

# Topical Psoriasis Therapies and Unmet Patient Needs: The Importance of Optimizing Methotrexate

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Although a wide variety of treatment modalities exist for the management of psoriasis, nontreatment, undertreatment, and treatment dissatisfaction represent key clinical challenges. Careful tailoring of therapeutic regimens to meet individual patient needs and priorities may therefore be critical to improving treatment adherence and clinical outcomes. Importantly, systemic therapies such as methotrexate (MTX) may be particularly useful for individualizing patient treatment regimens and appear to be underutilized components of treatment optimization.

A majority of psoriasis patients have mild to moderate disease and many are treated primarily with topical medications. Although these treatments generally are safe and effective, practical limitations (eg, formulation, ease of application) may affect patients' treatment adherence and satisfaction even in the context of high efficacy. Systemic therapies, although associated with a distinct set of risks and treatment challenges, may enable patients to overcome many of these limitations, particularly in patients with moderate to severe disease or impaired quality of life as well as those with an inadequate response to or dissatisfaction with topical treatments.

## Systemic Treatment Options

Among the systemic treatment options for psoriasis, biologic therapies often are most highly regarded due to their strong efficacy, although traditional systemic therapies such as MTX, cyclosporine, and acitretin remain important treatment options and have an extensive history in the treatment of psoriasis.

In addition to typically being required by insurance companies prior to the initiation of biologic therapies, traditional systemic therapies also may be preferred by patients because of the options for oral and subcutaneous administration and their relatively low costs. Furthermore, systemic therapies may be critical in patients for whom biologic therapies are relatively contraindicated, such as those with an increased risk of infection, history of malignancy, or hypersensitivity to any of the product's ingredients.

Among traditional systemic therapies, MTX is one of the most frequently used psoriasis treatment worldwide and can be highly effective for even severe cases. Importantly, MTX is a valuable component of combination treatments for psoriasis and is frequently coadministered with topical and biologic agents and phototherapy, suggesting that MTX may be a particularly useful option to consider when adjusting a patient's treatment regimen.

## Benefits of Subcutaneous Methotrexate Administration

Methotrexate can be delivered either orally or parenterally, contributing to its compatibility with a wide variety of psoriasis treatment regimens and patient preferences. Administration is predominantly oral in the United States, but parenteral MTX (most commonly delivered subcutaneously) can confer important benefits and is used regularly in countries outside of the United States.

An important advantage of subcutaneous versus oral MTX is greater bioavailability, particularly at higher doses. In studies of healthy volunteers or patients with rheumatoid arthritis, the bioavailability of MTX following oral administration appears to plateau at doses of 15 mg or higher,<sup>1</sup> whereas that of subcutaneous MTX appears to increase linearly at a wide range of doses and exceeds that of oral MTX at each dose examined.<sup>1,2</sup> A switch from oral

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to subcutaneous MTX may therefore benefit patients experiencing suboptimal disease control.

Another important benefit of subcutaneous versus oral MTX is the potential for reduced intensity of gastrointestinal adverse events.<sup>2,3</sup> In a study of patients with rheumatoid arthritis, those who received subcutaneous MTX reported less severe nausea, vomiting, abdominal pain, and diarrhea than those who received oral MTX,<sup>3</sup> which may improve treatment adherence and potentially enable patients to tolerate higher doses. Because gastrointestinal adverse events are a common cause of MTX treatment discontinuation, a switch from oral to subcutaneous MTX may be an important strategy to enable more patients to benefit from this treatment option.

Subcutaneous MTX presents some potential challenges, including patients' fear of needles and difficulties with drawing and administering an accurate drug dose using a vial, needle, and syringe. However, recent developments in autoinjector technology have produced MTX injection devices that largely mitigate many of these challenges. Methotrexate autoinjectors allow for the accurate administration of prespecified doses, and patients generally find them easy to use.<sup>4</sup> Furthermore, MTX autoinjectors have been associated with low levels of administration-site pain (median pain score on a visual analog scale, 1.0/100 mm in one study<sup>4</sup>), and the concealment of a needle from view may potentially lessen needle phobia.

### Role of Subcutaneous Methotrexate in Patient Care

The types of patients expected to benefit most from subcutaneous MTX include those with moderate to severe psoriasis and those who have experienced dissatisfaction with topical medications or phototherapy. The increased bioavailability of subcutaneous MTX as well as the reduced intensity of gastrointestinal adverse events compared with oral MTX may enable patients to achieve a greater clinical response, and the systemic route of administration may improve treatment adherence and patient satisfaction among those who are dissatisfied with topical treatment regimens. Notably, an additional benefit of optimizing MTX treatment may be the potential to prevent or delay progression to biologic therapies, which may be an important goal of both patients and physicians to prevent higher health care costs.

Another principal role of subcutaneous MTX is as a component of combination therapy with topicals or other systemic therapies for either long-term care

or periodic treatment of disease flares. Methotrexate is a frequent component of combination therapies, and subcutaneous administration may be preferable for many patients, particularly those who are already accustomed to injectable therapies (eg, biologic agents) and those who regularly visit a physician who can perform the injections (eg, for regular phototherapy treatments). Interestingly, the coadministration of MTX may be especially valuable in the context of biologic therapies, as concomitant MTX is associated with a reduced incidence of antidrug antibodies and may therefore enhance or prolong responses to biologic agents.

### Final Thoughts

Because subcutaneous MTX is infrequently used for the treatment of psoriasis in the United States, increased awareness of its unique advantages may provide new opportunities for patients to tailor treatment regimens to meet individual needs and preferences. Treatment optimization across a broad range of patient characteristics may be critical to improving adherence and satisfaction in psoriasis patients and may be considered a major therapeutic goal.

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