Northern Treatment Advisory Group

Northern (NHS) Treatment Advisory Group

Treatment Appraisal: Decision Summary

Date	28th February 2017
Appraisal & Details	The Northern (NHS) Treatment Advisory Group considered an appraisal of **Dimethyl Fumarate for moderate to severe chronic plaque psoriasis.**
Recommendation	**The Northern (NHS) Treatment Advisory Group recommends the use of dimethyl fumarate for those patients who are <u>not</u> suitable for a biologic and in whom conventional first and second line treatment options have failed and who would otherwise have been given Fumaderm®.** The group noted that dimethyl fumarate was superior to placebo and non-inferior to Fumaderm® at week 16. Monoethyl fumarate salts (Fumaderm®) are licensed for moderate to severe psoriasis in Germany. Although unlicensed in the UK, Fumaderm® is imported for use by specialist dermatology centres particularly in patients who fail or are intolerant to other non-biological systemic therapy. *Dimethyl fumarate has not yet been launched and this recommendation will apply once it's available and licensed.*
Clinical evidence summary	A pivotal phase III RCT compared dimethyl fumarate to placebo and Fumaderm® in 671 adults with moderate to severe plaque psoriasis, aiming to demonstrate superiority of dimethyl fumarate to placebo, and non-inferiority to Fumaderm®. At week 16, dimethyl fumarate was superior to placebo for the co-primary outcomes of Psoriasis Area Severity Index (PASI) 75 (37.5% vs 15.3%) and Physician Global Assessment response of 0 "clear" /1 "almost clear" (33.0% vs 13.0%); and non-inferior to Fumaderm® for PASI 75 (37.5% vs 40.3%, non-inferiority margin ±15%). Previous studies on compound FAE therapy also suggest that they are superior to placebo and possibly similar in efficacy to methotrexate but the overall quality of the evidence is low due to limitations such as small patient numbers and use of non-validated outcome measures.
Safety	The rates and types of treatment emergent adverse events (TEAEs) in the pivotal study were similar between the dimethyl fumarate and Fumaderm® groups and consistent with the known safety profile of FAE. TEAEs were mostly considered to be mild but led to discontinuation in nearly a quarter of patients receiving active treatment. The most common adverse effects were GI symptoms (nausea, vomiting, abdominal pain, flatulence, diarrhoea) occurring in about two thirds of patients followed by flushing.

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	Reduced leucocyte and lymphocyte counts were also observed. Cases of progressive multifocal leukoencephalopathy (PML) have been reported in patients on FAE with severe prolonged lymphopenia. Monitoring of full blood count (FBC), renal and hepatic function is recommended at baseline and during FAE treatment. The manufacturer is currently in discussion with regulatory authorities regarding monitoring requirements. There is lack of data on long-term efficacy and safety of dimethyl fumarate or compound FAE, or on comparison with other systemic treatments. Adverse effects may limit use.
Patient Perspective	Patients will be pleased that another licensed oral treatment option is now available for use; however they may have concerns about the adverse effects of this drug. Pros and cons will need to be discussed with patients prior to prescribing.
Cost analysis summary	The cost of dimethyl fumarate is not yet available. Assuming it will be 10% less expensive than Fumaderm®; this corresponds to an estimated annual maintenance cost of £1,655.64 to £4,966.92 depending on dose.
Financial impact PbR: non-tariff	As an additional licensed oral treatment option, dimethyl fumarate may delay or avoid the need for biologics. Therefore costs could be offset against potential savings realised through reduced use of biologics.