Psoriasis is a chronic autoimmune skin disease with multiple comorbidities that can have a considerable impact on quality of life (QoL). As therapeutic options evolve, physicians should look to treatment guidelines and consensus statements to keep their practice and management of psoriasis patients current with worldwide standards. This article reviews the most up-to-date general guidelines available for the management of psoriasis.

Psoriasis is a chronic autoinflammatory disorder affecting approximately 2% to 4% of the Western population.1 While there is no absolute cure for psoriasis, novel therapies allow for substantial reduction in symptoms and considerable improvement in quality of life (QoL). In the past few years, multiple treatment guidelines (recommendations based on evidence-based literature reviews) and consensus statements (a set of declarations determined and voted on by a panel of experts in the field) have been developed to guide physicians worldwide in treating psoriasis in the clinical setting (eTable).2-10

Psoriasis is a complex disease with multiple comorbidities, applicability of these guidelines may be limited. Although some basic treatment algorithms exist, patient preference, disease severity, and other variables including comorbidities (eg, psoriatic arthritis [PsA], risk of major cardiac events, inflammatory bowel disease [IBD]), history of nonmelanoma skin cancer (NMSC), pregnancy and lactation, and specific contraindications to therapy (eg, renal failure, liver disease, active malignancy) should be considered. In this article, we summarize common themes across existing guidelines and consensus statements for the treatment of psoriasis and highlight areas where there is consistent agreement or lack of sufficient information.

Disease Severity and Treatment Outcomes

There currently are no consensus definitions for mild, moderate, and severe psoriasis, but several consensus statements have attempted to standardize grading systems based on objective values, such as body surface area (BSA) and psoriasis area and severity index (PASI)(a scoring system used to grade the degree of redness, thickness, and scaling of psoriasis plaques), as well as subjective QoL measures.2,6 Although classification of disease severity varies, mild psoriasis generally is characterized as disease that can be managed with local and topical therapy, and moderate to severe psoriasis typically warrants consideration for escalated treatment with phototherapy or systemic agents.

Most definitions of disease severity in psoriasis reference 5% to 10% BSA involvement as a cutoff that should trigger consideration of systemic treatment; however, these criteria could result in undertreatment of patients with substantial disease. For example, patients who have limited BSA involvement but whose disease has a considerable impact on QoL, as well as those who have debilitating disease in localized areas (eg, palms, soles, scalp, nails) or substantial joint involvement may also be appropriate candidates for systemic treatment.5,8
Once therapy is initiated, patients should be evaluated for appropriate treatment response at dedicated intervals. While the time to maximum therapeutic benefit depends on the agent of choice, European guidelines recommend that patients be evaluated after an induction phase (typically 16–24 weeks) and define treatment success as either (1) at least 75% improvement in PASI or (2) at least 50% improvement in PASI and a Dermatology Quality of Life Index (DLQI) score of 5 or lower.

Alternatively, the National Psoriasis Foundation (NPF) recommended BSA as the preferred outcome measure in a recent consensus statement and concluded that an outcome of 3% or less BSA involvement or improvement in BSA of 75% or more is considered a desirable treatment response. Additionally, the Medicare Merit-based Incentive Payment System (MIPS) guidelines for successful systemic treatment response include at least 1 of the following: (1) physician global assessment score of 2 or lower, (2) BSA involvement of less than 3%, (3) PASI score lower than 3, or (4) DLQI score of 5 or lower.

Although an array of outcome measures have been utilized in clinical trials and proposed in psoriasis guidelines and consensus statements, BSA is typically a manageable measure of treatment response in a clinical setting; however, DLQI should also be assessed if possible, particularly in patients with debilitating localized disease.

Treatment Options
Because topical treatment regimens can be arduous and typically do not result in sustained clearance, patient expectations should be ascertained prior to initiation of therapy. Topical corticosteroids often can be used as monotherapy in patients with mild psoriasis. Topical vitamin D analogues and retinoids also can be effective; however, combined use of these agents with topical steroids should be considered to increase efficacy, and combination formulations can be prescribed to simplify application and improve adherence. Treatment with UVB or psoralen plus UVA phototherapy is recommended for patients with moderate to severe psoriasis as well as in those who have had minimal response to topical therapy. Targeted phototherapy with an excimer laser can be used in patients with BSA involvement of less than 10%.

Methotrexate (MTX), cyclosporine, and acitretin are the most commonly prescribed systemic medications for severe psoriasis in the United States. Despite the risk for hepatotoxicity, MTX appears to have the best combined safety and efficacy profile in terms of serious adverse events compared to other systemic agents. Guidelines for MTX monitoring, especially with regard to when to do a liver biopsy, have been substantially liberalized over time, and the recommended interval for biopsy has been extended by years; biopsy was previously recommended after a cumulative MTX dose of 1 to 1.5 g, but guidelines now suggest biopsy after 3.5 to 4 g in low-risk patients. While abnormally elevated function tests during treatment with MTX may necessitate liver biopsy, the use of transient elastography and a panel of serum biomarkers for liver function also can be used to monitor noninvasively for hepatotoxicity before biopsy is considered; these recommendations are likely to be incorporated into newer guidelines in development. Methotrexate has demonstrated safety and increased efficacy when used in combination with biologic agents such as adalimumab, etanercept, infliximab, and secukinumab and has been studied in combination with many biologics indicated for PsA.

Due to a considerable risk of glomerulonephritis, cyclosporine is approved for a maximum of 1 year of continuous treatment of psoriasis in the United States and 2 years in Europe. Cyclosporine is best used as induction therapy in psoriasis patients with severe disease who are seeking faster abatement of symptoms.

Acitretin is another systemic treatment option, although efficacy of this agent is dose dependent. Higher dosing often is limited due to lower tolerability.

Given that many insurance formularies primarily cover traditional systemic therapies and that MTX and phototherapy are generally well tolerated and cost effective, patients may need to be treated with traditional agents before escalating to biologics. Prior to starting treatment with any biologic, patients should typically be screened for tuberculosis (TB), human immunodeficiency virus infection, and immunization for, exposure to, and/or infection with hepatitis B and C virus, and any other active infections. In patients who do not demonstrate hepatitis immunity, the hepatitis B vaccine should be administered prior to starting treatment with a biologic. In psoriasis patients with latent TB, 2 months of treatment should be completed before initiating biologic therapy; once a biologic has been initiated, all patients should be screened annually for TB.

European guidelines for biologic treatment recommend that complete blood count and liver and renal function be evaluated at baseline, at months 1 and 3 of treatment, and then every 3 to 6 months thereafter while on the biologic agent. These recommendations are more stringent than those indicated in regulatory labeling and, based on the continual accumulation of data regarding the safety of these agents, some investigators have argued that laboratory testing might not be necessary at all.

Treatment in Special Populations
Psoriasis patients often present with comorbidities or a complicated medical history, which can make it challenging to decide which therapy is most suitable. Patients with comorbid diseases (eg, PsA, risk of major cardiac event, IBD) or a history of NMSC and those who are pregnant or are lactating require special considerations to ensure treatment safety and efficacy.

Tumor necrosis factor α (TNF-α) and IL-17 inhibitors are used in the treatment of joint disorders and should be considered in patients with PsA. IL-23/IL-12 inhibition appears to have less benefit in patients with PsA, but studies on IL-23 inhibition (p19 antibodies) alone are ongoing. It has been reported that TNF-α inhibition may be beneficial in patients at risk for major cardiac events. In patients with IBD, IL-17 inhibitors should be...
avoided because they may exacerbate the condition; how-
ever, TNF-α and IL-23/IL-12 inhibition have shown to be safe in patients with IBD and many agents in these classes are approved by the US Food and Drug Administration for use in this population.18,19

Although biologics may increase the risk of developing NMSC20 and should generally be avoided in patients with any active malignancy, specific guidelines for screening and initiation of treatment in patients with a history of cancer are not clearly outlined. Prior to initiating systemic therapy in any patient, a careful medical history should be obtained. These agents often are not prescribed in patients with a history of cancer until remission has been established for at least 5 years, with the exception of patients with a history of treated NMSC.8 Annual skin monitoring for NMSC should be undertaken for psoriasis patients on most immunomodulating systemic therapies.

Recommendations for biologic treatment in psoriasis patients who are pregnant or lactating also are limited. European guidelines have noted pregnancy as an absolute contraindication to treatment with biologics,7 but the regulatory guidance has recently changed for some agents, so this recommendation also may evolve.21 British8 and US guidelines do not consider pregnancy a contraindication for treatment with biologics.

Information on the safety of TNF-α antagonists during pregnancy comes primarily from use in patients with IBD and rheumatologic disease. To date, reports on the incidence of congenital malformations have been generally reassuring. Because IgG antibodies are actively transferred across the placenta in the late-second or the third trimesters, newborns born to mothers on biologic treatments may have high levels of some biologic drugs at birth. As a result, live vaccination should be avoided in neonates whose mothers were treated with IgG-based biologics.

Changing Treatment Agents
Patients may need to stop and change treatment agents due to ineffectiveness, personal preference, or worsening disease. When transitioning from any systemic or biologic agent to another (other than MTX), the British Association of Dermatologists recommends a washout period of at least 1 month before initiating a new therapy.8 Most guidelines do not define parameters for therapy escalation when patients fail multiple systemic agents, so physicians should use clinical judgment along with consideration of patient preference and comorbidity profile to ascertain which agent is most appropriate.

Conclusion
Keeping psoriasis treatment guidelines updated can be difficult, especially as new therapeutic options for psoriasis and treatment regimens rapidly evolve. Regulatory recommend-}


## eTABLE. Current Guidelines and Consensus Statements for the Treatment of Psoriasis

<table>
<thead>
<tr>
<th>Group (Year)</th>
<th>Type of Document</th>
<th>Proposed Classification of Disease Severity</th>
<th>Outcome Measure(s) For Evaluation After Treatment Initiation</th>
<th>Treatment Algorithm and Laboratory Monitoring Recommendations Provided?</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Psoriasis Foundation2 (2007)</td>
<td>Consensus statement</td>
<td>Candidates for localized therapy: BSA &lt; 5%; candidates for systemic or phototherapy (or both): BSA &gt; 5% or BSA &lt; 5% involving the face, genitals, palmoplantar surfaces, nails, scalp, or intertriginous areas</td>
<td>N/A</td>
<td>No</td>
</tr>
<tr>
<td>American Academy of Dermatology3-5 (2009)</td>
<td>Guidelines</td>
<td>Candidates for topical therapy: BSA &lt; 5%; candidates for phototherapy and systemic therapy: BSA &gt; 10%</td>
<td>Improvement in PASI of ≥75% from baseline</td>
<td>Yes</td>
</tr>
<tr>
<td>European consensus program6 (2011)</td>
<td>Consensus statement</td>
<td>Mild: BSA ≤ 10 + PASI ≤ 10 + DLQI ≤ 10; moderate to severe: BSA &gt; 10 + DLQI &gt; 10 or PASI &gt; 10 + DLQI &gt; 10</td>
<td>Treatment success: Improvement in PASI of ≥75% from baseline; treatment failure: Improvement in PASI &lt; 50%; for patients in whom treatment response is between PASI 50%-75%, a DLQI score &gt; 5 can indicate the need for change in therapeutic agent</td>
<td>No</td>
</tr>
<tr>
<td>European Dermatology Forum7 (2015)</td>
<td>Consensus statement and guidelines</td>
<td>Moderate to severe: PASI &gt; 10</td>
<td>After treatment induction: improvement in PASI of ≥75% from baseline, PGA ≤ 1; long-term: improvement in PASI of ≥90% from baseline, PGA ≤ 1, DLQI ≤ 5</td>
<td>Laboratory monitoring only</td>
</tr>
<tr>
<td>British Association of Dermatologists8 (2017)</td>
<td>Guidelines</td>
<td>Candidates for biologic therapy: DLQI &gt; 10 + PASI ≥ 10, or BSA &gt; 10</td>
<td>≥50% improvement in PASI or BSA from baseline, DLQI improvement of ≥4 points</td>
<td>Yes</td>
</tr>
<tr>
<td>National Psoriasis Foundation9 (2017)</td>
<td>Consensus statement</td>
<td>None</td>
<td>Acceptable: improvement in BSA ≥ 75% from baseline or ≥3% BSA; target: ≥1% BSA</td>
<td>No</td>
</tr>
<tr>
<td>MIPS (2018)10</td>
<td>Quality Measure</td>
<td>None</td>
<td>One of the following: PGA ≤ 2 (clear to mild skin disease), BSA &lt; 3%, PASI &lt; 3, DLQI ≤ 5</td>
<td>No</td>
</tr>
</tbody>
</table>

Abbreviations: BSA, body surface area; N/A, not available; PASI, psoriasis area and severity index; DLQI, Dermatology Quality of Life Index; PGA, physician global assessment; MIPS, Merit-based Incentive Payment System.