

A Boxed Warning for Inadequate Psoriasis Treatment

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The US Food and Drug Administration uses the term *boxed warning* to highlight potentially dangerous situations associated with prescription drugs. A boxed warning is used when “[T]here is an adverse reaction so serious in proportion to the potential benefit from the drug (e.g., a fatal, life-threatening or permanently disabling adverse reaction) that it is essential that it be considered in assessing the risks and benefits of using the drug.”¹ However, drugs are not the only potential cause of

severe adverse outcomes in patients with psoriasis. Untreated psoriasis also is a well-established cause of serious morbidity and mortality. What are the risks of inadequate psoriasis treatment?

Psoriasis is associated with an increased risk for cardiovascular disease.²⁻⁴ Patients with psoriasis also have a higher prevalence of classic cardiovascular risk factors including smoking, diabetes mellitus, hypertension, obesity, and hyperlipidemia.^{5,6} Psoriasis is a T-cell mediated disease process driven by IL-23 and T_H17 helper cell–derived proinflammatory cytokines, sharing certain genetic aspects with metabolic syndrome.⁶ Cytokine actions on insulin signaling, lipid metabolism, and adipogenesis may underlie the increased prevalence of metabolic syndrome and cardiovascular risk factors in patients with psoriasis. In addition to treating the cutaneous manifestations of psoriasis, reducing inflammation in these patients reduces C-reactive protein and lipid peroxidation and increases high-density lipoprotein levels.⁶ Tumor necrosis factor α blockers decrease the risk for cardiovascular disease in patients with psoriasis.^{7,8} Lower than expected rates of cardiovascular disease also have been reported in a large cohort of psoriasis patients (ie, PSOLAR [Psoriasis Longitudinal Assessment and Registry] registry) being treated with either ustekinumab or tumor necrosis factor α blockers.⁹

Psoriatic arthritis is a chronic inflammatory disease in which active inflammation results in progressive joint destruction.¹⁰ Tumor necrosis factor α inhibitors suppress disease progression, preserve function, and delay destruction of the joints. Ustekinumab also helps control psoriatic arthritis and inhibits radiographic progression of joint disease.¹¹

Importantly, untreated moderate to severe psoriasis is associated with several comorbidities that may lead to early death such as heart attacks and strokes.¹² Furthermore, patients not taking biologic medications may have higher death rates than patients taking biologic medications.⁹ Psoriasis also is associated

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Ms. Kagha and Ms. Anderson report no conflict of interest.

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with tremendous suffering and negative psychosocial effects. The mental and physical impact of the disease is comparable to other major medical conditions (eg, cancer, arthritis, hypertension, heart disease, diabetes, depression).¹³ Patients also may experience physical discomfort from pain and itching.¹⁴ Children with psoriasis may experience bullying, which is associated with an increased number of depressive episodes, thereby increasing their risk for developing psychiatric conditions such as depression and anxiety as adults.¹⁵ The stigma associated with psoriasis may affect patients' ability to build relationships. Patients with psoriasis experience higher divorce rates than patients with other chronic medical conditions, and direct involvement of genital regions may negatively impact patients' sex lives. Patients have noted that the stigma of psoriasis also is associated with the inability to obtain employment.¹⁵ Almost one-third of patients with psoriasis who are either not working or are retired base their work status on their skin condition.¹⁶ Furthermore, psoriasis may contribute to economic burden for patients due to indirect costs associated with work absenteeism.¹⁷

Adequate treatment of psoriasis improves patients' physical and psychological health as well as their ability to function in the workplace. However, despite the benefits of treatment, 30% of patients with severe psoriasis and 53% of patients with moderate psoriasis receive no treatment or only topical medications instead of systemic therapies.¹⁶ The potential adverse events of inadequate psoriasis treatment far outweigh any potential benefits of withholding treatment. Perhaps a boxed warning should be issued for inadequate treatment of psoriasis patients.

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