Health and Social Care Board

Interface Pharmacist Network Specialist Medicines

Dimethyl fumarate (Skilarence®)

Dermatology shared care guideline

Specialist details	Patient identifier
Name: _____	
Location: _____	
Tel: _____	**Date:** _____

NOTE – this guideline relates only to the use of dimethyl fumarate (Skilarence®) tablets. Other preparations of dimethyl fumarate are not covered by this guideline.

Introduction

Licensed indications: Dimethyl fumarate (Skilarence®) is indicated for the treatment of moderate to severe plaque psoriasis in adults.

Adult dosage and administration

Available as: 30 mg and 120 mg tablets.

The tablets must be swallowed whole with fluid during or immediately after a meal and should not be crushed, divided, dissolved or chewed.

A gradually increasing dose regimen is advised to improve tolerability:

Week	Number of tablets			Total daily dose of dimethyl fumarate
	Morning	Midday	Evening	
30mg tablets				
1	0	0	1	30mg
2	1	0	1	60mg
3	1	1	1	90mg
120mg tablets				
4	0	0	1	120mg
5	1	0	1	240mg
6	1	1	1	360mg
7	1	1	2	480mg
8	2	1	2	600mg
9+	2	2	2	720mg

If a particular dose increase is not tolerated, it may be temporarily reduced to the last tolerated dose.

If treatment success is observed before the maximum dose is reached, no further increase of dose is necessary. After clinically relevant improvement of the skin lesions has been achieved, consideration should be given to gradual reduction of the maintenance dose as advised by the specialist.

Hospital specialist responsibilities

- Assess if the patient is suitable for treatment with dimethyl fumarate (Skilarence®)
- Assess patient's current repeat medications for potential significant interactions with the new treatment and discuss with GP if any concerns
- Agree shared care with the patient's GP and document in patient's case notes.
- Advise GP on dose to be prescribed.
- Provide the patient/carer with relevant written information on use, side-effects and need for monitoring of medication, e.g. 'BAD Patient Information Leaflet – Dimethyl Fumarate'
- Provide shared care monitoring record booklet if required.
- Baseline tests:
  - FBC including differential blood count and platelet count
  - U&E and urinalysis
  - LFT
- Review results of safety monitoring and request additional tests as required.
- Monitor disease response to treatment and need to continue therapy. Advise GP of any changes to dose required.

- Continue to review the patient at agreed specified intervals sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP if required

GP responsibilities

- Prescribe dimethyl fumarate (Skilarence®), continued prescribing is appropriate for patients attending regular review
- Adjust the dose as advised by the specialist.
- Arrange and record ongoing monitoring as agreed with specialist, ensuring practice systems are in place to recall patients for monitoring the following tests **every 3 months**:
  - FBC including differential white cell count and platelet count
  - U&E
  - LFT
  - Urinalysis (* in terms of detecting Fanconi syndrome, in the event of glucosuria, ensure robust systems are in place to follow up blood glucose levels)
- Prevent ongoing prescription if patient is not compliant with monitoring. Liaise with specialist if appropriate.
- Report adverse drug reactions to initiating specialist and usual bodies (e.g. MHRA).
- Continue to monitor for significant drug interactions with other medicines.

Action required in event of monitoring abnormalities

Test	Results	Action required
Total white cell count	Greater than **3.0** x 10^9/L but recent unusual decrease or consistent downward trend	• Continue treatment but monitor FBC monthly until no further marked decreases.
	Less than **3.0** x 10^9/L	• **Stop dimethyl fumarate**, • Repeat test and inform specialist
Lymphocytes	Between **0.7** and **1.0** x 10^9/L	• Continue treatment and monitor FBC monthly until lymphocytes are ≥ 1.0 x 10^9/L for 2 consecutive tests
	Less than **0.7** x 10^9/L	• Repeat test. If the levels are confirmed to be below 0.7x10^9/L, then **stop dimethyl fumarate** and inform specialist. • Continue monitoring FBC every 3 months until levels return to normal.
Other haematological results	Clinically relevant change	• Continue treatment and contact initiating specialist
Liver function	AST/ALT between 2 - 3 times the upper limit of normal (ULN)	• Continue treatment • Repeat bloods and seek specialist advice
	AST/ALT greater than 3 x ULN	• **Stop dimethyl fumarate**, • Repeat test and inform specialist
Renal function	If renal impairment develops	• Continue treatment and contact initiating specialist

*** Detection of Fanconi Syndrome (see also adverse effects below)**		
Urinalysis	Proteinuria	• **Stop dimethyl fumarate** and contact initiating specialist
	Glucosuria	• In the event of glucosuria, check blood glucose levels **immediately** (eg using blood glucose finger prick test). • If glucosuria is present and blood glucose levels are ***NORMAL***, **stop dimethyl fumarate** and contact initiating specialist.

Results should be recorded in the patient's shared care monitoring record booklet (where in use).

Please note an unusual fall or rise or a consistent downward or upward trend in any value should prompt review of the patient and extra vigilance. Some patients may have abnormal baseline values, specialist will advise.

Adverse effects, precautions and contraindications

Gastrointestinal disturbances (diarrhoea, nausea, vomiting, abdominal distension, dyspepsia, abdominal pain/discomfort, constipation and flatulence) are common and are most likely to occur during the first 2 – 3 months of treatment. These are usually mild and should improve or resolve as treatment continues.

Flushing commonly occurs in the first few weeks of treatment and tends to lessen with time.

Other common adverse reactions include: lymphopenia, leukopenia, eosinophilia, leucocytosis, decreased appetite, headache, paraesthesia, erythema, skin burning sensation, pruritus, fatigue, feeling hot, asthenia and hepatic enzymes increased.

*** Fanconi syndrome,** a syndrome of inadequate reabsorption in the proximal renal tubules of the kidney, has been reported rarely with a related medicinal product containing dimethyl fumarate. Early diagnosis and discontinuation of dimethyl fumarate treatment are important to prevent the onset of renal impairment and osteomalacia, as the syndrome is usually reversible. Fanconi syndrome can present with polyuria, polydipsia, anorexia and vomiting – other important signs are: proteinuria, glucosuria (with normal blood sugar levels), hyperaminoaciduria and phosphaturia (possibly concurrent with hypophosphatemia).

Infection. Immunosuppressants can increase susceptibility to infection. It is advisable not to commence or continue treatment with dimethyl fumarate when patients have a confirmed or established local or systemic infection. It is advisable to recommence once the infection has been treated. Precise period of discontinuation depends on the nature and severity of infection and the activity of the underlying disease.

Opportunistic infections/progressive multifocal leukoencephalopathy (PML). Cases of opportunistic infections, particularly of progressive multifocal leukoencephalopathy (PML) have been reported with other dimethyl fumarate-containing products. Typical symptoms associated with PML are diverse, become worse over days to weeks and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision and changes in thinking, memory and orientation leading to confusion and personality changes. If PML is suspected, treatment with dimethyl fumarate should be stopped immediately and initiating specialist contacted.

Contraindications include:

- Hypersensitivity to dimethyl fumarate or excipients
- Severe gastrointestinal disorders
- Severe hepatic or renal impairment

Pregnancy: dimethyl fumarate is contraindicated in pregnancy. Women of child-bearing potential should use a reliable form of contraception. In patients experiencing diarrhoea during dimethyl fumarate treatment, the effect of oral contraceptives may be reduced and additional barrier methods of contraception may be necessary.

Breastfeeding: dimethyl fumarate is contraindicated during breastfeeding.

Common drug interactions

- **Alcohol** - Strong alcoholic drinks (more than 30% alcohol by volume) increase the risk of stomach irritation and should be avoided.
- **Live vaccines:** Immunosuppression is a risk factor for the use of live vaccines. The risk of vaccination should be weighed against the benefit. Discuss with initiating specialist.
- **Nephrotoxic medicines** (e.g. methotrexate, ciclosporin, aminoglycosides, diuretics, NSAIDs or lithium) may increase the potential for renal adverse reactions (e.g. proteinuria) in patients taking dimethyl fumarate.

Communication

For any queries relating to this patient's treatment with dimethyl fumarate (Skilarence®), please contact the specialist named at the top of this document.

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC or the BNF

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