Dapsone

Shared Care Guideline for Dapsone (FOR DERMATOLOGICAL INDICATIONS ONLY)

Introduction

Dapsone is a sulfone active against a wide range of bacteria. It is indicated for the following Dermatological Indications:

- Multibacillary leprosy in combination with rifampicin and clofazimine (3-drug regimen)
- Paucibacillary leprosy in combination with rifampicin (2-drug regimen)
- Dermatitis herpetiformis

However Leprosy is not managed by the Dermatology team at BHNFT (and patients diagnosed with this condition are referred to the Infectious Diseases team in Sheffield). It is therefore used primarily for Dermatitis herpetiformis as first line oral therapy after failure of at least two topical steroids.

Dosage and duration of therapy depends on the indication being treated, however it is as follows for **Adults and children over 12 years:**

1. Dermatitis herpetiformis:
    - Initially 50mg 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.
    - Maintenance dosage can often be reduced in patients receiving a gluten-free diet.

The mechanism of action of dapsone is probably similar to that of the sulfonamides which involves inhibition of folic acid synthesis in susceptible organisms. It is usually considered to be bacteriostatic against *M leprae* although it may also possess weak bactericidal activity. It is also active against *Plasmodium* and *Pneumocystis carinii*.

Dapsone is almost completely absorbed from the GI tract with peak plasma concentrations occurring about 2-8 hours after a dose. Steady-state concentrations are not obtained until after at least 8 days of daily administration.

About 50-80% of dapsone in the circulation is bound to plasma proteins. It undergoes enterohepatic recycling and is widely distributed i.e. is present in saliva, breast milk and crosses the placenta.

The half-life ranges from 10-80 hours. Dapsone is mainly excreted in the urine, with only 20% of a dose remaining as unchanged drug.

Dapsone is available as 50mg and 100mg Tablets.

Responsibilities of the specialist initiating treatment

Summary

- To assess the suitability of the patient for treatment (see pages 3 and 4 for clinical information).
- To discuss the benefits and side effects of treatment with the patient/carer and the need for long term monitoring if applicable.
- To perform baseline tests (FBC, reticulocyte count, U&E's, LFT's and G6PD deficiency) and if appropriate routine tests (e.g. FBC including reticulocyte count every 2 weeks, and LFT's monthly) until the patient is stable.
- To prescribe for the first 12 weeks of treatment
- To ask the GP whether they are willing to participate in shared care.
- To provide the GP with a summary of information relating to the individual patient to support the GP in undertaking shared care (See Shared care request form in Appendix A).
- To advise the GP of any dosage adjustments required, monitoring required, when to refer back, and when and how to stop treatment (if appropriate).
- To advise the GP when the patient will next be reviewed by the specialist.
- To monitor the patient for adverse events and report to the GP and where appropriate Commission on Human Medicines/MHRA (Yellow card scheme).
- To provide the GP with contact details in case of queries.

Baseline Monitoring Tests
It is recommended that regular blood counts be performed before and during treatment with dapsone. Baseline bloods (FBC, U&E's, LFT's) **including reticulocyte count** should be performed before commencing Dapsone. G6PD deficiency should also be tested for prior to initiation of Dapsone.

Routine Monitoring Tests
FBC (including reticulocyte count), U&E's, LFT's should be performed at 3 monthly intervals.

Disease monitoring
Patients will be reviewed by the specialist team every 6 months to monitor disease management.

Responsibilities of other prescribers

Acceptance of Responsibility by the Primary Care Clinician
It is optional for GPs to participate in taking on responsibility for shared care for the patient. GPs will take on shared care only if they are willing and able.

Summary

- To reply to the request for shared care as soon as possible.
- To prescribe and adjust the dose as recommended by the specialist.
- To ensure there are no interactions with any other medications initiated in primary care.
- To continue monitoring as agreed with secondary care.
- To refer back to the specialist where appropriate. For example:
  - Patient or general practitioner is **not** comfortable to continue with the existing regime due to either change in condition or drug side effects.
  - Advice in respect of concordance.
  - Special situations (e.g. Pregnancy)
- Discontinue the drug as directed by the specialist if required
- To identify adverse events if the patient presents with any signs and liaise with the hospital specialist where necessary. To report adverse events to the specialist and where appropriate the Commission on Human Medicines/MHRA (Yellow card scheme).
- To review the patient every 3 months for routine ongoing bloods and disease monitoring (see page 4).

Clinical Particulars

BNF therapeutic class	Chapter 5 - Infections > Section 2.2 - Leprosy > Antimycobacterials.
Indication	Dapsone is indicated for the following Dermatological Indications: • Multibacillary leprosy in combination with rifampicin and clofazimine (3-drug regimen) • Paucibacillary leprosy in combination with rifampicin (2-drug regimen) • Dermatitis herpetiformis
Dosage and administration	**Adults and children over 12 years:** Dermatitis herpetiformis: • Initially 50mg daily. • Maximum daily dose is 300mg. • 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. • Maintenance dosage can often be reduced in patients receiving a gluten-free diet in patients with coeliac disease.
Cautions and Contraindication	**Contraindications** 1. Known hypersensitivity to sulfonamides, sulfones, or any of the excipients; 2. severe anaemia; 3. porphyria; 4. severe glucose-6-phosphate dehydrogenase deficiency. 5. Dapsone contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine. **Cautions** Dapsone should be used with caution in patients with cardiac or pulmonary disease. Dapsone should be used with caution in anaemia. Severe anaemia should be treated before starting Dapsone. **Pregnancy and Lactation** It is now generally considered that the benefits of dapsone in the treatment of leprosy outweigh any potential risk to the pregnant patient. Some leprologists recommend 5mg folic acid daily for leprosy patients receiving dapsone during pregnancy. The BNF advises that high dose Folic Acid should be given to the mother throughout pregnancy as neonatal haemolysis and methaemoglobinaemia reported in third trimester. Dapsone diffuses into breast milk and there has been a report of haemolytic anaemia in a breast fed infant. While some feel that dapsone should not be used in lactating mothers, in general treatment for leprosy is continued in such patients.The risk to the infant is very small unless infant is G6PD deficient.
Adverse Drug Reactions	Varying degrees of dose-related haemolysis and methaemoglobinaemia are the most frequently reported adverse effects of dapsone and occur in most patients given more than 200mg daily; doses of up to 100mg daily do not cause significant haemolysis but patients deficient in glucose-6-phosphate dehydrogenase are affected by doses above about 50mg daily. Hypoalbuminaemia and haemolytic anaemia has also been reported. Although agranulocytosis has been reported rarely with dapsone when used alone, reports have been more common when dapsone has been used with other agents in the prophylaxis of malaria.

	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. Fixed drug eruptions have occurred. **A "dapsone syndrome" may occur after 3-6 weeks therapy**; symptoms include rash, which is always present, fever, and eosinophilia. If dapsone is not stopped immediately, the syndrome may progress to exfoliative dermatitis, hepatitis, albuminuria and psychosis. Deaths have been recorded. Most patients require steroid therapy for several weeks, possibly due to the prolonged elimination time of the drug. Peripheral neuropathy with motor loss has been reported in patients on dapsone for dermatological conditions. Peripheral neuropathy may occur as part of leprosy reaction states and it is not an indication to discontinue dapsone. Other adverse effects occur infrequently and include anorexia, headache, hepatitis, jaundice, changes in liver function tests, insomnia, nausea, psychosis, tachycardia and vomiting. Dapsone should be discontinued or reduced in dosage if severe lepra reactions affecting the eyes or nerve trunks occur.
Monitoring	It is recommended that regular blood counts be performed before and during treatment with dapsone <u>Baseline Bloods</u> Before commencing Dapsone it is recommended that patients undergo the following tests: **FBC including reticulocyte count, U&E's and LFT's.** Patients deficient in glucose-6-phosphate dehydrogenase, or methaemoglobin reductase, or with haemoglobin M are more susceptible to the haemolytic effects of dapsone. Therefore **glucose-6-phosphate dehydrogenase deficiency** should be checked for in all patients prior to commencing Dapsone (particularly in patients of middle and far eastern origin). **FBC including reticulocyte count will be monitored by the specialist team every 2 weeks, and LFT's monthly until stable.** <u>Ongoing Monitoring</u> Patients who are stable on long-term Dapsone therapy should have their FBC (including reticulocyte count) and LFT's monitored at 3 monthly intervals.
Interactions	Clinically relevant drug interactions include: • **Trimethoprim** – Increase in dapsone levels; increasing risk of side effects • **Probenecid** – Increase in dapsone levels; increasing risk of side effects • **Folic acid antagonists** – increase in dapsone levels; increasing risk of side effects e.g. methotrexate • **Rifampicin** – decrease in dapsone levels • **Sulphonamide** – increased risk of haemolysis • **Hydroxychloroquine** – increased risk of haemolysis
Counselling	On long-term treatment, patients and their carers should be told how to recognise signs of blood disorders and advised to seek immediate medical attention if symptoms such as: fever, sore throat, rash, mouth ulcers, purpura, bruising or bleeding develop.

Communication

Specialist to GP
The specialist will inform the GP when they have initiated Dapsone. When the patient is near completing the satisfactory initiation period, the specialist will write to the GP to request they take over prescribing and where possible give an indication as to the expected length of treatment. The Specialist will also send a Shared care request form to support the GP in undertaking shared care. (Appendix A)

GP to specialist
If the GP has concerns over the prescribing of Dapsone, they will contact the specialist as soon as possible.

Contact Details	Telephone number	Email
Consultant Dermatologists: Dr Kay Baxter	01226 432117	kay.baxter2@nhs.net
Medicines Information: Gillian Turrell	01226 432857	gilliansmith2@nhs.net

References

1. Summary of Product Characteristics. Dapsone Tablets BP 50mg. Accessed Online. Available at: https://www.medicines.org.uk/emc/product/5768/smpc (Accessed 20th April 2018).

2. BNF Online. Dapsone Monograph. Accessed Online. Available at: https://www.medicinescomplete.com/mc/bnf/current/PHP3641-dapsone.htm?q=dapsone&t=search&ss=text&tot=30&p=1#_hit (Accessed 20th April 2018).

Development Process

This guidance has been produced by Umar Patel, Senior Pharmacist - Interface following an AMBER classification status of Dapsone for Dermatological Indications by the Barnsley Area Prescribing Committee. This guideline has been subject to consultation and endorsement by the Area Prescribing Committee on 10th October 2018 and the LMC on 13th November 2018.

Appendix A – Shared Care request form (Amber)

- Specialist to complete when requesting GP to enter a shared care arrangement.
- GP to return signed copy of form.
- Both parties should retain a signed copy of the form in the patient's record.

From (**Specialist**): _____ **To** (**GP**): _____

Patient details

Name: _____ ID Number: _____

Address: _____ DOB: _____

Diagnosed condition: _____

Amber Drug details

Drug name: _____ Dose and frequency: _____

Date of initiation: _____ Length of treatment: _____

The patient will be reviewed by the Consultant on: _____

The patient should be reviewed by the GP by: _____

Monitoring

The following monitoring should be undertaken by the GP:

Parameter	Most Recent Result	Date Last Performed	Date next test due	Frequency
FBC (including Reticulocyte Count)	WCC = Neutrophils = Platelets = Hb = Reticulocyte =			3 monthly
U&E's	Na = Cr = K = Ur =			3 monthly
LFT's	Billirubin = ALT = AST = GGT =			3 monthly

Communication

Consultant
Telephone number: _____ Fax number:_____

Email address: _____

Specialist Nurse
Telephone number: _____ Fax number: _____

Email address: _____

Confirmation of acceptance of shared care

Specialist (Doctor/Nurse) name: _____

Specialist (Doctor/Nurse) signature: _____ Date: _____

I, Dr ……., can confirm I :

☐ accept the request to participate in shared care for the patient named above.

☐ reject the request to participate in shared care for the patient named above. The reason for this being ……..

GP signature: _____ Date: _____