

PRESCRIBING INFORMATION

(Please consult the Summary of Product Characteristics (SmPC) before prescribing.)

Skilarence 30 mg & 120 mg gastro-resistant tablets

Active Ingredient:

Skilarence 30 mg

Each gastro-resistant tablet contains 30 mg dimethyl fumarate. Also contains 34.2 mg lactose (as monohydrate).

Skilarence 120 mg

Each gastro-resistant tablet contains 120 mg dimethyl fumarate. Also contains 136.8 mg lactose (as monohydrate).

Indication: For the treatment of moderate to severe plaque psoriasis in adults in need of systemic medicinal therapy.

Dosage and Administration: For oral use. To improve tolerability, it is recommended to begin treatment with a low initial dose with subsequent gradual increases. In the first week, Skilarence 30 mg is taken once daily (1 tablet in the evening). In the second week, Skilarence 30 mg is taken twice daily (1 tablet in the morning and 1 in the evening). In the third week, Skilarence 30 mg is taken three times daily (1 tablet in the morning, 1 at midday, and 1 in the evening). From the fourth week, treatment is switched to only 1 tablet of Skilarence 120 mg in the evening. This dose is then increased by 1 Skilarence 120 mg tablet per week at different times of day for the subsequent 5 weeks. If a particular dose increase is not tolerated, it may be temporarily reduced to the last tolerated dose. The maximum daily dose allowed is 720 mg (3 x 2 tablets of Skilarence 120 mg). *Consult SmPC and package leaflet for the titration table and full method of administration.*

Contraindications, Warnings, etc:

Contraindications: Hypersensitivity to the active substance or to any of the excipients listed in SmPC section 6.1. Severe gastrointestinal disorders, Severe hepatic or renal impairment, Pregnancy and breast-feeding.

Precautions: Skilarence may decrease leukocyte and lymphocyte counts. It has not been studied in patients with pre-existing low leukocyte or lymphocyte counts. Prior to initiating treatment with Skilarence, a current complete blood count (including differential blood count and platelet count) should be available. Treatment should not be initiated if leukopenia below $3.0 \times 10^9/L$, lymphopenia below $1.0 \times 10^9/L$ or other pathological results are identified. During treatment a complete blood count with differential should be performed every 3 months. **Leukopenia:** Discontinue treatment if the total number of white blood cells is at levels below $3.0 \times 10^9/L$. **Lymphopenia:** If the lymphocyte count falls below $1.0 \times 10^9/L$ but is $\geq 0.7 \times 10^9/L$, blood monitoring should be performed monthly until levels return to $1.0 \times 10^9/L$ or higher for two consecutive blood tests at which point monitoring can again be performed every 3 months. If the lymphocyte count falls below $0.7 \times 10^9/L$, the blood test must be repeated and if the levels are confirmed to be below $0.7 \times 10^9/L$, then treatment must be stopped immediately. Patients developing lymphopenia should be monitored after stopping treatment until their lymphocyte count has returned to the normal range. **Infections:** Initiation of therapy should only be considered once a pre-existing infection has resolved. If a patient develops an infection during treatment with Skilarence, suspension of treatment should be considered and the benefits and risks should be reassessed prior to re-initiation of therapy. Patients receiving Skilarence should be instructed to report symptoms of infection to a physician.

Progressive multifocal leukoencephalopathy (PML)

Cases of opportunistic infections, particularly of PML have been reported with other dimethyl fumarate-containing products. PML is an opportunistic infection caused by the John-Cunningham virus (JCV) that can be fatal or cause severe disabilities. A modified or weakened immune system as well as genetic or environmental factors can also constitute risk factors. Persistent moderate or severe

lymphopenia during treatment with dimethyl fumarate is also considered a risk factor for PML. Patients who develop lymphopenia should be monitored for signs and symptoms of opportunistic infections, particularly for symptoms indicative of PML. If PML is suspected, Skilarence should be stopped and neurological and radiological examinations performed. Renal and hepatic function should be checked prior to initiation of treatment and every three months thereafter. **Fanconi syndrome:** Early diagnosis of Fanconi syndrome and discontinuation of Skilarence treatment are important to prevent the onset of renal impairment and osteomalacia, as the syndrome is usually reversible. **Flushing:** Patients should be made aware that they are likely to experience flushing in the first few weeks of taking Skilarence. **Lactose:** Skilarence contains lactose. Patients with rare hereditary problems of galactose intolerance, lactase deficiency or glucose-galactose malabsorption should not take this medicine. **Interactions:** Skilarence should be used cautiously in combination with other systemic antipsoriatic therapy (e.g. methotrexate, retinoids, psoralens, ciclosporin, immunosuppressants or cytostatics). During treatment with Skilarence, simultaneous use of other fumaric acid derivatives (topical or systemic) should be avoided. Concurrent therapy with nephrotoxic substances (e.g. methotrexate, ciclosporin, aminoglycosides, diuretics, NSAIDs or lithium) may increase the potential for renal adverse reactions (e.g. proteinuria). In cases of severe or prolonged diarrhoea during treatment with Skilarence, absorption of other medicinal products may be affected. Caution should be exercised when prescribing medicinal products with a narrow therapeutic index that require absorption in the intestinal tract. The efficacy of oral contraceptives may be reduced and the use of an alternative barrier contraceptive method is recommended to prevent possible failure of contraception. Consumption of large quantities of strong alcoholic drinks (more than 30% alcohol by volume) should be avoided because it may lead to increased dissolution rates of Skilarence and, therefore, may increase the frequency of gastrointestinal adverse reactions. Vaccination during treatment with Skilarence has not been studied. Immunosuppression is a risk factor for the use of live vaccines. There is no evidence for Skilarence interaction with cytochrome P450. **Fertility, pregnancy and lactation:** Skilarence is not recommended in women of child-bearing potential not using appropriate contraception. In patients experiencing diarrhoea during Skilarence treatment, the effect of oral contraceptives may be reduced and additional barrier methods of contraception may be necessary. There are limited data from the use of dimethyl fumarate in pregnant women. Animal studies have shown reproductive toxicity. Skilarence is contraindicated during pregnancy and breast-feeding. There are no human or animal data on the effects of Skilarence on fertility. **Ability to drive and use machines:** Skilarence may have a minor influence on the ability to drive and use machines. Dizziness and fatigue may occur. *Consult SmPC and package leaflet for more information.*

Adverse Reactions: *Very common ($\geq 1/10$):* Lymphopenia, leukopenia, flushing, diarrhoea, abdominal pain and distention, nausea. *Common ($\geq 1/100$ to $< 1/10$):* Eosinophilia, leukocytosis, headache, paraesthesia, vomiting, dyspepsia, constipation, abdominal discomfort, flatulence, erythema, skin burning sensation, pruritus, fatigue, feeling hot, asthenia, hepatic enzyme increased, decreased appetite. *Uncommon ($\geq 1/1,000$ to $< 1/100$):* dizziness, proteinuria, serum creatinine increased. *Rare ($\geq 1/10,000$ to $< 1/1,000$):* Allergic skin reactions. *Very rare ($< 1/10,000$):* Acute lymphatic leukaemia, irreversible pancytopenia, allergic skin reaction. *Not known (cannot be estimated from available data):* PML, renal failure, Fanconi syndrome. *Consult SmPC and package leaflet for other adverse reactions.*

Legal Category: POM

Marketing Authorisation Number(s): EU/1/17/1201/001,
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NHS Cost: 30 mg - 42 tablets = £89.04; 120 mg - 90 tablets =
£190.80, 180 tablets = £381.60 (excluding VAT).

Marketing Authorisation Holder:
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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Almirall Ltd.