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## Fumarates in psoriasis

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Psoriasis is a chronic, immune mediated inflammatory skin disease, characterized by hyperproliferation of keratinocytes and an increased dermal infiltration of immunologically active cells. Most patients with moderate to severe disease require long-term systemic treatment to control their psoriasis. Fumarates (dimethylfumarate (DMF) and monoethylfumarate (MEF)) are small molecules used as oral treatment in psoriasis for more than 25 years, mainly in Western Europe. Clinical studies have shown that 50 to 70% of fumarates treated psoriasis patients show a clinical improvement of at least 70% following 16 weeks of treatment. Data from long-term observational studies on treatment of psoriasis with fumarates indicate a favorable safety profile. *In vitro* studies have shown that DMF inhibits dendritic cell maturation and keratinocyte proliferation. DMF has several effects on mitochondria and signal transduction pathways. More recently DMF is registered as systemic therapy for relapsing-remitting multiple sclerosis.

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## Cutaneous adverse events associated with long term disease modifying therapy in multiple sclerosis

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Glatiramer acetate (GA) and interferon-beta (IFN-β) are disease-modifying therapies (DMTs) for multiple sclerosis (MS) that are administrated via subcutaneous (SC) or intramuscular (IM) injections. Cutaneous adverse events associated with DMTs are common and may have a major impact patient's quality of life. DMTs for MS are frequently associated with local injection-site reactions and a wide spectrum of generalized cutaneous adverse events, in particular, the subcutaneous formulations. The most common cutaneous events were local injection site reactions and lipoatrophy. Systematic review reveals sixty five case reports involving 106 MS patients described a wide spectrum of cutaneous adverse events, the most frequently reported being lipoatrophy, cutaneous necrosis and ulcers and various immune-mediated inflammatory skin diseases. Although some of the skin reactions may be severe and persistent, most of them are mild. We also performed the derMiS study, a cross sectional study conducted in 15 Dutch clinics. Eligible for inclusion were MS patients who had been treated with their first DMT for at least 2 years. Cutaneous events were assessed from digital photographs of injection sites by dermatologists blinded to DMT. A total of 229 patients were enrolled, of whom 44 (19%) were treated with SC GA, 60 (26%) with SC IFN-b-1b, 66 (29%) with SC IFN-b-1a and 59 (26%) with IM IFN-β-1a. Mean duration of DMT treatment was 6 years (range 2-18 years). Overall, 156 (68%) had at least one cutaneous adverse event. The prevalence of cutaneous adverse events was higher for the SC DMTs (75 to 82%) compared to IM DMT (41%, $P<0.001$). Local injection site reactions (erythema and ecchymosis) and lipoatrophy were the most common skin reactions, occurring in 156 (68%) and 45 (20%) patients, respectively. Less frequently occurring reactions were post-inflammatory hyperpigmentation (7%), eczema (6%), healed ulcers (3%), urticaria (2%) and skin necrosis (0.4%). Topical therapy with a potent corticosteroid, tacrolimus or vitamin D can all be beneficial in counteracting these benign cutaneous adverse events. The additional use of any emollients is recommended. Also topical brimonidine can be an interesting option in order to prevent the erythema as cutaneous adverse event of interferon therapy in MS.

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