation of methaemoglobin which interferes with the measurement HbA1c.

Action in the event of abnormal test result:

Test Result	**Recommended Action**
>2 fold rise in aspartate transaminase (AST), alanine transaminase (ALT) (from upper limit of reference range)	Refer to local guidelines on deranged liver function (e.g. Easter Liver Network) Check for other causes of deranged LFTs including infection / alcohol excess / other medications. If persistently elevated without other obvious cause: suggest stopping dapsone and contacting hospital specialist.
>4 fold rise in aspartate transaminase (AST), alanine transaminase (ALT) (from upper limit of reference range)	Refer to local guidelines on deranged liver function (e.g. Easter Liver Network) Stop dapsone and discuss with hospital specialist immediately.
White cell count <2.5 x 10*9/L Neutrophils <1.5 x10*9/L Haemoglobin fall of >20g/L from baseline	Stop dapsone and discuss with hospital specialist immediately. Ensure not G6PD deficient.
Hb fall >1g in 4 weeks or last reading below 10g Note: On initiation Hb typically drops by approximately 1g and tends to stabilise. A 1g drop occurring later in treatment would require further investigation/review	Check for increased disease activity. Ask about NSAID use and symptoms of GI blood loss or dyspepsia and stop NSAIDS if implicated. Check MCV and iron studies. Consider endoscopy
Platelets <150 x19*9/L	Consider other causes; discuss with hospital specialist
Secondary care testing only Methaemoglobin >20%	Stop dapsone and discuss with patient's direct hospital specialist immediately.
Secondary care testing only Methaemoglobin >30%	Stop dapsone, discuss with patient's direct hospital specialist immediately, and consider treatment in A&E with methylene blue.

Action in the event of abnormal signs/symptoms:

Sign / Symptom	Recommended Action
Sore throat / mouth ulcers / fever / pallor	Arrange urgent FBC. Consider stopping dapsone and contacting specialist.
Abnormal purpura / bruising / bleeding / jaundice	Stop dapsone and discuss with hospital specialist. Arrange urgent FBC, Clotting, and LFT.
Hypersensitivity reaction (e.g. widespread rash, pruritus, fever)	Stop dapsone and discuss with hospital specialist immediately. Check observations and arrange urgent FBC, LFT, Creatinine, and U&E. Likely to need treatment with oral prednisolone.
Light-headedness, headache, fatigue, dyspnoea, bluish-brown lips/skin colour	Stop dapsone and check serum and refer to hospital specialist to test methaemoglobin levels

11. Shared Care Responsibilities

Policy for Shared Care Shared care is only appropriate if it provides an optimum solution for the patient, and it meets the criteria outlined in the above Formulary document.

- Prescribing responsibility will only be transferred when the specialist and the patient's GP agree that the patient's condition is stable.
- Before prescribing responsibilities are transferred to primary care, all information required by the shared care framework for the individual medicine has been provided to the patient's GP.
- Patients will only be referred to the GP once the GP has agreed to the shared care agreement and returned signed copies. Inherent in any shared care agreement is the understanding that participation is at the discretion of the GP, subject to the availability of sufficient information to support clinical confidence.

a. Hospital specialist:

- Obtain patient informed consent for sharing of care between the specialist, primary care prescriber and patient. Consenting parties must have sufficient, accurate, timely information in an understandable form. Consent must be given voluntarily and must be documented in the patient's notes. Patients should be aware that shared care will not always be the best option for them. This is a mutual agreement between the specialist and primary care, which needs to be confirmed with the shared care agreement.
- To confirm the diagnosis.
- To confirm that the patient's care can be suitably maintained by primary care, following their medicine being optimised for approximately 3 months, with satisfactory investigation results.
- Initiate treatment with dapsone and continue to prescribe and monitor until the dose has been stable for four weeks and the condition is adequately controlled.

- Check the interactions with patient's medications and check there are no contra-indications prior to initiating treatment
- Send a letter to the GP requesting shared care for the patient; include the baseline blood results in this letter.
- Agreement to shared care will be assumed unless the GP advises otherwise (as per shared care guidelines).
- Inform GP of patients who do not attend clinic appointments and advise regarding arrangements for further follow up.
- To provide any advice to the patient/carer/GP when requested.
- Following the request to the patient's GP to initiate shared care; to ensure that the patient has an adequate supply of medication (usually 28 days) until shared care arrangements are in place. Further prescriptions will be issued if, for unforeseen reasons, arrangements for shared care are not in place at the end of 28 days. Patients should not be put in a position where they are unsure where to obtain supplies of their medication
- Routine clinic follow-up at least 6 monthly.
- Evaluation of any reported adverse effects by GP or patient.
- Send a letter to GP after each clinic appointment ensuring correct dose, most recent blood results, and frequency of monitoring are stated.

b. General Practitioner:

- Agreement to shared care guideline by the GP.
- To be familiar with the individual shared care framework, have the information and knowledge to understand the therapeutic issues relating to the patient's clinical condition and undergo any additional training if necessary.
- Monitor patient/blood tests in line with shared care guideline and recommendations from hospital specialist; recording results in the blood monitoring book.
- Report any adverse events to the hospital specialist, where appropriate.
- Request advice from the hospital specialist when necessary.
- Monitor patient's overall health and well-being.
- Prescribe the drug treatment as described.

c. Patient or parent/carer:

- Report to the hospital specialist or GP if they do not have a clear understanding of their treatment.
- Patients must not exceed the recommended dose.
- Patients must attend their scheduled clinic and blood test appointments (where relevant).
- Patients must carry their monitoring book and show to GP and/or hospital specialist for review and recording of results.
- Must inform other clinical staff that they are receiving treatment.
- Inform healthcare professionals of their current medications, both prescribed and purchased elsewhere prior to receiving any new prescribed or over-the-counter medication.
- Report any adverse effects to the hospital specialist or GP.
- Share any concerns they have in relation to treatment with dapsone.
- Store their medication securely away from children and according to the medication instructions.

12. Contact numbers for advice and support

Cambridge University Hospitals NHS Foundation Trust

Specialist	Post	Telephone
Medicines Information Department		01223 217502
Dermatology Specialist Nursing Staff	Dermatology specialist sisters	01223 217391
Dermatology Consultant team	Addenbrooke's Hospital	01223 216501 01223 216459

13. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service Equality and Diversity statement.

14. Disclaimer

It is your responsibility to check that this printed out copy is the most recent issue of this document.

15. Document Management

Ratification Process	Details
Authored by:	Cambridgeshire University Hospitals NHS Foundation Trust
Ratified by:	Cambridgeshire and Peterborough Joint Prescribing Group
Date ratified:	April 2024
Review date:	April 2027
Version number:	2

The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent **Summary of Product Characteristics** for Dapsone 50 mg Tablets.