

## Revisiting the safety profile: Understanding the link between Methotrexate and skin cancer in psoriasis patients

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Madam, Methotrexate (MTX) is an antimetabolite (formerly known as amethopterin) proven to be effective in managing autoimmune diseases by suppressing the hyperactive immune response, reducing inflammation, and alleviating associated symptoms. In the case of psoriasis, a chronic autoimmune skin disorder characterized by red, scaly patches on the skin, MTX is among the available treatment options. It is proven beneficial for moderate to severe psoriasis that does not respond adequately to other treatments by reducing the severity and extent of the skin lesions, relieving itching, and improving the overall quality of life. A recent study by Ravi Bharadwaj et al. found that MTX exerts its therapeutic effect on psoriatic skin inflammation by inhibiting the activity of the muropeptide transporter SLC46A2<sup>1</sup>. This mechanism interferes with two key inflammatory responses, namely the NOD1 and NOD2 pathways. It is administered orally, intramuscularly, intravenously, or subcutaneously. Doctors opt for a once-weekly oral dosage, which initiates at a low level to minimize adverse effects. Subsequently, the dosage is incrementally raised to attain the desired efficacy<sup>2</sup>.

Although MTX can be an effective treatment choice, its usage has raised concerns regarding the potential elevation of skin cancer risk. In recently published studies, researchers have concluded that the use of this drug in psoriatic patients might be doing more harm than good. In a meta-analysis performed by Margaret et al., it was found that psoriasis patients receiving MTX therapy have a 2.8-fold greater likelihood of developing non-melanoma skin cancer (NMSC) in comparison to those who do not undergo MTX treatment<sup>3</sup>. Moreover, there is evidence that prolonged use of MTX may be associated with an increased probability of developing basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC), following a dose-dependent trend<sup>4</sup>. Individuals

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with psoriasis who may require long-term systemic treatment could face a significantly elevated risk of developing skin cancer.

Despite multiple studies confirming the link between MTX and different skin malignancies, its usage remains alarmingly high in treating psoriasis. In resource-limited settings such as Pakistan, this drug is a cost-effective and efficient therapeutic option for managing various forms of psoriasis, including extensive plaque-type psoriasis, acute pustular psoriasis, and erythrodermic psoriasis<sup>5</sup>. Nevertheless, healthcare workers in Pakistan must prioritize establishing an accurate drug administration plan, to reduce morbidity and mortality rates, as well as the heightened risk of non-melanoma skin cancer (NMSC) among psoriasis patients receiving this treatment.

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