THE PSORIASIS AND PSORIATIC ARTHRITIS POCKET GUIDE

Treatment algorithms and management options

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psoriasis.org
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This is the fifth edition of The Psoriasis and Psoriatic Arthritis Pocket Guide: Treatment Algorithms and Management Options. Since the publication of the fourth edition, several new psoriatic disease treatments have become available, and the medical community has more experience with biological treatments in the management of psoriatic disease. The National Psoriasis Foundation has revised this publication again to provide more up-to-date guidance for managing patients with moderate to severe psoriasis and psoriatic arthritis to put the role of biologics, no longer new drugs, into perspective.

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CHAPTER 1 INTRODUCTION

EPIDEMIOLOGY
Psoriasis affects approximately 2.1% of U.S. adults, up to 7.5 million people, of whom about 25-30% will develop psoriatic arthritis. Approximately 1.5 million U.S. adults are considered to have moderate to severe psoriasis. Between 150,000 and 260,000 new cases of psoriasis are diagnosed each year. 1-3

Although psoriasis may be more prevalent in women than men, psoriasis affects all ages, genders, races and ethnicities. Most patients will present before age 35 with their first signs and symptoms of psoriasis. From an economic standpoint, people with psoriasis lose an estimated 56 million hours of work each year.

In addition, approximately $11.25 billion is spent annually treating the disease. 4 Without treatment, the disease can become more severe, which can lead to a lower quality of life. 5 Psoriasis treatment costs add up to more than those of other lifelong illnesses, such as emphysema and epilepsy. 6

PSORIASIS: A SYSTEMIC DISEASE
Psoriasis is a systemic, immunological, genetic disease manifesting in the skin and/or joints. Because of its systemic nature, patients exhibit a broad spectrum of symptoms that vary in severity. Although many patients, particularly those with the limited form of the disease, may be treated with topical therapy, those with extensive (moderate to severe) psoriasis eventually require phototherapy or systemic therapy to adequately suppress the systemic, immunopathogenic process.

Psoriasis may be defined by body surface area (BSA) alone, where 0-3% BSA = mild, 3 to 10% BSA = moderate, and greater than 10% BSA = severe. It can also be defined as less than 3% BSA = limited and greater than 3% BSA = extensive. In clinical trials, the standard for severe psoriasis is the presence of lesions over more than 10% BSA. These definitions do not consider the impact on a patient’s quality of life. Localized disease in certain areas (face, genitals) can also be severe, having a disproportionate impact on quality of life.

Physicians typically define the severity of psoriasis based on assessing body coverage, the degree of inflammation and scaling, the severity of the symptoms, the specific locations involved and the effect of the disease on the patient’s life. Severe psoriasis, and many cases of moderate psoriasis, can be treated effectively with systemic therapies.

When certain localized areas such as the hands, face and scalp (less than 3% BSA) are involved the impact on the patient is often of sufficient magnitude to warrant systemic therapy.

Psoriatic arthritis (PsA) is an inflammatory joint disease that can involve the spine (sacroiliac joints, lumbar, thoracic, cervical) and any of the joints in the extremities, shoulders or hips. Patients often develop inflammation where tendons, ligaments or joint capsules attach to bone (enthesitis) or diffuse swelling of a toe or finger (dactylitis). About 25-30% of psoriasis patients develop PsA, typically about 10 years after onset of psoriasis.

The disease is highly variable in presentation and course. Some patients have mild joint symptoms while others develop severe arthritis with joint damage that results in disability. In general, joint involvement is asymmetric, and patients often have nail changes typical of psoriasis.

NEGATIVE EFFECTS ON QUALITY OF LIFE
Psoriasis is a lifelong, chronic, recurrent disease. In patient surveys conducted between 2001 and 2008 by the National Psoriasis Foundation (NPF), 33% of patients with mild and 60% of patients with moderate-to-severe psoriasis reported that their disease was a significant problem in their everyday life. 7 The negative effect on physical, psychological and social dimensions of life can be greater than those from life-threatening illnesses such as myocardial infarction. 8

<table>
<thead>
<tr>
<th>TABLE 1-1</th>
<th>Physical and mental rankings of psoriasis and other diseases, from best functioning (1) to worst functioning (11)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical Rank</strong></td>
<td><strong>Mental Rank</strong></td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>11</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>10</td>
</tr>
<tr>
<td>Type 2 Diabetes</td>
<td>9</td>
</tr>
<tr>
<td>Chronic Lung Disease</td>
<td>8</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>7</td>
</tr>
<tr>
<td>Arthritis</td>
<td>6</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5</td>
</tr>
<tr>
<td>Depression</td>
<td>4</td>
</tr>
<tr>
<td>Cancer</td>
<td>3</td>
</tr>
<tr>
<td>Dermatitis</td>
<td>2</td>
</tr>
<tr>
<td>Healthy</td>
<td>1</td>
</tr>
</tbody>
</table>

0 5 10 15 20
COMORBIDITIES IN PSORIASIS

While psoriasis has traditionally been categorized as a disease of the skin and/or joints, multiple reports now attest the disease’s systemic inflammation has ramifications for other organ systems, including the cardiovascular, liver, respiratory, renal and hematological systems. Thus patients, particularly those with more severe disease, may be at increased risk for coronary artery disease, type II diabetes, elevated lipids, hypertension, fatty liver and its consequences, stroke, chronic obstructive pulmonary disease, sleep apnea and lymphoma. In addition, there is an increase in depression and anxiety, as well as increased alcohol consumption and smoking.

Finally, other significant autoimmune diseases such as Crohn’s disease, diabetes mellitus, and even multiple sclerosis, may be genetically linked to psoriasis.

Dermatologists, in consultation with primary care physicians and other specialists, are the front line in evaluating and in elucidating the comorbid conditions and medical consequences of this immune disease. As with psoriasis patients, PsA patients develop comorbidities such as diabetes, obesity, fatty liver, hypertension and metabolic syndrome at a higher rate than in the general population.

DIFFERENTIAL DIAGNOSIS

Several important dermatoses – including fungal infections, mycosis fungoides and drug eruptions – may mimic psoriasis.

Chapter 2 contains a related full differential diagnosis section.

SYSTEMIC THERAPY: GOING BEYOND TOPICALS

It is medically appropriate to use systemic therapies, alone or in combination with topicals and phototherapy, in patients who do not have extensive psoriasis, if:

- The patient is unresponsive to topicals and other therapies.
- Phototherapy is ineffective or impractical.
- The patient’s quality of life is negatively affected to a degree that justifies the potential adverse effects of systemic therapy.
- Significant psoriatic arthritis is present.

The decision to use systemic therapy requires a thorough discussion between the patient, the physician and the medical support staff. For more information regarding systemic therapy visit psoriasis.org/systemics.

THERAPY OPTIONS

Currently, physicians treating psoriasis patients have many therapeutic options available, including targeted immunologic therapies (biologics). Treating a chronic systemic immunologic disease such as psoriasis can be difficult for both patient and physician, and this handbook is designed to facilitate successful decisions. Chapter 4 includes suggested patient algorithms that are a quick reference to a variety of patient types, recommended treatments, side effects and management options plus suggested treatment sequences. The potential side effects of therapies reviewed in Chapter 4 vary in their seriousness, which must be weighed in the balance when considering a course of therapy.

HOW MUCH, HOW OFTEN AND AT WHAT DOSE?

After choosing a treatment strategy, the next step is to consider dosing, side effects, length of treatment and overall patient management, especially if the strategy includes switching from one systemic treatment to the next, as in sequential therapy.

Chapters 5 and 6 discuss each of these points relative to the therapies outlined in the patient algorithms. These chapters also discuss clinical pearls and transitional issues related to the systemic therapies.

TREAT TO TARGET

In 2016, the National Psoriasis Foundation developed treatment target recommendations for those with severe psoriatic disease. A rigorous, scientific Delphi process that involved 25 key opinion leaders, as well as practicing dermatologist and patient input, determined that treatment progress should be measured at 3 months after a treatment is initiated and thereafter at 6 month intervals. These goals stipulate that at the 3 month assessment, the BSA should be less than or equal to 1%. Understanding that occasionally medications have not reached their full potential at 12 weeks, an acceptable response was also stipulated which is a BSA improvement of 75% from the patient’s baseline level or a BSA of 3% or less. At 6 months it is expected that a BSA of 1% or less should be achieved. At each of these points of evaluation, it is understood that every patient is unique and has individual needs and comorbid diseases. Therefore, those who’ve not reached these target goals should have a conversation with their
provider about what next steps could be considered. These could include the addition of topical therapies, concurrent combination therapy such as the addition of methotrexate or phototherapy to a biologic regimen, a dose alteration of the systemic medication, or a complete change of systemic therapy. It is understood there are certain unique situations that may make achieving target goals not feasible such as during pregnancy or in the setting of a child with psoriasis.

This treat to target effort in psoriasis is by no means the first such effort. Championing goals have long been important in the areas of diabetes and hypertension. These goals have lead to enhanced outcomes as levels of glucose, hemoglobin A1c, and blood pressure measurements are brought closer to the normal range. Treat to target goals have also been highly effective in improving both quality measures and increasing ACR scores in both rheumatoid arthritis and psoriatic arthritis. Target goals have also been developed for psoriasis in both Europe and Canada, which have paved the way for improved outcomes for those with psoriasis. While these goals are the first such goals in psoriasis in the United States, we recognize that over time they will evolve as the understanding of psoriasis grows. We hope that they will, however, become the framework of discussion between the patient and his or her provider in the treatment of this inflammatory systemic disease.

**TREATING PATIENTS IN PRACTICE**

Patients should be fully educated about all aspects of their disease, including all potential systemic-related disorders. Each patient should also receive a specific, personalized treatment plan.

**OBJECTIVES**

After studying this handbook, physicians should be able to:

- Define the severity of psoriasis and develop an appropriate therapy plan.
- Explain the profound emotional, social and physical impact psoriatic disease has on the patient.
- Understand the important comorbidities associated with psoriasis.
- Differentiate psoriasis from other diseases after evaluating patients who present with similar types of skin lesions.
- Diagnose patients who have moderate disease (3% to 10% body involvement) and severe disease (>10% body involvement or <10% involvement but resistant to topical therapy) and identify those who will potentially benefit from systemic therapy.
- Discuss therapeutic options and appropriate doses for patients at various stages of severity.
- Describe toxicities expected with various therapies and ways to minimize and manage them.
- Understand the importance of assessing psoriasis patients for psoriatic arthritis, and how a diagnosis of psoriasis and psoriatic arthritis impacts therapeutic options.

---

**TABLE 1-2**

<table>
<thead>
<tr>
<th><strong>Systemic therapy algorithm</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.</strong> Does the psoriasis affect &gt;3 percent body surface area (BSA)?</td>
</tr>
<tr>
<td><strong>2.</strong> Is the patient disabled by the psoriasis?</td>
</tr>
<tr>
<td><strong>3.</strong> Does the psoriasis have a significant impact on the patient’s quality of life?</td>
</tr>
<tr>
<td><strong>4.</strong> Does the patient have psoriatic arthritis?</td>
</tr>
</tbody>
</table>

**YES TO ANY OF THE ABOVE.**

- 5. Does the patient have psoriatic arthritis?*
- 6. Was systemic treatment required in the past?
- 7. Is phototherapy contraindicated or unavailable, or is the psoriasis resistant to phototherapy?

**NO TO ALL.**

- The patient is not a candidate for total body phototherapy or systemic treatment.

**YES TO ANY OF THE ABOVE.**

- The patient is a candidate for systemic treatment.

**NO TO ALL.**

- The patient is not a candidate for systemic treatment, but may be a candidate for phototherapy if they have greater than 3 percent BSA.

*Phototherapy can be used for treatment of psoriasis skin lesions in patients with psoriatic arthritis, but these patients also require systemic treatment for the joint involvement.
CHAPTER 2

ASSESSING A PSORIASIS PATIENT
CHAPTER 2 ASSESSING A PSORIASIS PATIENT

CLINICAL PRESENTATION

The clinical manifestations of psoriasis are usually recognized easily, although presentation and the location of the psoriasis may vary at different stages of the disease. (See Table 2-1.)

INITIAL WORK-UP

Unless the patient prefers otherwise, the physician should perform a complete skin examination, including the nails and scalp, at the first visit. Physicians should routinely ask patients with psoriasis about joint symptoms and back pain, which might be indicative of psoriatic arthritis. They should also discuss clinical presentation factors and encourage patients to take advantage of NPF resources to help address psychosocial and patient education issues. (See Table 2-2.)

DETERMINING DISEASE SEVERITY

The severity of psoriasis is determined by the extent and character of the lesions (measuring the percentage of BSA affected, determining the location of lesions) and by the effect of psoriasis on the patient’s quality of life and ability to function. (See Table 2-3.)

ASSESSING A PATIENT

Psoriasis is traditionally classified as mild-to-moderate or as moderate-to-severe. About 65% of patients have mild disease as defined by body surface area involvement and about 35% have moderate-to-severe disease (Table 2-3). 1-3 The NPF defines moderate-to-severe disease not only in terms of BSA (>3%), but also includes patients with a BSA of <3% who are being treated with a systemic medication or with phototherapy.

For treatment purposes, it is helpful to define psoriasis as either limited (BSA <3%) or extensive (BSA >3%). In practical terms, limited disease means few enough spots that the patient feels they can reasonably apply topicals to all the lesions. Extensive psoriasis (as well as palmoplantar psoriasis) generally cannot be treated with topical treatments alone. Patients with extensive psoriasis are candidates for phototherapy and/or systemic treatment, often along with topical treatments to the worst areas.

TABLE 2-1
The most common locations of lesions in patients with psoriasis

<table>
<thead>
<tr>
<th>Percent of Psoriasis Patients</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>Scalp</td>
</tr>
<tr>
<td>78</td>
<td>Elbows</td>
</tr>
<tr>
<td>74</td>
<td>Legs</td>
</tr>
<tr>
<td>57</td>
<td>Knees</td>
</tr>
<tr>
<td>54</td>
<td>Arms</td>
</tr>
<tr>
<td>53</td>
<td>Trunk</td>
</tr>
<tr>
<td>47</td>
<td>Lower part of the body</td>
</tr>
<tr>
<td>38</td>
<td>Base of the back</td>
</tr>
<tr>
<td>38</td>
<td>Other</td>
</tr>
<tr>
<td>12</td>
<td>Palms and soles</td>
</tr>
</tbody>
</table>

Adapted from van de Kerkhof (2003) 16

TABLE 2-2
Discussion points for provider/patient on initial visit

<table>
<thead>
<tr>
<th>Symptoms/lesions/diagnosis</th>
<th>Hereditary aspect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic manifestations</td>
<td>Exacerbating factors</td>
</tr>
<tr>
<td>Ameliorating factors</td>
<td>Past treatment responses</td>
</tr>
<tr>
<td>Range of therapeutic options</td>
<td>Chronic long-term disease</td>
</tr>
<tr>
<td>Psychological ramifications</td>
<td>Optimism for tomorrow</td>
</tr>
<tr>
<td>Support/services available from NPF</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Menter and Weinstein 17

TABLE 2-3
Prevalence in psoriasis patients of mild, moderate and severe disease

<table>
<thead>
<tr>
<th>Percent of Body Surface</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Mild BSA, treated with systemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>65%</td>
<td>25%</td>
<td>8%</td>
<td>2%</td>
</tr>
</tbody>
</table>

TABLE 2-4
Severity of psoriasis and percent of body surface affected

<table>
<thead>
<tr>
<th>Severity</th>
<th>Percent of Body Surface</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Up to 3 percent</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 percent - 10 percent</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;10 percent</td>
</tr>
</tbody>
</table>

Adapted from Menter and Weinstein 17
MEASURING BSA

The patient’s hand—including the palm, fingers and thumb—is used as a rough, general guide for measuring how much of their skin is affected by psoriasis, representing roughly 1% of the body’s surface.

- Mild psoriasis: Affects up to 3% of the body, generally in isolated patches on the knees, elbows, scalp, hands and feet. It can often be controlled with topical therapy.

- Moderate psoriasis: Affects 3% to 10% of the body’s surface. It often appears on the arms, legs, torso, scalp and other areas. Topical agents, phototherapy, and systemic medications, including biologics, may be appropriate.

- Severe psoriasis: Affects >10% of the body. It may be extensive with plaques, pustules or erythroderma. Phototherapy, systemic medications, including biologics or a combination of these, with or without a topical agent, are usually necessary to achieve adequate results.

QUALITY OF LIFE AND SEVERITY

Psoriasis can profoundly affect a person’s life and negatively affect lifestyle, emotional well-being, social life and ability to work.

- Clinical assessment should include the patient’s perspective on subjective factors such as itching, pain, loss of sleep and effect on daily activities, as well as the clinician’s perspective.

- A patient may have psoriasis that covers only a small area, but if it is highly visible or debilitating, it could be considered a severe case despite the small area involved.

The Koo-Menter Psoriasis Instrument (KMPI) is a practical assessment tool that physicians can use in clinical decision-making and documentation for third-party payers. The KMPI is short enough for the patient and the physician to complete quickly, with items that are easy to understand and answer. At the same time, it is comprehensive enough to include a Validated Health Related Quality of Life (HRQOL) index, a Psoriasis Quality of Life questionnaire (PQOL-12) and other assessments from both the patient’s and the physician’s perspective. The patient completes one side (prior to being seen by the physician) and then the physician completes the other.

IMPACT COMPARED TO OTHER MAJOR DISEASES

Psoriasis affects physical and mental functions of patients to a similar degree that other diseases affect patients with cancer, arthritis, hypertension, heart disease, diabetes and depression.

- Physical- and mental-functioning scores for psoriasis patients are among the lowest of all groups (10/11 for physical and 9/11 for mental functioning, 11 being the lowest).

- Burning sensations, joint pain and appearance were negative physical factors.

- Itching, skin soreness and a negative or dismissive attitude from a doctor regarding psoriasis negatively affected mental function.

Physicians planning treatment options should consider psychological and social aspects of the disease, as well as the physical aspects (e.g., severity of skin lesions and the possibility of associated joint disease). It is important to work as a rheumatology/dermatology team that can diagnose psoriasis and psoriatic arthritis, and either treat or refer for care.
Patient self-assessment

Name: ____________________________  Date: __________

**Part 1: Quality of life**

Please answer each of the following questions as they pertain to your psoriasis during the past month.

<table>
<thead>
<tr>
<th>Circle one number per question</th>
<th>Not at All</th>
<th>Somewhat</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How self-conscious do you feel with regard to your psoriasis?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. How helpless do you feel with regard to your psoriasis?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. How embarrassed do you feel with regard to your psoriasis?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. How angry or frustrated do you feel with regard to your psoriasis?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. To what extent does your psoriasis make your appearance unsightly?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. How disfiguring is your psoriasis?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. How much does your psoriasis impact your overall emotional well-being?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Overall, to what extent does your psoriasis interfere with your capacity to enjoy life?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

How much has each of the following been affected by your psoriasis during the past month?

<table>
<thead>
<tr>
<th>Circle one number per question</th>
<th>Not at All</th>
<th>Somewhat</th>
<th>Very Much</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. Itching?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Physical irritation?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Physical pain or soreness?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Choice of clothing to conceal psoriasis?</td>
<td>0 1 2 3 4 5 6 7 8 9 10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Patient self-assessment

<table>
<thead>
<tr>
<th>Part 1: Total quality-of-life score (from part 1 of previous page)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Part 2: Area of involvement: percent BSA (body surface area)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head: Up to 9 percent total BSA</td>
</tr>
<tr>
<td>Anterior trunk: Up to 18 percent</td>
</tr>
<tr>
<td>Posterior trunk: Up to 18 percent</td>
</tr>
<tr>
<td>Right leg: Up to 18 percent (includes buttock)</td>
</tr>
<tr>
<td>Left leg: Up to 18 percent (includes buttock)</td>
</tr>
</tbody>
</table>

Note: Patient’s open hand (from wrist to tips of fingers) with fingers tucked together and thumb tucked to the side equals approximately 1 percent body surface area.

<table>
<thead>
<tr>
<th>Part 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Please answer the following questions by marking the appropriate checkbox</td>
</tr>
</tbody>
</table>

A. Have you ever been diagnosed with psoriatic arthritis?  
   Yes [ ]  No [ ]

B. Do you have swollen, tender, or stiff joints (e.g. hands, feet, hips, back)?  
   Yes [ ]  No [ ]

   If yes, how many joints are affected? (Check one box)  
   1 [ ]  2 [ ]  3 [ ]  4 [ ]  More than 4 [ ]

   If yes, how much have your joint symptoms affected your day-to-day activities?  
   Not at all [ ]  A little [ ]  A lot [ ]  Very much [ ]

When completed, please return to medical staff.
**Part 3: In terms of psoriasis severity, does the patient have:**

<table>
<thead>
<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque, erythrodermic, or pustular psoriasis with &gt;10 percent BSA involvement?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gluttate psoriasis?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized (&gt;10 percent BSA) psoriasis but resistant to optimized attempts at topical therapy or physically disabling (e.g., palmoplantar psoriasis)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized (&gt;10 percent BSA) but serious subtype with possibility of progression (e.g., pustular or pre-erythrodermic psoriasis)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical evidence of psoriatic joint disease as assessed by physician (e.g., examine IP, MCP and MT joints of hands, wrists, feet and ankles, plus patient responses from Part 3 of patient self-assessment)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Substantial psychosocial or quality-of-life impact documented by patient Quality-of-Life self-assessment score of ≥50?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Part 4: Is phototherapy an option?**

<table>
<thead>
<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is a suitable phototherapy unit readily accessible to the patient?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does the anatomical location or form of psoriasis (e.g., scalp, inverse, erythrodermic) preclude phototherapy?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does the patient have the dedication, time, stamina, or transportation for phototherapy?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Has phototherapy, as monotherapy, failed in the past?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is phototherapy contraindicated (e.g., photosensitive drugs, history of multiple skin cancers)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In your clinical judgment, is phototherapy likely to yield substantial improvement to justify its use before systemic therapy?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Physician/Nurse comments**

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

If at least one of the shaded boxes in both part 3 and part 4 on the previous page are checked, then the patient is a candidate for systemic therapy.

**Conclusion:** The patient is a candidate for systemic therapy.

**YES** | **NO**
EFFECTS ON SOCIAL AND ECONOMIC WELL-BEING

In a mail survey conducted by NPF, patients assessed the effects of psoriasis on their lifestyle, emotional well-being and social interactions with others. They identified the following problems:

- Difficulty finding a job
- Job complications (e.g., an average of 2.3 days/year missed due to psoriasis)
- Financial distress [reported by about one-third of respondents]
- Suicide contemplation
- Sexual activity concerns
- Emotional turmoil, including: embarrassment when people saw their psoriasis (81% of respondents); frustration with ineffective treatments (90%); feeling unattractive (75%); depression (54%)

In a 2002 study conducted by the NPF, patients with moderate to severe psoriasis said that their disease affected their quality of life in the following ways:

- 26% had to alter or stop their normal daily activities
- 40% chose clothing to cover up their condition
- 36% had problems with sleep

These studies confirm that psoriasis has a major impact on patients’ lives. Comprehensive treatment should account for this impact to control both the disease and all the sequelae.

TYPES OF PSORIASIS

A patient’s psoriasis may present in varying degrees of severity during the course of the disease. Individual lesions may range from pinpoint lesions to large plaques. The morphology of the lesions helps determine the psoriasis type. Some patients may have more than one type of psoriasis at a given time.

Plaque psoriasis is the most common type of psoriasis.

- Diagnosed in 80% to 90% of patients.
- Characterized by sharply defined erythematous plaques that are distributed somewhat symmetrically.

- Most commonly seen on the scalp.
- Coin-sized to palm-sized plaques, usually present for months to years. Lesions larger than palm-sized are often due to coalescence of individual plaques, as seen in geographic psoriasis.
- Nail involvement in up to 55% of patients, with findings such as pitting, onycholysis, subungual hyperkeratosis and “oil drops.”

Erythrodermic psoriasis consists of inflammation of the skin with replacement of the skin surface by generalized erythema, scaling and exfoliation. This type is sometimes called exfoliative psoriasis.

It is diagnosed in about 10% of patients at certain points in their lifetime; repeated episodes are not uncommon.

- Patients may be ill and have hypo- or hyperthermia, protein loss, dehydration, renal failure and cardiac abnormalities. Death may occasionally ensue. Gross nail deformations are frequent.
- Previous history of psoriasis, skin findings of psoriasis and information from a skin biopsy may all help in the differential diagnosis (e.g., eczema, Sézary’s syndrome, pityriasis rubra pilaris [PRP], etc.).
- It may occur at any age.

Pustular psoriasis is characterized by individual or coalescing sterile pustules.

- When inflammatory processes dominate, patients may develop either generalized (von Zumbusch psoriasis) or localized pustules, most often on the palms or soles (palmoplantar).
- Pustular palmoplantar psoriasis occurs in less than 5% of patients, often presenting with erythematous, scaly plaques with pustules on palms and soles. Pustules vary in size from 1 mm to 1 cm and are yellow at first, turning to brown.
- Pustular psoriasis, seldom seen in children, affects mostly the elderly. Only 12% of patients develop it before age 60. Between 70% and 90% of patients are female; 10% to 25% have a positive family history.
- Generalized forms of the disease (e.g., von Zumbusch), though uncommon, are frequently associated with arthritis and a stormy course of disease.
**Guttate psoriasis** is characterized by mostly small papules of short duration (weeks to months).  
- It usually affects children and young adults.
- Many patients suffer from an infection before the lesions appear, particularly an upper respiratory infection, commonly of the streptococcal variety.
- “Droplet” lesions occur over the entire body surface. The trunk is most commonly affected with the palms and soles usually being spared.

**Inverse/flexural psoriasis** is a seborrheic-dermatitis-like form that occurs in the armpit, under the breast and in skin folds around the groin, buttocks and genitals. Scaling is often not visible.

**NAIL AND MUCOSAL MANIFESTATIONS OF PSORIASIS**
- Both the nail bed (onycholysis, yellowish discoloration and/or hyperkeratosis) and the nail matrix (pitting) can be observed in psoriasis.  
- Fingernails are more often involved than toenails.
- Most patients with psoriatic arthritis have coexistent nail involvement. Nail involvement can be associated with pain and can cause restriction of daily activities.
- About 50% of all patients with psoriasis have fingernail involvement.
- Lesions can occur on mucosal membranes, including the geographic tongue in psoriasis patients.

**Triggers for psoriasis**
Various factors that may trigger or exacerbate psoriasis are listed in **Table 2-5**.

<table>
<thead>
<tr>
<th><strong>Table 2-5</strong> Trigger for psoriasis</th>
<th><strong>PSORIATIC ARTHRITIS</strong></th>
</tr>
</thead>
</table>
| Stress | - As many as 30% of patients with psoriasis also have psoriatic arthritis (PsA). PsA is characterized by inflammation and stiffness in the soft tissue around the joints and is often characterized by joint stiffness in the morning or after inactivity. There are five clinical subtypes of joint involvement. Frequently, this type of arthritis involves the fingers and toes.  
- In addition to joint pain and swelling, patients may develop enthesitis, pain and tenderness at the insertion of tendons or ligaments on to bone (Achilles tendonitis, tennis elbow, plantar fasciitis) and dactylitis, diffuse swelling and pain in a toe or finger.  
- Assessing musculoskeletal signs and symptoms is a key component of evaluating psoriasis patients. Psoriatic skin lesions tend to occur before joint symptoms. Joint involvement can also cause irreversible damage to the joint, so early recognition and treatment is important.  
- Patient evaluation should determine if the psoriasis and joint pain features are consistent with psoriatic arthritis or another form of joint disease. It is important to distinguish psoriatic arthritis from rheumatoid arthritis, systemic lupus erythematosus, osteoarthritis and gout.  
- When evaluating a patient with potential psoriatic arthritis, important first steps include examining peripheral joints, the spine and soft tissues (ligaments, tendons and digits) followed by blood tests and radiographs of affected joints and often the pelvis and spine. Determining the extent of joint damage strongly influences treatment selection.  

One of the major challenges in PsA is early diagnosis and referral since joint damage can occur in almost half of patients within two years of arthritis onset. Several questionnaires (PACE, PEST, TOPAS) can be administered to psoriasis patients in dermatology or primary care offices to help identify patients who may have psoriatic arthritis.

The diagnosis is based on the history, physical exam, X-rays and sometimes other imaging studies, such as musculoskeletal ultrasound or MRI, and blood tests. Unlike rheumatoid arthritis, there is no blood marker for this disease though negative RF testing for RA is a point in favor of PsA. Treatment is guided by the degree of pain, extent of joint involvement and the impact of the disease on function and quality of life. Many PsA patients suffer from additional disorders including obesity, metabolic syndrome, diabetes, hypertension and depression/anxiety.

*Adapted from Menter and Weinstein* 17
Working as a rheumatology/dermatology team is essential for diagnosing and addressing the psoriasis and arthritis, plus other diseases or comorbidities.\(^{20-22}\)

**DIFFERENTIAL DIAGNOSIS OF PSORIASIS**

Patients with typical psoriatic lesions are relatively easy to diagnose, but difficulties may arise when asymmetrical, individual lesions are present; when eruptive, pustular or erythematous phases are evolving; or when the patient has concomitant diseases. [See Table 2-6.]\(^{24}\)

**Diagnoses to rule out:**

**Bowen’s disease** (in situ squamous cell carcinoma), often presenting as a single lesion, is found in both sun-exposed and sun-protected areas of the body.

- The plaque is well demarcated, pink to red in color, with varying amounts of scale.
- A biopsy of the skin lesion is diagnostic.

**Eczema** may be confused with plaque psoriasis, erythrodermic psoriasis, generalized pustular psoriasis (von Zumbusch) or palmoplantar psoriasis.

- Primary lesions may include papules, patches and plaques; in severe eczema, weeping and crusting may predominate. Long-staying eczema may become lichenified, characterized by thickened, scaling skin that resembles psoriasis.
- Acute eczema with vesiculation is easily differentiated from psoriasis, as vesiculation is seldom seen with psoriasis.

**Hyperkeratotic eczema** of the palms and soles is more of a problem, as it is not a specific diagnosis but is used to describe several disorders, such as the following:

- Chronic palmoplantar eczema (e.g., allergic contact dermatitis, irritant dermatitis or atopic dermatitis).
- “Dermatitis” of palms and soles that is not eczema or psoriasis, i.e., overlap.
- Dyshidrotic eczema of palms and soles.
- A skin biopsy may sometimes help differentiate chronic hyperkeratosis and erythema of the palms and soles from psoriasis. Unfortunately, biopsies often reveal a combination of spongiotic and psoriasiform changes that are not specific to either psoriasis or allergic/irritant dermatitis.

**Mycosis fungoides**, patch or plaque stage (cutaneous T cell lymphoma):

- In its early stages, cutaneous T cell lymphoma (CTCL) may be confused with psoriasis; but unlike psoriasis, it tends not to have the “true” micaceous scale.
- CTCL may present as erythroderma (Sezary’s syndrome) and should be considered when no apparent cause of erythroderma is found.
- As CTCL develops within plaque lesions, the palpable component of the plaque increases.\(^{25}\)
- A skin biopsy in which atypical T lymphocytes are found in the epidermis and dermis is diagnostic.

**Pityriasis rubra pilaris** (PRP) may be confused with erythrodermic psoriasis.

- Follicular papules are characteristic, with follicular hyperkeratosis on the back of the finger.\(^{26}\) The scalp may show psoriasis-like changes.
- Patients with PRP are differentiated by having islands of unaffected skin (“skip areas”) surrounded by involved skin or yellowish or palmoplantar keratoderma.
- Classic psoriatic nail changes are absent.
- Histologic examination of a hyperkeratotic papule may be diagnostic.

**PsEMA** is a term coined to describe signs and symptoms of a combination of psoriasis and eczema.\(^{27}\)

- An overlap syndrome with clinical features of both diseases.
- Not widely accepted at present. It is not a recognized diagnosis.

**TABLE 2-6**

<table>
<thead>
<tr>
<th>Differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of Psoriasis</strong></td>
</tr>
<tr>
<td><strong>Differential Diagnosis</strong></td>
</tr>
<tr>
<td>Chronic plaque</td>
</tr>
<tr>
<td>Guttate</td>
</tr>
<tr>
<td>Erythrodermic</td>
</tr>
<tr>
<td>Pustular</td>
</tr>
<tr>
<td>PSA</td>
</tr>
</tbody>
</table>
Secondary syphilis-psoriasiform type may be difficult to differentiate from guttate psoriasis. Syphilis may involve the face and often involves the palms and soles, producing psoriasiform papules with "collarette" of scale.

- Patients may also have nonscarring alopecia, mucous patches in the mouth, lymphadenopathy, malaise, fever, headache and myalgias.
- The primary lesion may or may not still be evident.
- Lab tests: Veneral Disease Research Laboratory (VDRL) and skin biopsies are diagnostic.

Subacute cutaneous lupus erythematosus (SCLE) is characterized by a widespread photosensitive, non-scarring eruption that can present in two different forms.

- The first form is a psoriatic-like papulosquamous eruption with discrete erythematous patches on the back, chest, shoulders, arms and the backs of the hands. The scaling patches tend to merge into large plaques.
- The second is an annular form with central clearing and peripheral scale.
- Acute SCLE is characterized by a "butterfly" rash on the face, which consists of erythema of the nose and cheeks.
- Lab tests: a panel of antibody tests helps differentiate various forms of lupus erythematosus (Ro and La also called SSA and SSB).

Tinea corporis is a localized-to-widespread fungal infection of non-hairbearing skin with a varying presentation, depending on the severity of the inflammatory response.

- It may have the appearance of "ringworm" or appear as deep inflammatory nodules or granulomas.
- Characterized by papulosquamous pink-red skin lesions with central clearing and peripheral scale.
- Lab tests: KOH stain and/or fungal culture of scale or biopsy.

Differential Diagnosis of Psoriatic Arthritis

Rheumatoid arthritis (RA) differentiated from psoriatic arthritis. These two diseases have some similarities, but differ significantly in their clinical presentation and natural history. RA is more common in females and more symmetric in distribution. It does not involve the sacroiliac joints, lumbar or thoracic spine. RA patients often have a positive test for rheumatoid factor or anti-cyclic citrullinated peptide antibodies which are usually negative in PsA.

Reactive arthritis can also be confused with PsA. PsA is more gradual in onset, affects the upper extremities and is not associated with mouth ulcers, urethritis or bowel symptoms. In reactive syndrome, the onset of arthritis is acute, with symptoms occurring in new joints over a period of a few days to a few weeks. The arthritis is asymmetric and additive. Joint symptoms may persist in as many as 30% to 60% of patients.

The most common sites of involvement in reactive arthritis are the knee, ankle and toe joints, but the wrist and fingers can also be affected. A “sausage digit” – a diffuse swelling of a single finger or toe – is typical of both reactive arthritis and PsA. Low back and spinal pain are common. Patients with reactive arthritis often have conjunctivitis, mucocutaneous lesions and genitourinary disease. Nail changes are common. Infection with Shigella, Salmonella, Yersinia, Campylobacter species, clostridium difficile, and Chlamydia trachomatis may initiate psoriatic arthritis among other infections. In the majority of cases, a history will reveal an infection one to four weeks before symptoms appear; however, some show no signs or fail to recall of an earlier infection. Reactive arthritis can have a more severe presentation in the setting of HIV disease.

Ankylosing spondylitis (AS), an inflammatory disease of the spine, shares many features with PsA. Involvement of peripheral joints [hands, feet, elbows] is atypical in AS and most patients are positive for the genetic marker HLA-B27. Enthesitis and dactylitis are also observed in some patients. Involvement of the sacroiliac joints tends to be bilateral compared to PsA, where the disease is more commonly unilateral. Females with this disease are more likely to have fewer X-ray changes in the sacroiliac joints than males. Eye inflammation, uveitis, is more common in AS compared to PsA patients.

Osteoarthritis can be confused with PsA, particularly when it involves the distal joints of the fingers (DIP joints). PsA patients may also have concomitant osteoarthritis.

Gout in either one or multiple joints is more common in psoriasis patients than in the general population and can mimic PsA. It typically comes on suddenly and tends to involve joints in the feet in an asymmetric manner. Diagnosis...
is dependent on isolation of crystals in the joint fluid of an inflamed joint and often by the presence of an elevated uric acid. Gout has a waxing and waning course with periodic flares. Co-occurrence of gout and PsA has also been reported.

COMORBIDITIES AND PSORIASIS
Psoriasis and psoriatic arthritis are systemic inflammatory diseases associated with increased cardiovascular morbidity and mortality. Diabetes, obesity and metabolic syndrome, as well as myocardial infarction and depression, are more common in patients with psoriasis and psoriatic arthritis than in the general population.12,14

Screening for these comorbidities is appropriate. While definitive guidelines have not been established, physicians should at the very least carry out the recommended evaluations and prevention strategies that are appropriate for the patient’s age (Table 2-7). Patients should be encouraged to quit smoking and to tell their primary care physician about their psoriasis, as it is an independent cardiovascular risk factor. Depending on other risk factors, blood pressure, body mass index and cholesterol levels may be checked more frequently in this at-risk population.31 It may also be valuable to look for signs of depression during the history and physical examination.

<table>
<thead>
<tr>
<th>Measurement Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure evaluated at least every 2 years; target &lt;120/80 mmHg</td>
</tr>
<tr>
<td>Body mass index evaluated at least every 2 years; target &lt;25 Kg/m²</td>
</tr>
<tr>
<td>Waist circumference evaluated least every 2 years; target • &lt;35 inches for women • &lt;40 inches for men</td>
</tr>
<tr>
<td>Pulse evaluated at least every 2 years</td>
</tr>
<tr>
<td>Fasting serum lipoprotein or total and HDL cholesterol evaluated at least every 5 years or every 2 years if risk factors, such as a positive family history, presence of diabetes or smoking habits are present: • Total Cholesterol = &lt; 200 mg/dL • HDL = 50 mg/dL or higher • LDL Optimal &lt; 100 mg/dL Near Optimal/Above Optimal 100 to 129 mg/dL Borderline High 130 to 189 mg/dL Very High 190 mg/dL and above</td>
</tr>
<tr>
<td>Fasting blood glucose evaluated at least every 5 years or every 2 years if risk factors are present; target &lt;100 mg/dL</td>
</tr>
</tbody>
</table>
AHA recommendations for cardiovascular risk factor screening (Kimball et al) 31
CHAPTER 3

CHOOSING A TREATMENT
There are multiple treatment options, as well as several strategies for treating patients. The options are topical therapy, phototherapy and systemic therapy. (See Table 3-1.)

**Therapy goals are to:**

- Gain initial rapid control of the disease.
- Decrease BSA involvement.
- Decrease erythema, scaling and the thickness of lesions of individual plaques.
- Maintain the patient in long-term remission and avoid relapse.
- Avoid adverse effects as much as possible.
- Improve the patient’s quality of life.

**TABLE 3-1**

<table>
<thead>
<tr>
<th>Psoriasis Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topical Therapy</strong></td>
</tr>
<tr>
<td>Anthralin</td>
</tr>
<tr>
<td>Corticosteroid creams, lotions, ointments, gels, foams, shampoo, patches &amp; solutions</td>
</tr>
<tr>
<td>Tars</td>
</tr>
<tr>
<td>Vitamin D</td>
</tr>
<tr>
<td>Retinoid gel and creams</td>
</tr>
<tr>
<td>Topical immunomodulators</td>
</tr>
<tr>
<td><strong>Phototherapy</strong></td>
</tr>
<tr>
<td>Goeckermanb (tar and UVB)</td>
</tr>
<tr>
<td>Broad-band UVB</td>
</tr>
<tr>
<td>Narrow-band UVB</td>
</tr>
<tr>
<td>PUVA</td>
</tr>
<tr>
<td>Excimer laser</td>
</tr>
<tr>
<td><strong>Systemic Therapy</strong></td>
</tr>
<tr>
<td>Retinoids</td>
</tr>
<tr>
<td>Methotrexate immune-modulating therapy</td>
</tr>
<tr>
<td>Other cytotoxic immune-modulating therapy</td>
</tr>
<tr>
<td>Cyclosporine</td>
</tr>
<tr>
<td>Biologics IL-17 TNF blockers IL-12/23 IL-23</td>
</tr>
<tr>
<td>Phosphodiesterase 4 inhibitors</td>
</tr>
</tbody>
</table>

In addition to choosing a treatment option, the physician must also determine which treatment strategy is most appropriate for the patient. Following are the four types of therapeutic strategies to use when prescribing the various agents listed in Table 3-1:

- Monotherapy, the use of one therapeutic agent during one treatment time.
- Combination therapy, the use of two or more agents in combination during one treatment time. In combination, the agents are sometimes used at lower doses than when they are used in monotherapy.
- Rotation therapy, the use of therapeutic agents for a specified period of time (usually 1-2 years), after which they may be switched to alternative agents to avoid cumulative toxicity (not favored in PsA or with biologics in PsO).
- Sequential therapy, the use of a stronger agent[s] initially to clear the psoriasis rapidly, followed by a less toxic agent[s] for maintenance therapy; a transitional strategy minimizes the risk of psoriasis flare between the clearing and maintenance phases.

**MONOTHERAPY**

Monotherapy is often used as initial therapy.

- The advantage of one drug is that it may limit side effects, decrease costs and improve adherence to the treatment regimen.
- Long-term monotherapy with some agents may lead to toxicity at high doses. Risk factors may accumulate with continuing therapy.
- When monotherapy fails or toxicity develops, another agent or several agents may be added in combination, rotation or sequential therapy.

**COMBINATION THERAPY**

Combination therapy generally allows lower doses of individual agents to be used, helping to minimize toxicity and improve efficacy. Topicals are often used in combination with a systemic agent; however, combinations of systemic agents are often underused. The combination of two systemic agents, or of a systemic agent with phototherapy, is often more effective than each agent individually. When deciding what combination to use or to continue to use, you should evaluate product safety or the agent with the most favorable side-effect profile.
Combination therapy:

- Could allow for a lower dose of each agent to be used. One agent may be discontinued after the psoriasis has cleared and the “safer” of the two agents used for maintenance therapy. Treatment-resistant patients may continue with both agents.\(^3^3\)

- Can help maintain the efficacy of a TNF inhibitor. However, the combined use of these medications carries the risks of both medications. It is not known whether this increased efficacy improves the long-term outcome of treatment with other biologic agents.

Table 3-2 lists frequently used combination therapies, and those to be used with caution.

### TABLE 3-2

<table>
<thead>
<tr>
<th>Combination Therapy</th>
<th>Combinations with Increased Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequently Used Combinations</td>
<td>Retinoids and broad-band UVB</td>
</tr>
<tr>
<td></td>
<td>Retinoids and narrow-band UVB</td>
</tr>
<tr>
<td></td>
<td>Retinoids and PUVA (Ultraviolet light A with the drug psoralen)</td>
</tr>
<tr>
<td></td>
<td>Retinoids and methotrexate</td>
</tr>
<tr>
<td></td>
<td>Retinoids and cyclosporine to decrease cyclosporine dose</td>
</tr>
<tr>
<td></td>
<td>Cyclosporine and methotrexate (low doses of both)</td>
</tr>
<tr>
<td></td>
<td>Mycophenolate mofetil and cyclosporine in order to taper off cyclosporine</td>
</tr>
<tr>
<td></td>
<td>Oral agents [methotrexate, retinoids, cyclosporine] with any biologic</td>
</tr>
<tr>
<td></td>
<td>Cytotoxics (e.g., methotrexate) and phototherapy</td>
</tr>
<tr>
<td></td>
<td>Topicals and retinoids</td>
</tr>
<tr>
<td></td>
<td>Methotrexate + TNF antagonists</td>
</tr>
</tbody>
</table>

Combining two biologic agents has not been studied in PsO or PsA and may increase the risk of immunosuppression. Physicians should avoid this option whenever feasible, or strictly limit its duration.

### ROTATIONAL THERAPY WITH CONVENTIONAL SYSTEMIC AGENTS

Rotational therapy is used primarily with conventional systemic agents and may facilitate long-term treatment. In theory, it helps minimize chronic toxicity by periodically rotating various therapies before respective drug toxicities occur. \(\text{See Table 3-3.}\) Biological medications that do not have long-term risks to kidneys and liver have reduced the need for rotational therapy.

- Historically, treatments with known cumulative toxicity like methotrexate or cyclosporine might be rotated, usually at intervals of one to two years, possibly returning to the original therapy thereafter.

- Side effects [e.g., methotrexate-induced hepatic changes, cyclosporine-induced hypertension and renal changes, and phototherapy-induced skin changes] may be fully or partially reversed by discontinuing a drug or stopping therapy.\(^3^3\)

- Retinoid mucocutaneous side effects are completely reversed when the drug is discontinued.

### TABLE 3-3

<table>
<thead>
<tr>
<th>Rotational Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>PUVA</td>
</tr>
<tr>
<td>Acitretin</td>
</tr>
</tbody>
</table>

*In patients who have developed multiple skin cancers as a result of long-term PUVA, cyclosporine should be avoided, as it may produce further skin cancers.

The rotational therapy concept was developed before biologics. Rotation is not recommended with biologics, because some of them lose efficacy if they are discontinued and then restarted. In the case of infliximab, not only does efficacy reduce, but infusion reactions increase.
SEQUENTIAL THERAPY

Sequential therapy uses specific therapeutic agents in a deliberate sequence to maximize improvement initial speed and success probability. This minimizes side effects by smoothly transitioning from an initial rapid improvement strategy to a long-term maintenance strategy. It also allows the combination of a more potent, "less safe" agent for initial clearing with a "safer agent" for use in long-term control. Sequential therapy is administered in three steps:

Step 1: Clearing or "quick-fix" phase.
Step 2: Transitional phase.
Step 3: Maintenance phase.

Topical therapy can be administered sequentially to maximize initial clearing, minimize psoriasis recurrence and avoid steroid rebound. For example, halobetasol propionate and calcipotriene may be used as shown in Table 3-4. Sequential therapy regimens are also used with systemic agents.

When considering systemic therapy, the rationale for the sequential therapy method is that some therapies are better suited for rapid clearance (e.g., methotrexate and cyclosporine), whereas others are less toxic and more appropriate for long-term maintenance (e.g., acitretin). (See Table 3-4.)

TRANSITIONING

Transitioning between medications has traditionally been an issue when using medications with treatment-limiting potential toxicities as are seen with methotrexate and cyclosporine. A more effective, but potentially more toxic medication is started for a brief period of time to help gain control of the psoriasis. Once this control is achieved, then a transition occurred to a potentially less potent, but less risky second medication is undertaken. In the case illustrated by Table 3-5, cyclosporine is started initially. Once the skin improves, then the patient is treated with a medication with less risk of toxicity such as acitretin. Subsequently if a loss of efficacy occurs while on acitretin monotherapy, then UVB can then be considered. Using a biologic in this way for a short period followed by a transition to a second agent is generally not recommended because stopping and restarting a biologic is often associated with a loss of response.

<table>
<thead>
<tr>
<th>TABLE 3-4</th>
<th>Sequential Therapy Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase</td>
<td>Topical</td>
</tr>
<tr>
<td>Phase 1</td>
<td>1-month for clearing Calcipotriene or Calcitriol in combination with superpotent topical corticosteroid*, BID†</td>
</tr>
<tr>
<td>Phase 2</td>
<td>Calcipotriene or Calcitriol BID on weekdays Superpotent topical corticosteroid BID on weekends</td>
</tr>
<tr>
<td>Phase 3</td>
<td>Maintenance Calcipotriene or Calcitriol BID, which may be tapered to once/day and discontinued if appropriate</td>
</tr>
</tbody>
</table>

*Superpotent topical or corticosteroid and topical tazarotene may be combined in a similar fashion. †Brand name calcipotriene and halobetasol are compatible. They can be mixed fresh in equal proportions just prior to application, they can be applied separately or at the same time or different times, or they can be mixed and used over a prolonged period.
Psoriasis is a complex, multi-faceted disease with a diverse array of clinical manifestations and patient expectations. The authors spent considerable time creating the following algorithms to assist physicians with specific situations encountered in clinical practice. These algorithms serve as an outline for clinicians managing individual patients. The goal is to help every patient to gain comprehensive treatment, using the algorithms as a general guide to therapy.

This guide presents a full scope of treatment algorithms for various types of patients to assist in choosing optimal treatments. Chapter 5, “Therapeutic Treatment Options and Their Side Effect Profiles,” lists more detailed information on drug dosing and side effects for individual agents.

In general, topicals are used for limited disease or as adjunct to systemic, small molecule, biologic, or phototherapy treatments. Limited information may be known about some of the newer agents in specific situations; however, general guidance is provided based on current understandings.

There is no universally effective therapy or therapy combination for psoriasis and psoriatic arthritis. All treatment must be individually tailored to each patient’s needs and the type of disease being addressed. The following algorithms offer guidelines for treating specific patient types but are not meant to be restrictive.

**Key points to remember:**
- Patients should not be forced to fail one therapy in order to qualify for a more appropriate therapy.
- Ongoing therapy is often required to maintain remission.
- Life factors such as employment, childbearing potential, alcohol intake, access to therapies, concomitant conditions such as arthritis or diabetes, response to sunlight, and response to prior therapies must be considered in selecting the ideal treatment for a patient.
- Psoriasis can cause disability equal to cancer, diabetes and other major diseases.
### Healthy Male Adult with Chronic Plaque Psoriasis (>5 percent BSA), Without Psoriatic Arthritis

**FIRST LINE**
- UVB phototherapy
- UVB phototherapy alone
- UVB phototherapy + adjuvant topical agents
- UVB phototherapy + systemic retinoids
- Goeckerman

**SECOND LINE**
- Combination Therapies
  - CsA + MTX
  - MTX + biologic
  - CsA + biologic
- Systemic retinoid
  - biologic
- UVB + biologic
- apremilast + UVB

### Healthy Children Under 18 with Chronic Plaque Psoriasis (>5 percent BSA), Without Psoriatic Arthritis

**FIRST LINE**
- UVB phototherapy (NB more effective than BB)
- UVB phototherapy alone
- UVB phototherapy + adjuvant topical agents
- UVB phototherapy + systemic retinoids
- Goeckerman

**SECOND LINE**
- Apremilast
- Brodalumab
- Certolizumab pegol
- Cyclosporine
- Etanercept
- Gusekumab
- Risankizumab
- Infliximab
- Ixekizumab
- Methotrexate
- PUVA
- Secukinumab
- Systemic retinoids
- Tildrakizumab
- Ustekinumab

### TREATING SPECIFIC PATIENT TYPES ALGORITHMS

- **Healthy Children Under 18 with Chronic Plaque Psoriasis (>5 percent BSA), Without Psoriatic Arthritis**
  - If UVB phototherapy available, feasible, practical and suitable
  - If UVB phototherapy unavailable, contraindicated, ineffective, or patient unable to comply

**FIRST LINE**
- UVB phototherapy (NB or BB)
- UVB phototherapy alone
- UVB phototherapy + adjuvant topical agents
- UVB phototherapy + systemic retinoids [for special cases]*
- Goeckerman

**SECOND LINE**
- Apremilast*
- Brodalumab*
- Certolizumab pegol*
- Cyclosporine*
- Etanercept*
- Gusekumab*
- Risankizumab*
- Infliximab*
- Methotrexate*
- PUVA [dark skin]*
- Tildrakizumab*
- Ustekinumab**†

**SYSTEMIC RETINOIDS**
- Adalimumab*  
- Certolizumab pegol*
- Cyclosporine*  
- Etanercept*
- Gusekumab*
- Risankizumab*
- Infliximab*
- Methotrexate*
- PUVA*
- Secukinumab*
- Systemic retinoids
- Tildrakizumab*
- Ustekinumab*†

*Not approved for treatment of psoriasis in children.
†Approved in adolescents

While all of the systemic therapies are appropriate consideration in this setting, a loss of response is sometimes seen in the biologic agents when these medications are stopped and then restarted. This should be considered when choosing a medical regimen.
## Sequential Therapy Examples

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosing Regimens</th>
<th>FDA-approved in pediatric populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids</td>
<td>Various strengths and formulations available</td>
<td>Patients &gt;12 years of age</td>
</tr>
<tr>
<td>Narrow-band UVB Phototherapy</td>
<td>Initial dose 50 of minimal erythema dose, then gradual increase to maximum tolerated dose or 2000 to 5000 mJ/cm² two to five times/week</td>
<td>Patients &gt; 6 years of age</td>
</tr>
<tr>
<td>Acitretin</td>
<td>&lt;0.5 to 1mg/kg/day</td>
<td>Not approved in pediatric populations</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>0.1 to 0.4mg/kg/week with a maximum of 25mg/week</td>
<td>Treatment of juvenile idiopathic arthritis in patients &gt;2 years of age</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>1.5 to 5 mg/kg per day with a maximum of 4mg/kg per day. Limited to 1 year of treatment.</td>
<td>Pediatric transplant patients &gt;6 months of age</td>
</tr>
<tr>
<td>Etanercept</td>
<td>SC injection of 0.8mg/kg per week</td>
<td>Treatment of psoriasis in patients &gt;4 years of age</td>
</tr>
<tr>
<td>Infliximab</td>
<td>IV infusion of 3.3 to 5 mg/kg at weeks 0, 2, and 6, then once every 7-8 weeks</td>
<td>Treatment of Crohn’s disease in patients &gt;6 years of age</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>SC injection of 0.4 to 0.8mg/kg with a maximum of 40mg every 2 weeks</td>
<td>Treatment of juvenile idiopathic arthritis in patients &gt;2 years of age, treatment of Crohn’s disease in patients &gt;6 years of age</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>SC injection of 0.75mg/kg for patients &lt;60kg, of 45mg for patients 60-100kg, and 90mg for patients &gt;100kg at week 0, 4, and then every 12 weeks</td>
<td>Treatment of psoriasis in patients &gt;12 years</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>Case report: SQ injection of 75-150mg/week at week 1, 2, 3 and 4 then every 4 weeks after</td>
<td>Not approved in pediatric populations</td>
</tr>
<tr>
<td>Apremilast</td>
<td>Case report: oral 30mg dose daily</td>
<td>Not approved in pediatric populations</td>
</tr>
</tbody>
</table>
### Women Trying To Become Pregnant with Chronic Plaque Psoriasis (>5 percent BSA), Without Psoriatic Arthritis

**FIRST LINE**
- Moisturizers and UVB phototherapy (NB and BB)
- Topical corticosteroids

**SECOND LINE**
- Certolizumab pegol
- Etanercept*

**THIRD LINE**
- Adalimumab
- Brodalumab
- Guselkumab
- Risankizumab
- Infliximab
- Ixekizumab
- Secukinumab
- Tildrakizumab
- Ustekinumab
- Topical calcipotriene/calcitriol

*Placental transfer of certolizumab pegol is known to be poor due to the pegolation. Etanercept is less abundant in cord blood than IgG monoclonals such as adalimumab. Safety improvements due to reduced placental transport remain unproven, however, and neonatal events attributable to biologics on board are not common in any case.

### Guttate Psoriasis (>5 percent BSA), Without Psoriatic Arthritis

**FIRST LINE**
- UVB phototherapy (NB or BB)

**SECOND LINE**
- Adalimumab
- Brodalumab
- Certolizumab pegol
- Cyclosporine
- Etanercept
- Guselkumab
- Risankizumab
- Infliximab
- Ixekizumab
- Secukinumab
- Tildrakizumab
- Ustekinumab

While all of the systemic therapies are appropriate consideration in this setting, a loss of response is sometimes seen in the biologic agents when these medications are stopped and then restarted. This should be considered when choosing a medical regimen.

Methotrexate and acitretin are contraindicated in pregnancy. While all of the other systemic therapies are appropriate consideration in this setting, a loss of response is sometimes seen in the biologic agents when these medications are stopped and then restarted. This should be considered when choosing a medical regimen.
### Erythrodermic Psoriasis in Males or Females Not of Childbearing Potential

**FIRST LINE**
- Brodalumab
- Cyclosporine
- Infliximab
- Ixekizumab
- Methotrexate
- Secukinumab
- Systemic Retinoids

**SECOND LINE**
- Adalimumab
- Certolizumab pegol
- Etanercept
- Guselkumab
- Risankizumab
- Tildrakizumab
- Combinations: MTX and TNF, retinoids and TNF, retinoids and CsA, CsA and MTX
- Ustekinumab

Adjunctive topicals such as wet compresses, cool baths, mid-potency steroid ointment, hospitalization

Once stable, initiate maintenance with plaque psoriasis algorithm

---

### Currently Heavy Alcohol Intake with Chronic Plaque Psoriasis (>5 percent BSA), Without PSA in Males or Females not of Childbearing Potential*

**FIRST LINE**
- UVB phototherapy available, feasible, practical and suitable

**SECOND LINE**
- Adalimumab
- Apremilast
- Brodalumab
- Certolizumab pegol
- Etanercept
- Infliximab
- Ixekizumab
- PUVA
- Systemic retinoids
- Secukinumab
- Combination therapies

*If patient is unreliable, consideration should be given for providing in-office treatments only.

**Liver studies should be monitored**
**TREATING SPECIFIC PATIENT TYPES ALGORITHMS**

<table>
<thead>
<tr>
<th>Hepatitis C* with Chronic Plaque Psoriasis (&gt;5 percent BSA), Without Psoriatic Arthritis in Males or Females Not of Childbearing Potential</th>
<th>Healthy Adults with Palmoplantar Psoriasis, Without Psoriatic Arthritis in Males or Females Not of Childbearing Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FIRST LINE</strong></td>
<td><strong>FIRST LINE</strong></td>
</tr>
<tr>
<td>If UVB phototherapy available, feasible, practical and suitable</td>
<td>If UV phototherapy unavailable, contraindicated, ineffective, or patient unable to comply</td>
</tr>
<tr>
<td>• UVB phototherapy [NB or BB]</td>
<td>• Topical corticosteroids</td>
</tr>
<tr>
<td>x UVB phototherapy alone</td>
<td>• Topical calcipotriene-steroid combination</td>
</tr>
<tr>
<td>x UVB phototherapy</td>
<td>• Keratolytics</td>
</tr>
<tr>
<td>+ adjuvant topical agents</td>
<td>• Moisturization</td>
</tr>
<tr>
<td>x UVB phototherapy</td>
<td><strong>SECOND LINE</strong></td>
</tr>
<tr>
<td>+ systemic retinoids (for special cases)</td>
<td>• Adalimumab</td>
</tr>
<tr>
<td>x Goeckerman</td>
<td>• Apremilast</td>
</tr>
<tr>
<td><strong>SECOND LINE</strong></td>
<td>• Brodalumab</td>
</tr>
<tr>
<td>• Apremilast</td>
<td>• Cyclosporine</td>
</tr>
<tr>
<td>• Azathioprine***</td>
<td>• Certolizumab pegol</td>
</tr>
<tr>
<td>• Brodalumab</td>
<td>• Etanercept**</td>
</tr>
<tr>
<td>• Cyclosporine***</td>
<td>• Infliximab**</td>
</tr>
<tr>
<td>• Combination therapies***</td>
<td>• PUVA</td>
</tr>
<tr>
<td><strong>THIRD LINE</strong></td>
<td>• Systemic retinoids</td>
</tr>
<tr>
<td>• CsA + MTX</td>
<td>• Ixekizumab</td>
</tr>
<tr>
<td>• CsA + biologic</td>
<td>• Methotrexate</td>
</tr>
<tr>
<td>• MTX + biologic</td>
<td>• PUVA/topical or systemic</td>
</tr>
<tr>
<td></td>
<td>• Secukinumab</td>
</tr>
<tr>
<td></td>
<td>• Systemic retinoids</td>
</tr>
<tr>
<td></td>
<td>• Targeted UVB phototherapy/excimer laser</td>
</tr>
<tr>
<td></td>
<td>• Tildrakizumab</td>
</tr>
<tr>
<td></td>
<td>• Ustekinumab</td>
</tr>
</tbody>
</table>

*New treatments for Hepatitis C allow complete and permanent clearing of the virus which will hopefully make the algorithm for Hepatitis C obsolete*

**Strength of data regarding safety of use greater for etanercept than adalimumab or infliximab**

***Monitor viral load and consider antiviral prophylaxis**
### HIV Infection with Chronic Plaque Psoriasis (>5 percent BSA), Without PSA in Males or Females Not of Childbearing Potential

#### FIRST LINE
- Adequate HIV control with antiviral treatment

#### SECOND LINE
- UVB phototherapy (NB or BB)
  - UVB phototherapy alone
  - UVB phototherapy + adjuvant topical agents
  - Goeckerman
- PUVA photochemotherapy
- PUVA photochemotherapy alone
- PUVA photochemotherapy + adjuvant topical agents

#### THIRD LINE
- Adalimumab
- Apremilast
- Brodalumab
- Certolizumab pegol
- Cyclosporine
- Etanercept
- Guselkumab
- Risankizumab

### Pustular Psoriasis in Males or Females Not of Childbearing Potential

#### FIRST LINE
- Brodalumab
- Cyclosporine
- Infliximab
- Ixekizumab
- Secukinumab

#### SECOND LINE
- Adalimumab
- Apremilast
- Certolizumab pegol
- Etanercept
- Guselkumab
- Risankizumab
- Methotrexate
- PUVA photochemotherapy
- Tildrakizumab
- Ustekinumab

*UC reports of TNF blocker & Ustekinumab-induced pustular psoriasis exist.*

In conjunction with adjunctive topicals such as wet compresses, cool baths, mid-potency steroid ointment, hospitalization.

Rule out sepsis.

Sequential treatment can be used – for example, using Cyclosporine at first, then switching to something milder long-term.

---

**Note:**
- **Hydroxyurea**
- **Infliximab**
- **Ixekizumab**
- **Methotrexate**
- **Secukinumab**
- **Tildrakizumab**
- **Ustekinumab**
### Hypertension with Chronic Plaque Psoriasis (>5 percent BSA), Without Psoriatic Arthritis in Males or Females not of Childbearing Potential

<table>
<thead>
<tr>
<th>FIRST LINE</th>
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<tbody>
<tr>
<td>- UVB phototherapy (NB or BB)</td>
<td>- Adalimumab</td>
</tr>
<tr>
<td>- UVB phototherapy alone</td>
<td>- Apremilast</td>
</tr>
<tr>
<td>- UVB phototherapy + systemic retinoids</td>
<td>- Brodalumab</td>
</tr>
<tr>
<td>- UVB phototherapy + adjuvant topical agents</td>
<td>- Certolizumab pegol</td>
</tr>
<tr>
<td>- Goeckerman</td>
<td>- Etanercept</td>
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<tr>
<td></td>
<td>- Guselkumab</td>
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<tr>
<td></td>
<td>- Risankizumab</td>
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<tr>
<td></td>
<td>- Infliximab</td>
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<tr>
<td></td>
<td>- Ixekizumab</td>
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<tr>
<td></td>
<td>- Methotrexate</td>
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<td></td>
<td>- PUVA</td>
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<tr>
<td></td>
<td>- Secukinumab</td>
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<tr>
<td></td>
<td>- Systemic retinoids</td>
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<tr>
<td></td>
<td>- Tildrakizumab</td>
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<tr>
<td></td>
<td>- Ustekinumab</td>
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<tr>
<th>SECOND LINE</th>
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<tbody>
<tr>
<td>- UVB phototherapy (NB or BB)</td>
<td>- Adalimumab</td>
</tr>
<tr>
<td>- UVB phototherapy alone</td>
<td>- Apremilast</td>
</tr>
<tr>
<td>- UVB phototherapy + systemic retinoids</td>
<td>- Brodalumab</td>
</tr>
<tr>
<td>- UVB phototherapy + adjuvant topical agents</td>
<td>- Certolizumab pegol</td>
</tr>
<tr>
<td>- Goeckerman</td>
<td>- Etanercept</td>
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<tr>
<td></td>
<td>- Guselkumab</td>
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<tr>
<td></td>
<td>- Risankizumab</td>
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<td></td>
<td>- Infliximab</td>
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<td></td>
<td>- Ixekizumab</td>
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<tr>
<td></td>
<td>- Methotrexate</td>
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<tr>
<td></td>
<td>- PUVA</td>
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<tr>
<td></td>
<td>- Secukinumab</td>
</tr>
<tr>
<td></td>
<td>- Systemic retinoids</td>
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<td></td>
<td>- Tildrakizumab</td>
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<tr>
<td></td>
<td>- Ustekinumab</td>
</tr>
</tbody>
</table>

*When using these medications, screen for possible impairment of renal and/or hepatic function.

### Healthy Elderly Patient with Chronic Plaque Psoriasis (>5 percent BSA), Without Psoriatic Arthritis

<table>
<thead>
<tr>
<th>FIRST LINE</th>
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</tr>
</thead>
<tbody>
<tr>
<td>- UVB phototherapy (NB or BB)</td>
<td>- Adalimumab</td>
</tr>
<tr>
<td>- UVB phototherapy alone</td>
<td>- Apremilast</td>
</tr>
<tr>
<td>- UVB phototherapy + systemic retinoids</td>
<td>- Brodalumab</td>
</tr>
<tr>
<td>- UVB phototherapy + adjuvant topical agents</td>
<td>- Certolizumab pegol</td>
</tr>
<tr>
<td>- Goeckerman</td>
<td>- Etanercept</td>
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<tr>
<td></td>
<td>- Guselkumab</td>
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<td></td>
<td>- Risankizumab</td>
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<td></td>
<td>- Infliximab</td>
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<td></td>
<td>- Ixekizumab</td>
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<tr>
<td></td>
<td>- Secukinumab</td>
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<tr>
<td></td>
<td>- Systemic retinoids*</td>
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<tr>
<td></td>
<td>- Tildrakizumab</td>
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<tr>
<td></td>
<td>- Ustekinumab</td>
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</table>

<table>
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<tr>
<th>SECOND LINE</th>
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</thead>
<tbody>
<tr>
<td>- Methotrexate*</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>THIRD LINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>- MTX + CsA*</td>
</tr>
<tr>
<td>- MTX + biologic*</td>
</tr>
<tr>
<td>- CsA + biologic (short term only)*</td>
</tr>
</tbody>
</table>

*When using these medications, screen for possible impairment of renal and/or hepatic function.*

*Cyclosporine should be avoided in patients with uncontrolled hypertension.*
### TREATING SPECIFIC PATIENT TYPES ALGORITHMS

#### Healthy Adult with Severe Nail Psoriasis, Without Psoriatic Arthritis

<table>
<thead>
<tr>
<th>Patients desiring non-invasive treatment</th>
<th>Patients desiring more aggressive treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cosmetic treatment</td>
<td>• Intraleisional steroids</td>
</tr>
<tr>
<td>• Topical steroids</td>
<td></td>
</tr>
</tbody>
</table>

#### FIRST LINE

- UVB phototherapy (NB or BB)
- Adalimumab
- Apremilast
- Brodalumab
- Certolizumab pegol
- Etanercept
- Guselkumab
- Risankizumab
- Infliximab
- Ixekizumab
- Methotrexate
- PUVA
- Secukinumab
- Systemic retinoids
- Tildrakizumab
- Ustekinumab

#### SECOND LINE

- Combination therapies
  - CsA + MTX
  - CsA + biologic
  - Biologic + systemic retinoid

#### Healthy Person of Color with Chronic Plaque Psoriasis (>5 percent BSA), Without Psoriatic Arthritis in Males or Females Not of Childbearing Potential

If UVB phototherapy available, feasible, practical and suitable

- Adalimumab
- Apremilast
- Brodalumab
- Certolizumab pegol
- Cyclosporine
- Etanercept
- Guselkumab
- Risankizumab
- Infliximab
- Ixekizumab
- Methotrexate
- Secukinumab
- Systemic retinoids
- Tildrakizumab
- Ustekinumab

If UVB phototherapy unavailable, contraindicated, ineffective, or patient unable to comply

- Adalimumab
- Apremilast
- Brodalumab
- Certolizumab pegol
- Cyclosporine
- Etanercept
- Guselkumab
- Risankizumab
- Infliximab
- Ixekizumab
- Methotrexate
- Secukinumab
- Systemic retinoids
- Tildrakizumab
- Ustekinumab

- MTX + biologic
- Biologic + UVB phototherapy
- Apremilast + UVB phototherapy
Healthy Adults with Chronic Plaque Psoriasis (>5 percent BSA), and History of Skin Cancer, Without Psoriatic Arthritis in Males or Females Not of Childbearing Potential

**FIRST LINE**

- Systemic retinoids, if baseline lipids WNL

**SECOND LINE**

- UVB phototherapy (NB or BB)
- UVB phototherapy alone
- UVB phototherapy + systemic retinoids
- UVB phototherapy + adjuvant topical agents
- Goeckerman
- Apremilast

- Brodalumab
- Guselkumab
- Risankizumab
- Ixekizumab
- Secukinumab
- Tildrakizumab
- Ustekinumab
- IL-17*
- IL-23*

**THIRD LINE**

- Adalimumab
- Certolizumab pegol
- Etanercept
- Infliximab
- Methotrexate
- Combination Therapies
  - MTX + biologic
  - Biologic + UVB phototherapy [only if absolutely necessary]
  - Apremilast + UVB phototherapy

*Women of childbearing potential should be informed about the need to abstain from becoming pregnant and remain on appropriate contraception for the recommended interval after the discontinuation of these medications. Other oral retinoids with a short half-life similar to isotretinoin would also be appropriate for short-term use if needed in this setting.

Cyclosporine and PUVA should be avoided if possible as they may increase the risk for both non-melanoma skin cancer, especially in fair-skinned patients, and melanoma. At the present time there is no known contraindication to biologic therapies in patients with a significant past medical history of various skin cancers. However, as experience with these agents increases, this recommendation may need to be modified as there have been case reports about the development of skin cancers when some of these agents are used.

---

Women of Childbearing Potential Using Appropriate Contraception with Chronic Plaque Psoriasis (>5 percent BSA), Without Psoriatic Arthritis

**FIRST LINE**

- UVB phototherapy available, feasible, practical and suitable

**SECOND LINE**

- UVB phototherapy alone
- UVB phototherapy + systemic retinoids
- UVB phototherapy + adjuvant topical agents
- UVB phototherapy + short-term isotretinoin, if necessary*
- Goeckerman

- Brodalumab
- Apremilast
- Certolizumab pegol
- Cyclosporine
- Etanercept
- Guselkumab
- Risankizumab
- Infliximab
- Ixekizumab
- Methotrexate
- PUVA
- Secukinumab
- Tildrakizumab
- Ustekinumab

*Based on limited data.
Healthy Adult with Scalp Psoriasis, Without Psoriatic Arthritis, in Males or Females Not of Childbearing Potential

FIRST LINE
- Medicated shampoos including tar, salicylic acid, selenium, topical steroid, zinc or ketoconazole
- Topical steroids - variety of vehicles
- Topical tar
- Topical calcipotriene
- Topical tazarotene
- Anthralin

SECOND LINE
- Adalimumab
- Apremilast
- Brodalumab
- Certolizumab pegol
- Cyclosporine
- Etanercept
- Guselkumab
- Risankizumab
- Infliximab
- Ixekizumab
- Methotrexate
- Secukinumab
- Systemic retinoids
- Targeted UVB phototherapy
- Tildrakizumab
- Ustekinumab

PSORIATIC ARTHRITIS TREATMENT OPTIONS

Over the last decade, significant advances in the treatment of psoriatic arthritis have translated into less pain and greater mobility for patients with this disorder. Nevertheless, challenges remain, particularly in regards to the variability of disease presentation and course. As outlined earlier, psoriatic arthritis can involve any joint in the body including the entire spine and sacroiliac region along with dactylitis, enthesitis, nail disease and psoriasis. The major goals of treatment are to relieve pain and swelling, improve function and lessen progressive joint damage. In addition, comorbid diseases such as hypertension, obesity, fatty liver, diabetes and elevated cholesterol may influence treatment decisions.

A wide array of treatment options are now available for the treatment of PsA. Treatment decisions, however, are individualized due to the distinct blend of manifestations in the skin and joints observed in each patient. Treatment algorithms fail to capture the complexity of involvement or the impact of comorbid diseases. The various treatment options are summarized in Table 4-1.

When choosing a specific therapy, it is important to consider evidence of bone damage (erosions, joint space narrowing on X-ray), extent of psoriasis and nail disease, presence of enthesitis or dactylitis, spinal involvement and relevant comorbidities such as hypertension, diabetes or obesity. A close working relationship between the patient and treating rheumatologist and dermatologist will help to improve treatment response and minimize side effects.

Therapeutic Options for Patients with Psoriatic Arthritis

**Non-steroidal anti-inflammatory agents (NSAIDs), oral or topical**
- Physical Therapy
- Corticosteroid injections into tendons, joints or sacroiliac joints

**Disease modifying anti-rheumatic agents (DMARDs)**
- Sulfasalazine
- Leflunomide
- Cyclosporine
- Methotrexate
- Hydroxychloroquine

**Biologic Agents**

<table>
<thead>
<tr>
<th>Anti-Tumor Necrosis Factor (TNF)</th>
<th>Methotrexate</th>
<th>Hydroxychloroquine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>Infliximab</td>
<td></td>
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<tr>
<td>Golimumab</td>
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<tr>
<td>Certolizumab</td>
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<tr>
<td>Etanercept</td>
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</tbody>
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<tr>
<th>Anti-Interleukin (IL) - 12,23 Antibody</th>
<th>Risankizumab</th>
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<tr>
<td>Ustekinumab</td>
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<tr>
<th>Anti-IL 23</th>
<th>PDE4 Inhibitor</th>
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<tr>
<td>Tildrakizumab</td>
<td>Apremilast</td>
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<td>Guselkumab</td>
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<tr>
<th>Anti-IL-17</th>
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<tr>
<td>Secukinumab</td>
<td>Abatacept</td>
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<tr>
<td>Ixekizumab</td>
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<tr>
<td>Brodalumab</td>
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</tr>
</tbody>
</table>

*In some patients, antimalarials like hydroxychloroquine results in exacerbation of psoriasis
CHAPTER 5

THERAPEUTIC TREATMENT OPTIONS
AND THEIR SIDE EFFECT PROFILES
The three types of therapies available for treating psoriasis:

1. **Topical therapies**
2. **Phototherapies**
3. **Systemic therapies**

### TOPICAL THERAPIES

Topical treatments are highly potent and can provide rapid improvement in psoriasis lesions. With some topical agents, such as superpotent topical steroids, lesions may clear in just two to four weeks. Topical treatments are most successful when patients adhere to the treatment regimen. There are many types of topical treatments, which means physicians can help patients find an option they are most comfortable using. Physicians should encourage patients to use the medication as directed, and to report treatment progress with a return visit, phone call or other contact shortly after a new topical treatment is prescribed. This follow-up contact should help improve adherence and outcomes.

**Steroids:** Topical corticosteroids – formulated as lotions, solutions, creams, foams, ointments, gels, sprays and shampoos – are the most commonly prescribed agents for treating mild to moderate psoriasis. In patients with moderate-to-severe psoriasis, topical corticosteroids may be prescribed as adjunctive therapy along with systemic therapy or phototherapy.

**Dosing**

Apply to affected area twice daily (once daily may also be effective).

Topical corticosteroids are available in many different strengths, ranging from class 7 steroids such as 1% hydrocortisone to superpotent class 1 corticosteroids such as clobetasol propionate, halobetasol propionate, diflorasone diacetate and some formulations of betamethasone dipropionate and fluocinonide.

Superpotent corticosteroids should not be used continuously for more than two to four weeks, and dosage should not exceed 50 g/week.

**Side Effects**

- Suppression of the hypothalamic-pituitary-adrenal (HPA) axis may occur with medium-to-superpotent topical corticosteroids.

- Infants and children are more susceptible to HPA suppression because of their high ratio of skin surface to body mass.

- Atrophy of the epidermis and dermis may occur.

- Long-term use may result in thin, shiny, fragile skin that is easily lacerated and subject to purpura and striae.

- Tachyphylaxis can result from long-term reliance on use of topical corticosteroids. Gradual, reduced effectiveness may be due in part to poor treatment adherence. This drawback has led to the development of intermittent therapy, in which a superpotent topical steroid is only applied in pulses (e.g., on weekends).

**Vitamin D Analogs:** Calcipotriene, Cream and Scalp Solution, 0.005% (Dovonex®), Calcitriol Ointment (Vectical®)

Calcipotriene is a vitamin D analog indicated for the topical treatment of plaque psoriasis and moderately severe psoriasis of the scalp. Calcipotriene does not stain like anthralin and is less irritating. Calcipotriene does not have corticosteroid side effects. Calcipotriene combination therapy with a superpotent corticosteroid is superior to either agent alone.

Calcitriol, a naturally occurring form of vitamin D, is comparable to calcipotriene in efficacy, but is less irritating when applied to intertriginous psoriasis. Like calcipotriene, it does not have corticosteroid side effects.

**Dosing**

Apply to affected area twice daily.

**Side Effects**

- May cause irritant contact dermatitis at the site of application.

- In rare cases, hypercalcemia has been reported in patients who applied large quantities over much of their body (>120 g/week for calcipotriene, 200 g/week for calcitriol).

**Clinical Pearls**

- Topical vitamin D analogs may be used on the face or the genital area without risk of atrophy; however, there is increased risk of irritation in these areas. Diluting with petrolatum or concomitant treatment with a topical corticosteroid may prevent irritation of the face.
or intertriginous areas. Calcitriol is less irritating on intertriginous sites.

- Topical vitamin D analogs should not be combined with salicylic acid or other acids, as these can inactivate vitamin D drugs.
- Topical vitamin D analogs should be used after, not immediately before phototherapy sessions. Calcipotriene is inactivated by UVA and may cause a burning sensation if applied just before UVB phototherapy. Calcitriol is inactivated by UVA and by UVB and blocks transmission of ultraviolet light.

**Combination Corticosteroid/vitamin D Products:**
Calcipotriene/betamethasone dipropionate (Taclonex® ointment and suspension and Enstilar® foam)

Fixed combination products of betamethasone dipropionate plus calcipotriene are available. They are labeled for once daily use. The combination is more effective than the individual ingredients. The safety of use on an as-needed basis has been studied for up to a year.

**Side Effects**

The expected side effects are based on the individual ingredients including topical corticosteroids and calcipotriene as listed above. The presence of the topical corticosteroid reduces the risk of irritation associated with topical vitamin D monotherapy.

**Combination Corticosteroid/retinoid products:**
Halobetasol Propionate and Tazarotene Lotion 0.01%/0.045% (Duobrii®)

Indicated for adults with plaque psoriasis, this combination of halobetasol propionate and tazarotene is more effective than the individual ingredients. It is labeled for once daily use. The safety of use has been studied for up to a year.

**Side Effects**

May cause birth defects if used during pregnancy. A negative pregnancy test must be obtained before females of child-bearing age start using this product, and they must use effective birth control during treatment. If too much of the lotion passes through the skin, the adrenal glands could stop working. Other side effects include Cushing’s syndrome, hyperglycemia, effects of growth and weight in children, skin irritation and vision problems. The most common side effects include: redness, itching, swelling, burning, stinging, application site pain, inflamed hair follicles [folliculitis], thinning of the skin [atrophy], peeling and rash.

**Coal Tar Preparations:** Psorent®, Scytera®, over-the-counter products

Tar preparations have been used for many years as adjunctive therapy. They are messy, smelly and used less often since the introduction of calcipotriene and tazarotene. Their effectiveness may be mediated via aryl hydrocarbon receptors.

**Dosing**

Tar-containing compounds are available as shampoos, creams, gels, solutions, foams or ointments that can be applied to lesions or as solutions to be added to the bath.

**Side Effects**

- Stains skin and clothing; preparations are usually smelly.
- Increases sensitivity to sun.

**Clinical Pearls**

- Tar preparations increase skin sensitivity to ultraviolet light; they are often combined with UVB phototherapy to enhance efficacy.

The tar is applied after UVB as tar can block transmission of UV light.

**Anthralin:** Psoriatec®

Anthralin is a yellowish cream used to treat mild to moderate psoriasis and refractory scalp psoriasis. Its use has declined considerably since the introduction of the less messy non-corticosteroid alternatives calcipotriene and tazarotene.

**Dosing**

Anthralin in concentrations <1% is applied overnight. Anthralin 1% is applied for a shorter period of time (for only a few minutes up to 60 minutes). Short-contact anthralin therapy (SCAT) may minimize staining and irritation.

**Side Effects**

Anthralin stains skin, clothing and furniture, even ceramic bathtubs. Anthralin irritates skin. After anthralin is washed off, triamcinolone or other topical steroid may be applied to prevent or lessen irritation.

**Retinoids:** Tazarotene Topical Gel and Cream 0.05% and 0.1% (Tazorac®)

Tazarotene, a topical retinoid, does not produce the side effects of corticosteroids. Topical tazarotene is indicated for the treatment of stable-plaque psoriasis involving up to 20% of BSA. Topical tazarotene can be irritating; combining tazarotene with corticosteroid therapy helps avoid irritant dermatitis and produces better results than corticosteroid monotherapy.
**Dosing**

Apply once a day, usually in the evening.\(^\text{43}\)

**Side Effects**

- Causes retinoid dermatitis at the site of application, especially with 0.1% gel.
- Increases sunburn risk.

**Clinical Pearls**

- If irritation occurs, it may help to minimize the application amount and frequency and to add topical corticosteroids.
- Combining it with UVB may make UVB more effective; however, when adding a retinoid to an ongoing UV regimen, UV doses should be reduced by at least one-third to reduce risk of burning.\(^\text{48, 49}\)

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**PHOTOTHERAPY**

**Broadband UVB**

In the U.S., broadband ultraviolet light B (UVB) phototherapy has been used for a century for treating moderate to severe psoriasis or localized areas of stubborn plaques. UVB can be combined with other topical and/or systemic agents to enhance efficacy, but some of these may increase photosensitivity and burning, or shorten remission.\(^\text{37, 50}\) Combining UVB with systemic therapies may increase efficacy dramatically and support lower doses of the systemic. (See Table 5-1 for combinations and monitoring.)

Goeckerman (tar and UVB) is a very safe and effective regimen. Suberythemogenic doses of UVB can be used with up to 10% crude coal tar and up to 10% salicylic acid in petrolatum. This preparation is messy and difficult to use at home; however, highly motivated patients with local resistant lesions – such as those on the elbows – may benefit.\(^\text{51}\)

**Dosing**

Dosing is based on minimal-erythema dose (MED) testing or skin types. Broad-band UVB is administered three to five times a week for one to two months or longer, especially if maintenance therapy is indicated. Maintenance UVB phototherapy is recommended at whatever frequency that maintains control of psoriasis. Often, this minimal frequency is once a week.

**Combination Therapy Dosing**

- The combination of phototherapy with an oral retinoid is a highly effective way to manage psoriasis. UVB plus low-dose acitretin: 10 to 30 mg/day (most often 25 mg QD of QOD with food) and lower doses of UVB.
- UVB plus low-dose methotrexate: The entire dose can be taken at one time; alternatively, if not tolerated as one single dose the dose may be administered as three doses taken within 24 hours (total: 15 mg or less per week) until clearing. Avoid taking methotrexate just prior to UVB phototherapy (rare methotrexate-induced acute photosensitivity may result in a burn).
- UVB plus apremilast: 30 mg twice daily

**Side Effects**

May cause increased photosensitivity and burning unless UVB dosing is individualized. If acitretin is added to an ongoing UVB regimen, the UVB dose should be decreased (by \(\frac{1}{3}\) to \(\frac{1}{2}\)) to prevent burning at the same dose tolerated before acitretin was added.
Clinical Pearls

- Can be used for long-term maintenance. If unable to return for office UVB treatments, the patient may consider using a home UVB unit. If this is not an option, natural sunlight with adequate sun protection for unaffected areas may be an alternative.

- Salicylic acid blocks UVB.

- Combination therapy requires increased monitoring. (See Table 5-1.)

- Pregnancy category X: Retinoids should not be used by women who are or may become pregnant.

Narrowband UVB (nbUVB)

Narrowband UVB phototherapy uses 311 nm light for the treatment of moderate to severe psoriasis. The efficacy is superior to broadband UVB and safer than PUVA treatment. The efficacy of nbUVB is similar to that of PUVA in the initial clearing phase, but remissions are not as durable. nbUVB, like broadband UVB, can be used in conjunction with low dose acitretin, but the UV dose must be reduced by 1/3 to ½ if the oral retinoid is added to an ongoing UV regimen.

Side Effects

Rarely causes burns but nbUVB burns can be more severe and longer lasting than those caused by broadband UVB.

Clinical Pearls

- Particularly useful in treating psoriasis refractory to broadband UVB.

- Caution is required for patients taking drugs that increase photosensitivity.

- Home narrowband phototherapy devices are a highly cost-effective treatment for long-term management of psoriasis.

When appropriately used, home nbUVB can be as effective as office nbUVB treatment. Handheld devices are suitable for localized involvement; full-body devices can be used for patients with extensive disease. Full-body home phototherapy devices come in two-dimensional panels, partial three-dimensional panels and full wrap-around devices. For many patients, the partial three-dimensional panels offer the best reimbursement coverage.

- Laser devices are an efficient way to administer nbUVB to localized areas of psoriasis. Their use for large areas may be possible with high fluence/output UV laser devices.

UVA

Treatment with ultraviolet light A (UVA) exposes the patient to an indoor artificial source of UVA (320-400 nm) radiation. UVA radiation as monotherapy produces only mild to moderate improvement and is not recommended if other forms of phototherapy are available. Office UVA treatment is most often used as a component of PUVA therapy.

PUVA

This approach uses methoxsalen (Oxsoralen®) prior to UVA radiation to treat moderate-to-severe psoriasis. Treatments are administered two to three times a week; after 20 to 30 treatments, nearly 90% of patients are markedly improved or clear. Despite being one of the most effective treatments for psoriasis, PUVA use is declining because of its association with cutaneous malignancies. However, this association has been demonstrated only in Caucasian patients. None of the studies on non-Caucasian patients has shown evidence of cutaneous malignancies, including squamous cell skin cancers. PUVA therapy may be used in combination with acitretin or methotrexate. Very rarely, methotrexate can induce acute photosensitivity. Therefore, it is best not to do PUVA or any other phototherapy during and for 24 to 48 hours after the last dose of methotrexate.

Dosing

- Oxsoralen-Ultra® 0.4 mg/kg PO 90 minutes before UVA.

- Oxsoralen (crystalline) 0.6 mg/kg orally two hours before UVA.

- UVA dosing depends on Fitzpatrick skin type and calls for monitoring the output of the UVA box with a photometer.

- RePUVA (retinoid plus PUVA) may be an option for patients who want faster and more effective PUVA photochemotherapy.

Side Effects

- Squamous cell carcinoma (SCC): PUVA increases SCC risk in Caucasians. This increase was not seen if the patient had less than 150 cumulative PUVA sessions. SCC risk was moderately increased if the patient had between 150-350 PUVA sessions. The risk of SCC is markedly increased if the patient had 350 or more cumulative PUVA sessions. SCC or any other skin cancer risk has not been demonstrated with PUVA in non-Caucasians.
• Basal cell carcinoma (BCC): PUVA increases BCC risk moderately if the patient had more than 450 cumulative PUVA sessions. BCC or any other skin cancer risk has not been demonstrated with PUVA in non-Caucasians.\(^{56}\)

• Melanoma: One U.S. study found that PUVA increased the risk of malignant melanoma, especially among those who received more than 250 treatments.\(^{57}\) However, other U.S. and European studies have not shown the same association. A large Swedish study with the same length of follow-up as the U.S. study did not demonstrate an association between melanoma and PUVA.\(^{58}\)

• Phototoxicity: Patients should avoid sun or be instructed to wear UVA-blocking sunscreens on days they are given methoxsalen.

• Nausea after methoxsalen dose: To avoid nausea, the methoxsalen dose is divided and given over a 15-minute period with food. Also, the patient may take 1,500 mg of ginger 20 minutes before methoxsalen treatment. Antiemetics such as trimethobenzamide HCL (Tigan\(^{®}\)) 250 mg may be given 30 minutes before methoxsalen, or promethazine suppositories 12 to 25 mg (which may cause drowsiness) may be used.

PUVA bath therapy, which obviates GI tract exposure, can be used as an alternative to oral methoxsalen if UVA exposure is practical within 30 minutes of PUVA bath therapy at home. In PUVA bath therapy, 50 mg of 8-methoxypsoralen (Oxsoralen-Ultra) is dissolved in a cup of hot water, which is then mixed with about 100 liters of water in a bathtub. The tub must be filled to the same height each time. Non-oral or bath delivery of psoralen has the following advantages:\(^{59}\)

• No facial exposure to PUVA.

• No nausea.

• Minimal risk of ocular changes.

• Less total UVA irradiation.

• Possible reduction in the risk of PUVA-induced cutaneous cancers (long-term bath PUVA studies have uniformly failed to show increase in skin cancer risk).

• A disadvantage of bath PUVA is a local risk of burns, in part because it is particularly difficult to assure that the exact same area of skin is exposed to the bath at each session.

Clinical Pearls

• No increase in skin cancer of any type in non-Caucasians.\(^{56}\)

• Patients should not use tanning beds in conjunction with psoralens. The combination of Oxsoralen and tanning beds can result in life-threatening burns. Patients receiving PUVA treatment should avoid all unnecessary sun exposure such as deliberate sun tanning.

• Patients taking a photosensitizing drug (e.g., quinolones) should take it only after PUVA therapy, not before, and only if such agent cannot be discontinued.

• Phototherapy should be used carefully in patients taking drugs that increase photosensitivity. The initial dose of UV should be reduced, smaller incremental doses should be used, and the time period between the ingestion of photosensitizing drugs and phototherapy should be maximized.

• For maintenance therapy, the frequency of PUVA phototherapy sessions can be less than once a week and sometimes as seldom as once a month due to a much longer duration of therapeutic effect than UVB phototherapy.
SYSTEMIC THERAPIES

Small Molecule

Acitretin (Soriatane®)

Acitretin is a synthetic retinoid that is effective for plaque, pustular, palmoplantar, guttate and erythrodermic psoriasis. A 57% improvement in PASI was observed by week 12 of acitretin treatment. Seventy% of patients with severe disease showed marked improvement after one year of treatment. However, these results were obtained with a relatively high dose of acitretin (e.g., 50 mg to 75 mg per day). Often patients do not tolerate such a high dose. Because patients better tolerate 25 mg per day or less, a lower dose is more often recommended. Long-term use is safe; there are no time-limit restrictions, making acitretin useful for maintenance therapy.

Acitretin is a potent teratogen and should not be used in women of childbearing potential if avoidable. Acitretin can be converted to etretinate which has a long half-life. Patients should avoid pregnancy during and for three years after taking acitretin.

Although infrequent, symptoms related to bone changes or calcified ligaments or tendons may limit long-term use in selected patients. In long-term, low-dose use of acitretin in psoriasis patients there was no increased risk of hyperostosis such as bone spurs.

Combination therapy regimens with acitretin enhance efficacy:

- Combination with PUVA or UVB light therapies enhances efficacy in plaque or guttate psoriasis and limits UV treatment frequency, duration and cumulative doses.
- Combination with methotrexate is effective for severe, generalized pustular psoriasis.
- Sequential therapy with cyclosporine and acitretin is effective for severe, generalized psoriasis. Cyclosporine is used initially to clear the psoriasis; acitretin is used for maintenance and cyclosporine is tapered.

Dosing

- Monotherapy: 10 to 50 mg/day.
- Combination therapy: 10 to 25 mg PO, QD to QOD.

Side Effects and Management Options

Table 5-2 details the side effects of acitretin and corresponding management options.

Clinical Pearls

- Essentially there are no known drug interactions with other psoriasis therapies except for possible enhanced hepatotoxicity with methotrexate [FDA considers this combination "contraindicated"]. Acitretin (and

<table>
<thead>
<tr>
<th>Therapy Being Added</th>
<th>Current Therapy</th>
<th>MTX</th>
<th>CsA</th>
<th>Acitretin</th>
<th>UVB</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX</td>
<td>Monitor CBC &amp; renal function, electrolytes, Mg²⁺; use lower doses of both drugs</td>
<td>Monitor LFTs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CsA</td>
<td>Monitor CBC &amp; renal function, electrolytes, Mg²⁺; use lower doses of both drugs</td>
<td>Monitor lipids, renal function, electrolytes and Mg²⁺</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acitretin</td>
<td>Monitor LFTs, lipids and CBC</td>
<td>Monitor lipids, electrolytes, renal function and Mg²⁺</td>
<td>Decrease acitretin dose by 50 percent if given daily or give full dose every other day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UVB</td>
<td>Monitor for squamous cell carcinoma</td>
<td></td>
<td>Decrease acitretin dose by 25mg/day or every other day; decrease UVA by 50 percent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PUVA</td>
<td>Monitor for squamous cell carcinoma</td>
<td>Not recommended</td>
<td>Monitor for photodamage</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key: MTX = Methotrexate  CsA = Cyclosporine A  CBC = Complete Blood Count  LFT = Liver Function Test
other oral retinoids] should not be combined with tetracycline-class antibiotics due to increased risk of pseudotumor cerebri.

- Acitretin can be combined with almost any other psoriasis treatment at lower doses to enhance efficacy.

- Women who may become pregnant should avoid use of acitretin due to teratogenicity. In the rare instances where a woman of child-bearing potential is given acitretin, alcohol consumption should be avoided because alcohol facilitates the conversion of acitretin to the much longer acting etretinate.

- Lipid-lowering agents easily manage acitretin-induced lipid changes.

- Hyperostosis data is contradictory and subject to controversy.

- Retinoid with phototherapy (acitretin-UV) is more effective, better tolerated and perhaps safer for long-term therapy than phototherapy alone. UVB and UVA doses can be lowered by about 50% and acitretin doses of 10 to 25 mg/day can be used. Better tolerated by patients, the treatment also limits the frequency, duration and cumulative doses of individual therapy.

- When adding acitretin to ongoing therapy to enhance efficacy, the dosimetry (i.e. the amount of light given to the patient) should be decreased by 50% or more right away to avoid burning the patient later on at the same dose that was tolerated before acitretin was added.

- If the patient shows no sign of burning, the dosimetry can gradually increase to the pre-acitretin dose and beyond, as tolerated.

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**TABLE 5-2**

<table>
<thead>
<tr>
<th>Side Effects Requiring Therapy</th>
<th>Management Tips</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Eye exam; discontinue if papilledema</td>
</tr>
<tr>
<td></td>
<td>If severe, discontinue acitretin</td>
</tr>
<tr>
<td>Increased LFTs</td>
<td>Often transient and reversible</td>
</tr>
<tr>
<td></td>
<td>Ask if taking ASA, acetaminophen, alcohol</td>
</tr>
<tr>
<td></td>
<td>If LFT greater than 2.5x normal, decrease dose and re-check</td>
</tr>
<tr>
<td></td>
<td>Evaluate for other causes (e.g. hepatitis C)</td>
</tr>
<tr>
<td>Pyogenic granulomas (frequently periungual)</td>
<td>Lower dose</td>
</tr>
<tr>
<td></td>
<td>Consider using steroid gels, silver nitrate, cryotherapy, C&amp;D or surgical removal</td>
</tr>
<tr>
<td>Bone changes* Hyperostosis (DISH syndrome) Osteoporosis</td>
<td>If symptomatic, X-ray</td>
</tr>
<tr>
<td></td>
<td>Treat according to National Osteoporosis Guidelines</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Check triglycerides (TG) at baseline; monitor every 2 to 4 weeks until stable, every 3 to 6 months after that.</td>
</tr>
<tr>
<td></td>
<td>TG&gt;400 mg/dl; gemfibrozil (Lopid®) 600mg, BID</td>
</tr>
<tr>
<td></td>
<td>TG&gt;700 mg/dl; discontinue acitretin, start lipid lowering drugs</td>
</tr>
<tr>
<td></td>
<td>Cholesterol&gt;300 mg/dl; atorvastatin (Lipitor®) 10-80mg, fenofibrate (TriCor®)</td>
</tr>
<tr>
<td>Depression †</td>
<td>Discontinue acitretin</td>
</tr>
<tr>
<td>Important drug interactions</td>
<td>Glibenclamide, ethanol, progestin contraceptives</td>
</tr>
<tr>
<td>Mucocutaneous Changes</td>
<td>Emollients (Bag Balm®, Aquaphor®), antifungal (Mycostatin), mild topical steroids, lower dose</td>
</tr>
<tr>
<td>Hair loss</td>
<td>Reversible and dose dependent, lower dose</td>
</tr>
<tr>
<td>Skin fragility</td>
<td>Lower dose if symptomatic</td>
</tr>
<tr>
<td>Sticky skin</td>
<td>None</td>
</tr>
<tr>
<td>Dry eye</td>
<td>Lacri-Lube®, artificial tears, cleansing</td>
</tr>
<tr>
<td>Hair nose</td>
<td>Petroleum jelly</td>
</tr>
<tr>
<td>Thin nails</td>
<td>Clear nail polish</td>
</tr>
<tr>
<td>Pregnancy Considerations</td>
<td>Category X, cannot use if pregnant or thinking of becoming pregnant</td>
</tr>
<tr>
<td>Female on acitretin</td>
<td>No action, reassure female exposure to male semen not associated with birth defects</td>
</tr>
<tr>
<td>Partner of male on acitretin</td>
<td></td>
</tr>
</tbody>
</table>

*Association with retinoids is questionable and subject to controversy, especially in low-dose combinations or maintenance therapy for psoriasis patients.

†To date, only isoretinoin, not acitretin, has been associated with depression.

ASA = acetylsalicylic acid  DISH = diffuse idiopathic skeletal hypertosis
Apremilast (Otezla®)

Apremilast is a phosphodiesterase 4 (PDE4) inhibitor approved for psoriasis and psoriatic arthritis. It is an oral therapy which selectively inhibits the enzyme phosphodiesterase 4 (PDE 4). PDE4 regulates the conversion of cyclic adenosine monophosphate (cAMP) to AMP within the cell; the inhibition of this enzyme results in an increase in cAMP intracellularly which modulates the network of pro-inflammatory and anti-inflammatory mediators within the cell.

In pivotal phase 3 studies, apremilast treatment achieved an ACR 20 score of 41% at week 16 using the 30 mg twice daily oral dosage. In psoriasis, 33% of patients achieved PASI 75 versus 5.3% in control patients.

**Dosing**

30 mg tablets twice daily without regards to meals. In the setting of renal failure the dosage should be reduced to 30 mg daily.

**Side Effects**

- Diarrhea: predominately in the first two weeks of dosing in up to 10% of patients.
- Depression: approximately 1% of patients in clinical trials.
- Headache
- Weight decrease: 10% of patients in clinical trials lost 5 to 10% of their body weight.
- Pregnancy category C

**Drug interactions**

Use with strong cytochrome P450 enzyme inducers (e.g. rifampin, phenobarbital, carbamazepine, phenytoin) is not recommended because loss of efficacy may occur.

Cyclosporine (Neoral®)

The immunosuppressant cyclosporine was introduced in the 1970s to prevent kidney transplant rejection. Since then, a microemulsion form of cyclosporine called Neoral® was developed that is absorbed better from the GI tract and is indicated for the treatment of severe, recalcitrant plaque psoriasis. Cyclosporine is highly effective against psoriasis and in short-term therapy may be safer than methotrexate, as bone marrow toxicity is not a concern and it is not usually hepatotoxic. Owing to nephrotoxicity concerns, cyclosporine use is limited in the U.S. to one year of therapy. With the availability of biologic treatments for psoriasis, cyclosporine treatment is rarely needed.

A 16-week study compared methotrexate and cyclosporine’s effectiveness in treating moderate to severe chronic plaque psoriasis. Complete remission (defined as a reduction in a baseline PASI score of more than 90%) occurred in 40% of those patients treated with methotrexate and 33% in the patients treated with cyclosporine. Partial remission (defined as a reduction in the baseline score of more than 75%) was achieved in 60% of the methotrexate-treated patients and 71% of the cyclosporine-treated patients. In this study, there was no significant difference in efficacy found between methotrexate and cyclosporine for the treatment of moderate to severe chronic plaque psoriasis; however, many more patients dropped out of the methotrexate arm of the study due to hepatotoxicity and other adverse events.

**Dosing**

Starting dose is 4 to 5 mg/kg/day for erythroderma, 3 to 5 mg/kg/day for severe psoriasis and 3 to 5 mg/kg/day for chronic thick plaques.

Reduce dose if creatinine rises >30%, if hypertension develops or if potassium (K+) is persistently above normal.

**Side Effects**

- It is nephrotoxic unless psoriasis guidelines (as above) are followed. Uninterrupted long-term use for more than two years may produce irreversible vasculopathy and interstitial fibrosis even if the creatinine is kept within acceptable range.
- In one study, no patient treated for more than two years with cyclosporine had a normal kidney biopsy. Another renal biopsy study showed features of nephrotoxicity in six of eight patients treated with 1 to 6 mg/kg/day of cyclosporine for an average of five years.
- Irreversible kidney damage is extremely unlikely if dermatologic guidelines are followed.
- Malignancies, including skin cancers and lymphoma, have been reported in transplant patients on long-term, high-dose therapy. However, no increase in internal cancers, including lymphoma, has been seen in psoriasis patients treated according to the dermatologic guidelines. These guidelines, developed at an international consensus meeting, are as follows:
  - Use cyclosporine for no longer than two years at a time.
  - Keep serum creatinine increase to <30% of the pretreatment baseline creatinine.
  - Start at 2.5 mg/kg/day in BID or TID divided doses. Based on patient response, increase up to a maximum of 5 mg/kg/day in BID or TID divided doses.
If the patient is in a crisis and in need of rapid movement, cyclosporine can be started at 4 to 5 mg/kg/day in BID or TID divided doses.

Table 5-3 details the side effects of cyclosporine, drug interactions and corresponding management options.

### Clinical Pearls
- When adding drugs that interact with cyclosporine, the physician should monitor blood pressure, renal function and clinical response.
- Cyclosporine should not be used for more than one year at a time, according to FDA recommendations.
- International guidelines approve up to two years of continued use at a time.
- If longer than one-year, uninterrupted use is contemplated, consider checking GFR annually (not required by international guidelines).
- In patients with relative contraindications (older patients, diabetes or controlled hypertension), practice caution.
- Grapefruit juice can raise cyclosporine levels.
- Cyclosporine is usually given in two divided doses but may be given as a single daily dose or three times a day. If the patient misses one of two daily doses, he/she can double up on the next dose.
- Calcium channel blockers may limit nephrotoxicity.

### Methotrexate
In the United States, methotrexate as treatment for psoriasis was originally approved in 1971. It is also indicated for the management of severe erythrodermic and pustular psoriasis. However, it is hepatotoxic, teratogenic and immunosuppressive.

### Dosing
- Consider test dose: 2.5 to 5.0 mg
- Average dose: 10 to 15 mg/week
- Maximum dose: 30 mg/week
- Upon improvement, taper by 2.5 mg every four weeks

### Table 5-3: Side Effects of Cyclosporine and Management Options

<table>
<thead>
<tr>
<th>Side Effects Requiring Therapy</th>
<th>Management Tips</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased K&lt;sup&gt;+&lt;/sup&gt;</td>
<td>- Discontinue K&lt;sup&gt;+&lt;/sup&gt;-rich foods (e.g., bananas)</td>
</tr>
<tr>
<td></td>
<td>- Consider HCTZ (50mg, QOD); may reduce creatinine clearance</td>
</tr>
<tr>
<td></td>
<td>- K&lt;sup&gt;+&lt;/sup&gt; &gt;5.5mEq/L, discontinue drug</td>
</tr>
<tr>
<td>Decreased Mg&lt;sup&gt;2+&lt;/sup&gt;</td>
<td>- Give OTC Mg&lt;sup&gt;+&lt;/sup&gt; supplements</td>
</tr>
<tr>
<td>Hypertension (DBP&gt;90 mmHg)</td>
<td>- Common, easily controlled; monitor weekly</td>
</tr>
<tr>
<td></td>
<td>- Use of calcium channel blockers nifedipine (Adalat®, Procardia®) and felodipine (Plendil®) may help limit nephrotoxicity</td>
</tr>
<tr>
<td></td>
<td>- No ACE inhibitors; may increase creatinine and decrease GFR</td>
</tr>
<tr>
<td></td>
<td>- No thiazide diuretics</td>
</tr>
<tr>
<td>Increased CrCl &gt;30 percent</td>
<td>- Reduce CsA dose</td>
</tr>
<tr>
<td>Drug Interactions</td>
<td>- Some antibiotics, melphalan (alkeran®), antifungals, NSAIDS, cimetidine (Tagamet®), ranitidine (Zantac®), tacrolimus (Prograf®), calcium channel blockers, methylprednisolone, anticonvulsants and others</td>
</tr>
<tr>
<td>Parasthesias</td>
<td>- Educate patients; often transient divide dose further to reduce peak CsA blood levels</td>
</tr>
<tr>
<td>Gingival hyperplasia</td>
<td>- Good dental hygiene; consider adding retinoids</td>
</tr>
<tr>
<td>Hypertrichosis</td>
<td>- Hair removal methods</td>
</tr>
<tr>
<td>Acne</td>
<td>- Treat accordingly</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>- Not contraindicated in pregnant women, but has been associated with reduced birth weight and premature labor</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>- Rarely requires treatment, if so, consider a statin such as atorvastatin; however, be careful about possible drug interaction</td>
</tr>
<tr>
<td>Increased bilirubin, nausea,</td>
<td>- No treatment</td>
</tr>
<tr>
<td>headache, fatigue, myalgia</td>
<td>- Nothing unless symptomatic or has history of gout</td>
</tr>
</tbody>
</table>

HCTZ = hydrochlorothiazide   GFR = glomerular filtration rate
Side Effects and Management Options

- For low-risk patients whose liver function tests have remained in normal range, a liver biopsy may not be required. This should be judged on an individual basis. For high risk patients, methotrexate treatment can be avoided. If methotrexate is used in patients at high risk of liver disease, liver biopsy may be required after 1.5g of methotrexate. As an alternative to a liver biopsy, consider switching to another agent or discontinuing therapy.

- Bone marrow suppression can be lethal, especially in elderly patients with impaired renal function. Additional risk factors include: renal insufficiency, lack of folate supplementation, medication errors, drug interactions, hypoalbuminemia and excess alcohol intake.

- Acute photosensitive reactions may follow dosing, especially in patients who developed burns during prior phototherapy.

- Lymphoma risk increased according to FDA “black box” warning in package insert. It is not yet defined; however, how much of this risk is appropriately attributed to the methotrexate versus that associated with having psoriatic disease.

Table 5-5 details the side effects of methotrexate and corresponding management options.

Clinical Pearls

Physicians should provide the risks of methotrexate in writing to patients. The NPF brochure on systemic treatments is a convenient, free resource: psoriasis.org/systemics

- MTX should not be discontinued abruptly, unless doing so is essential.

- Drug interactions are numerous. NSAIDs impair the excretion of MTX, causing bone marrow suppression, but the most lethal combination is MTX with trimethoprim/sulfamethoxazole.

- Physicians should use special care when prescribing for the elderly.

- The liquid formulation has a bioavailability similar to or better than that of the tablets – and is less expensive – but is more difficult to titrate for elderly patients with poor eyesight.

- Investigations into the use of noninvasive monitoring procedures – such as serologic markers of hepatic fibrosis including serum aminoterminal propeptide of type III procollagen (PIIINP) – may help reduce the need for biopsies.
### Table 5-6

<table>
<thead>
<tr>
<th>Grade 0 Toxicity (none)</th>
<th>ALT/AST &lt;1.25x normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (mild)</td>
<td>ALT/AST 1.26-2.5x normal; re-check in 2-4 weeks</td>
</tr>
<tr>
<td>Grade 2 (moderate)</td>
<td>ALT/AST 2.6-5x normal; lower MTX dose</td>
</tr>
<tr>
<td>Grade 3 (severe)</td>
<td>ALT/AST 5.1-10x normal; stop MTX and re-check in 2 weeks</td>
</tr>
<tr>
<td>Grade 4 (life-threatening)</td>
<td>ALT/AST &gt;10x normal; stop MTX, life threatening</td>
</tr>
</tbody>
</table>

ALT = alanine aminotransferase  
AST = aspartate aminotransferase

### Table 5-7

<table>
<thead>
<tr>
<th>Liver Biopsy Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I (normal; mild fatty infiltration, nuclear variability, portal hypertension)</td>
</tr>
<tr>
<td>Grade II (moderate-severe; fatty infiltration, nuclear variability, portal tract inflammation)</td>
</tr>
<tr>
<td>Grade IIIA (mild fibrosis)</td>
</tr>
<tr>
<td>Grade IIIB (moderate-severe fibrosis)</td>
</tr>
<tr>
<td>Grade IV (cirrhosis)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Management Tips</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continue MTX</td>
</tr>
<tr>
<td>Continue MTX; these changes are relatively common pre-therapy</td>
</tr>
<tr>
<td>Continue MTX; repeat biopsy in six months</td>
</tr>
<tr>
<td>May continue MTX; repeat biopsy in six months</td>
</tr>
<tr>
<td>Discontinue MTX</td>
</tr>
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### Table 5-5 continued

<table>
<thead>
<tr>
<th>Side Effects Requiring Therapy</th>
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</tr>
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<tbody>
<tr>
<td>Platelets 100,000 to normal</td>
<td>Reduce dose or discontinue MTX</td>
</tr>
<tr>
<td>Platelets &lt; 100,000</td>
<td>Discontinue MTX</td>
</tr>
<tr>
<td>WBC &lt; normal</td>
<td>Reduce dose or discontinue MTX</td>
</tr>
<tr>
<td>WBC 3,000 to normal</td>
<td>Discontinue MTX</td>
</tr>
<tr>
<td>WBC &lt; 3,000</td>
<td>Discontinue MTX</td>
</tr>
<tr>
<td>Pulmonary toxicity - acute pneumonitis</td>
<td>Monitor for new cough</td>
</tr>
<tr>
<td></td>
<td>Stop MTX; obtain chest X-ray immediately</td>
</tr>
<tr>
<td>Pregnancy/ reproduction contraindicated</td>
<td>Men and women must be off MTX for three months before conception</td>
</tr>
<tr>
<td></td>
<td>If women become pregnant during therapy, discontinue MTX; seriously discuss with the patient all risks to fetus and appropriate courses of action</td>
</tr>
<tr>
<td></td>
<td>If partner of man on MTX becomes pregnant, man stays on MTX, uses condoms, gets genetic counseling</td>
</tr>
<tr>
<td>Important drug interactions</td>
<td>Barbiturates, phenylbutazone, phenothi (Dilantin®), probencid (Benemid®), salicylates, and sulfonamides may raise free MTX levels; NSAIDs, phenylbutazone, probencid, salicylates, sulfonamids, dipyridamole (Persentine®) increase half-life of MTX; Trimethorprim (in Sepra® and Bactrim®) and MTX can cause severe bone marrow suppression and should be avoided</td>
</tr>
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**WBC** = White Blood Count

---

**TABLE 5-6**

**WHO Guidelines for Liver Toxicity**

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**TABLE 5-7**

**Liver Biopsy Findings**

| Grade I (normal; mild fatty infiltration, nuclear variability, portal hypertension) |
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</tr>
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**WBC** = White Blood Count
Adalimumab (Humira®)

Adalimumab inhibits tumor necrosis factor-alpha (TNF-alpha), a key cytokine involved in the pathogenesis of psoriasis. Adalimumab is FDA-approved for adults and adolescents with psoriasis, psoriatic arthritis, rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, Crohn’s disease and ulcerative colitis and hidradenitis suppuritiva. Adalimumab is a recombinant IgG1 monoclonal antibody that binds to TNF-alpha. Adalimumab also lyses surface TNF-expressing cells in vitro in the presence of complement. In the REVEAL 2008 clinical study, 71% of patients achieved a PASI 75 at week 16.81 In this study, 240 patients were taken off treatment at week 33 and followed until week 52. Forty-five% of these patients retained a PASI 75 over this 20-week period off therapy.

Dosing

In psoriasis, the standard dosing is: an 80-mg loading dose followed by 40 mg one week later and thereafter 40 mgs every other week. Dosing can be increased safely to 40 mg weekly in some patients depending on the response or loss of response to treatment.

Side Effects

- Patients on TNF blockers have an increased risk of developing serious infections. These patients should be monitored during and after treatment for signs and symptoms of a developing infection.
- Malignancies, including lymphoma, have been reported in children and adolescents treated with TNF blockers. Some of these malignancies have been fatal.
- Treatment with TNF blockers has been associated with the development of antinuclear antibodies and rarely can be associated with a lupus-like syndrome. If a lupus-like syndrome develops on one anti-TNF agent, the patient is disqualified from all anti-TNF agents.
- In rare cases, use of TNF blockers has been associated with new onset or exacerbation of central nervous system demyelinating disease, warranting caution when considering TNF blockers for patients with a history of these disorders. Anti-TNF should not be used in persons with a history of demyelinating disease.
- Patients generally tolerate injection site reaction and pain.
- Anaphylaxis
- Pregnancy category B
- Non-melanoma skin cancer

Clinical Pearls

- A 2012 review of more than 70 studies across all seven adalimumab indications, including psoriasis, encompassing 23,000 patients over an average of nine years of therapy did not show any new side effects
or an increase in the baseline lymphoma risk in the psoriasis population.82

• Patients should not receive live vaccinations while on adalimumab.

**Monitoring Information**

Physicians should test for Tuberculosis at baseline and repeat annually thereafter. Hepatitis B and Hepatitis C screening is recommended prior to initiating therapy.

**Certolizumab pegol (Cimzia®)**

Certolizumab pegol is FDA-approved for treatment of psoriatic arthritis and moderate-to-severe plaque psoriasis. Other FDA-approved indications include Crohn's disease, rheumatoid arthritis, and ankylosing spondylitis.

Certolizumab pegol is a pegylated Fab fragment of an anti-TNF monoclonal antibody. In studies of psoriasis patients, following a loading dose of 400 mg, 75% of patients treated with 200 mg every other week achieved 75% improvement in PASI (PASI 75), and 83% of patients treated with 400 mg every other week achieved 75% improvement in PASI (PASI 75).

**Dosing**

Certolizumab pegol is provided as 200mg in 1ml syringes. For psoriatic arthritis, 400 mg is administered subcutaneously, given as two 200-mg subcutaneous injections, at weeks 0, 2, and 4, then 200 mg subcutaneously every other week. A maintenance dose of 400 mg every month can be considered.

**Side Effects**

• Patients on TNF blockers have an increased risk of developing serious infections. These patients should be monitored closely during and after treatment for signs and symptoms of a developing infection.

• Malignancies, including lymphoma, have been reported in children and adolescents treated with TNF blockers. Some of these malignancies have been fatal.

• Treatment with TNF blockers has been associated with the development of antinuclear antibodies and rarely can be associated with a lupus-like syndrome.

• In rare cases, use of TNF blockers has been associated with new onset or exacerbation of central nervous system demyelinating disease, warranting caution when considering TNF blockers for patients with a history of these disorders.

• Pregnancy category B

**Clinical Pearls**

• Concurrent therapy with anakinra is not recommended due to increased risk of infection.

• Patients should not receive live vaccinations while on certolizumab pegol.

**Monitoring information**

Physicians should test for tuberculosis at baseline and monitor for signs and symptoms of tuberculosis thereafter (annual tuberculosis is usually performed, though not required by the FDA-approved label).

**Etanercept (Enbrel®)**

Etanercept is FDA-approved for treatment of adult and pediatric patients (ages 4+) with chronic moderate to severe plaque psoriasis and psoriatic arthritis. Other FDA-approved indications include ankylosing spondylitis, polyarticular-course juvenile rheumatoid arthritis, and moderate to severe rheumatoid arthritis. Etanercept is a fusion protein consisting of TNF-alpha receptor components bound to the Fc portion of IgG. Etanercept binds and inactivates TNF-alpha. It is available in 25 and 50 mg syringes and in a lyophilized powder. In phase III studies of adult psoriasis patients, approximately 30% of patients treated with 25 mg twice a week and 50% of patients treated with 50 mg twice a week had 75% improvement in PASI (PASI 75) after 12 weeks of treatment.

**Dosing**

For plaque psoriasis in adults, the dose is 50 mg SQ given once or twice weekly for three months followed by a maintenance dose of 50 mg once weekly. The approved dose is 50 mg SQ weekly for psoriatic arthritis. Rotate injection sites (thigh, abdomen, upper arm). Do not inject in areas where skin is tender, bruised, red or hard. Dosing can be increased up to 50 mg twice weekly longer term in some patients based on response to treatment with no increase in side effects. In adolescents and children over the age of 2, administer 0.8 mg/kg per week subcutaneously (up to 50 mg/week). Pediatric patients weighing 63 kg (138 pounds) or more may receive 50 mg subcutaneously once weekly. For pediatric doses other than 25 mg or 50 mg, use reconstituted etanercept lyophilized powder.

**Side Effects**

• Mild to moderate injection-site reactions are the most common side effect. They are generally well-tolerated and can be treated symptomatically. They do not require discontinuation of treatment.
• Patients on TNF blockers have an increased risk of developing serious infections. These patients should be monitored during and after treatment for signs and symptoms of a developing infection.

• Malignancies, including lymphoma, have been reported in children and adolescents treated with TNF blockers. Some of these malignancies have been fatal.

• Treatment with TNF blockers has been associated with the development of antinuclear antibodies and rarely can be associated with a lupus-like syndrome. If a lupus-like syndrome develops on one anti-TNF agent, the patient is disqualified from all anti-TNF agents.

• In rare cases, use of TNF blockers has been associated with new onset or exacerbation of central nervous system demyelinating disease, warranting caution when considering TNF blockers for patients with a history of these disorders. Anti-TNF should never be used in persons with a history of demyelinating disease.

• Rare cases of pancytopenia including aplastic anemia have been reported.

• Pregnancy category B.

Clinical Pearls

• Concurrent therapy with anakinra or any other biologic is not recommended due to increased risk of infection.

• Patients should not receive live vaccinations while on etanercept.

• Concomitant methotrexate as well as narrowband UVB therapies improves clinical responses.

Monitoring Information

Physicians should test for Tuberculosis at baseline and repeat annually thereafter. Hepatitis B and Hepatitis C screening is recommended prior to initiating therapy.

Golimumab (Simponi®)

Golimumab is a fully human IgG monoclonal antibody with specificity for TNF-alpha that is FDA-approved for the treatment of active psoriatic arthritis alone or in combination with methotrexate. Other FDA-approved indications include active moderate-to-severe rheumatoid arthritis (in combination with methotrexate) and active ankylosing spondylitis. It is not approved for psoriasis.

In the pivotal phase III clinical trial of golimumab in patients with active psoriatic arthritis, 51% of patients treated with 50 mg every four weeks and 45% of patients treated with 100 mg every four weeks achieved a 20% improvement in the American College of Rheumatology criteria (ACR20) response at week 14, compared to 9% of patients in the placebo control group. Patients in the same study with psoriasis affecting 3% or more of their body surface area were also evaluated for changes in the PASI score. At week 14, 40% of the patients receiving 50 mg and 58% of the patients receiving 100 mg of golimumab achieved a PASI 75 compared to 3% of the placebo-treated patients.

Dosing

Golimumab is administered in doses of 50 mg by subcutaneous injection once per month. It may be given alone or in combination with methotrexate.

Side Effects

• Patients on TNF blockers have an increased risk of developing serious infections. These patients should be monitored closely during and after treatment for signs and symptoms of a developing infection.

• Malignancies, including lymphoma, have been reported in children and adolescents treated with TNF blockers. Some of these malignancies have been fatal.

• Treatment with TNF blockers has been associated with the development of antinuclear antibodies and rarely can be associated with a lupus-like syndrome.

• In rare cases, use of TNF blockers has been associated with new onset or exacerbation of central nervous system demyelinating disease, warranting caution when considering TNF blockers for patients with a history of these disorders.

• Injection-site reactions can occur

• Anaphylaxis

• Pregnancy category B

Clinical Pearls

• Patients should not receive live vaccinations while on golimumab.

• It is not to be used in combination with abatacept or anakinra or any other biologic.

Monitoring Information

Physicians should test for Tuberculosis at baseline and repeat annually thereafter. Hepatitis B and Hepatitis C screening is recommended prior to initiating therapy.

Infliximab (Remicade®)

Infliximab, also a TNF-alpha inhibitor, is a monoclonal
antibody currently used to treat psoriasis, psoriatic arthritis, Crohn’s disease, ulcerative colitis, rheumatoid arthritis and ankylosing spondylitis.

The safety and efficacy of infliximab was assessed in three randomized, double-blind, placebo-controlled studies. In the pivotal EXPRESS II study of 835 patients, 75% of the 5 mg/kg group achieved a PASI 75 compared to 2% of the placebo group at week 10. At week 52, the PASI 75 rate was 59%.87

Dosing

Infliximab is used in doses of 5 mg/kg infusions at 0, 2 and 6 weeks, then every 8 weeks. Patients should be observed for side effects for at least one hour after infusion. Appropriate staff, medication and emergency equipment should be available for managing possible infusion reactions.

Dosing can be increased up to 10 mg/kg or the frequency increased up to every 4 weeks.

Side Effects

- Acute infusion reactions can develop during the infusion or within a few hours thereafter.

- A delayed hypersensitivity reaction (myalgia, arthralgia with fever, rash, pruritus, edema, dysphagia, urticaria, sore throat, and headache) may occur. This has been observed most commonly in patients with Crohn’s disease with re-administration of infliximab after a drug-free interval of two to four years following a previous infusion, but is also seen in psoriasis and psoriatic arthritis patients.

- Patients on TNF blockers have an increased risk of developing serious infections. These patients should be monitored closely during and after treatment for signs and symptoms of a developing infection.

- Malignancies, including lymphoma, have been reported in children and adolescents treated with TNF blockers. Some of these malignancies have been fatal.

- Treatment with TNF blockers is associated with the development of antinuclear antibodies and rarely can be associated with a lupus-like syndrome.

- In rare cases, use of TNF blockers has been associated with new onset or exacerbation of central nervous system demyelinating disease, warranting caution when considering TNF blockers for patients with a history of these disorders.

- Rare cases of pancytopenia including aplastic anemia have been reported.

- Pregnancy category B

Clinical Pearls

- Formation of antibodies and loss of response to infliximab will likely be reduced when the drug is given at regular intervals and when used concurrently with methotrexate, azathioprine or 6-mercaptopurine.

- Patients should not receive live vaccinations while on infliximab.

Monitoring Information

- Physicians should test for Tuberculosis at baseline and repeat annually thereafter. Hepatitis B and Hepatitis C screening is recommended prior to initiating therapy.

- Liver function tests should be monitored periodically. If >5 times the upper limit of normal, the dose should be withheld until LFTs are lower.

- Patients should be observed for side effects for at least one hour after infusion. Infusion reactions may be ameliorated in some patients by pre-medicating with acetaminophen and/or diphenhydramine and/or steroids.

Ustekinumab (Stelara®)

Ustekinumab is a monoclonal antibody directed against the p40 subunit of IL-12 and IL-23, thus blocking the interaction between those cytokines and their respective receptors. Ustekinumab is approved for psoriasis, psoriatic arthritis, and Crohn’s disease. In pivotal phase 3, multicenter, double-blind, placebo controlled trials for psoriatic arthritis, at week 24, ACR 20 was achieved 42.4% of the time, ACR 50 was achieved 24.9%, and ACR 70 was 12.2% at 45 mg dosing, whereas ACR 20 was achieved 49.5%, ACR 50 was 27.9%, and ACR 70 was 14.2% of the time at the 90 mg dose.88, 89

Dosing

Patients weighing less than 100 kg (220 lb.) receive 45 mg at weeks 0, 4, and then every 12 weeks thereafter. Those weighing more than 100 kg should be given 90 mg at the same intervals. For those who do not achieve adequate responses, dosing every 8-10 weeks is effective without any significant increase in side effects noted.89

Side Effects

- As with all biologic drugs, patients should be cautioned about the risk of infection and malignancy; however, a large, long-term registry (PSOLAR registry) found no detectable increased risk of serious infection or malignancy as compared to moderate-to-severe
psoriasis patients not on a systemic treatment.

- Patients taking this medication do not appear to be at an increased risk of salmonella and mycobacterial infections; an increased risk of these infections has been identified in genetically IL-12/23 genetically deficient patients.

- Pregnancy category B

- Ustekinumab has been linked to noninfectious pneumonitis.

Clinical Pearls

- Five years of safety data have shown no significant increase in side effects, with the majority of patients maintaining clinical response.

- Patients should not receive live vaccinations while on ustekinumab, as there are no data demonstrating safety (however there are also no data to suggest there would be a problem).

- PsA responses are approximately 25% lower than TNF-alpha agents.

Monitoring Information

Physicians should test for Tuberculosis at baseline monitor for signs and symptoms of tuberculosis thereafter (annual tuberculosis is usually performed, though not required by the FDA-approved label).

Brodalumab (Siliq®)

Brodalumab is an interleukin-17 receptor antagonist approved for the treatment of moderate-to-severe plaque psoriasis. The medication is highly effective in treating patients with psoriasis, achieving an excellent response in approximately 80% of patients (PASI=75), as well as being able to clear approximately one-third of patients.

Dosing

The recommended dose for psoriasis is 300 mg at weeks 0, 1, 2, 3, and 4, followed by 300 mg every 4 weeks. Each 300 mg dose is given as two subcutaneous injections of 150 mg each. For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, use the dosage and administration for plaque psoriasis. For other psoriatic arthritis patients, the recommended dosage with a loading dose is 150 mg at weeks 0, 1, 2, 3, and 4, and every 4 weeks thereafter. The recommended dosage without a loading dose is 150 mg every 4 weeks. If a patient continues to have active psoriatic arthritis, consider a dosage of 300 mg.

Side Effects and Monitoring

- As with all biologic drugs, patients should be cautioned about the risk of infection.

Cautions

IL17 antagonists are associated with a risk of exacerbating inflammatory bowel disease. Caution must be exercised in the setting of concurrent inflammatory bowel disease. 95, 96

During the clinical study for brodalumab, a small number of patients experienced suicidal ideation and behaviour, including four patients who completed suicides. Because of this, it is important to weight the risk and benefit of this treatment in the patients who have a history of depression and/or suicidal ideation or behavior. Patients that have worsening suicidal ideation behavior, depressive symptoms, or thoughts of harm should be seen by a mental health professional. This medication is only available under a restricted program known as the Risk Evaluation and Medication Strategy (REMS), which requires administration by a suitably trained dermatologist and via specialized pharmacies.

Ixekizumab (Taltz®)

Ixekizumab is an interleukin-17A inhibitor. It is a humanized IgG4 monoclonal antibody which acts by binding and neutralizing the IL-17. It is approved for moderate to severe psoriasis. It is not approved at this time for PsA. At week 12 87-90% of patients with psoriasis achieved a PASI 75 response and 68-71% achieved a PASI 90 response.

Dosing

160 mg loading dose, followed by 80 mg every 2 weeks x 6 times (weeks 2-12), and 80 mg every 4 weeks thereafter.

Side Effects and Monitoring

- As with all biologic drugs, patients should be cautioned about the risk of infection.

Cautions

IL-17 antagonists are associated with a risk of exacerbating inflammatory bowel disease. Caution must be exercised in the setting of concurrent inflammatory bowel disease. 95, 96
Secukinumab (Cosentyx®)

Secukinumab is a recombinant, high-affinity, fully human immunoglobulin G1k monoclonal antibody inhibitor of interleukin-17A (IL-17) that selectively binds and neutralizes interleukin-17A. It is approved for moderate-to-severe plaque psoriasis and psoriatic arthritis. In clinical trials, about 82% of the individuals taking 300 mg doses of Cosentyx experienced a PASI score of 75% after 12 weeks. About 72% of patients taking 150 mg doses of Cosentyx also achieved a PASI 75. In phase 3 pivotal trials for psoriatic arthritis, ACR 20 was met 54% of the time using secukinumab 300 mg subcutaneously dosing as compared with ACR 20 of 51% using secukinumab 150 mg dosing.

**Dosing**
The recommended dose for psoriasis is 300 mg at weeks 0, 1, 2, 3, and 4, followed by 300 mg every 4 weeks. Each 300 mg dose is given as two subcutaneous injections of 150 mg each. For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, use the dosage and administration for plaque psoriasis. For other psoriatic arthritis patients, the recommended dosage with a loading dose is 150 mg at weeks 0, 1, 2, 3, and 4, and every 4 weeks thereafter. The recommended dosage without a loading dose is 150 mg every 4 weeks. If a patient continues to have active psoriatic arthritis, consider a dosage of 300 mg.

**Side Effects and Monitoring**
- As with all biologic drugs, patients should be cautioned about the risk of infection.
- Physicians should test for tuberculosis at baseline and monitor for signs and symptoms of tuberculosis thereafter.

**Cautions**
IL-17 antagonists are associated with a risk of exacerbating inflammatory bowel disease. Caution must be exercised in the setting of concurrent inflammatory bowel disease.95,96

Guselkumab (Tremfya®)

Guselkumab is a human monoclonal antibody to the p19 component of IL-23 approved for psoriasis. The safety and efficacy of guselkumab 100mg administered at weeks 0, 4 and every 8 weeks thereafter was assessed in a phase 3 trial (VOYAGE 1) comparing it to adalimumab and placebo. At week 16, 86% of guselkumab-treated patients achieved PASI 75; 70% achieved PASI 90 and 34% achieved PASI 100.

**Dosing**
Guselkumab was used in 100mg syringes administered subcutaneously at weeks 0,4 and every 8 weeks thereafter.

**Side Effects**
- Mild-to-moderate injection-site reactions can occur. They are generally well-tolerated and can be treated symptomatically. They do not require discontinuation of treatment.

**Monitoring Information**
- Physicians should test for tuberculosis at baseline and monitor for signs and symptoms of tuberculosis thereafter (annual tuberculosis is usually performed, though not required by the FDA-approved label).

Risankizumab (Skyrizi®)

Risankizumab is an IL-23 antagonist indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

The recommended dose is 150 mg (two 75 mg injections) administered by subcutaneous injection at Week 0, Week 4, and every 12 weeks thereafter.

Four multicenter, randomized, double-blind studies enrolled 2109 subjects 18 years of age and older with moderate to severe plaque psoriasis. Overall, subjects had a median baseline PASI score of 17.8 and a median BSA of 20.0%. In two studies, 80% of the subjects who continued on risankizumab had PASI 100 at Week 52. For PASI 90 responders at Week 16, 88% (398/450) of the subjects had PASI 90 at Week 52. In the third study, subjects who were originally on risankizumab and had sPGA 0 or 1 at Week 28 were re-randomized to continue risankizumab every 12 weeks or withdrawal of therapy. At Week 52, 87% of the subjects re-randomized to continue treatment with risankizumab had sPGA 0 or 1 compared to 61% who were re-randomized to withdrawal of risankizumab.

**Dosing**
The recommended dose is 150 mg (two 75 mg injections) administered by subcutaneous injection at Week 0, Week 4, and every 12 weeks thereafter.

**Side Effects**
The most common side effects of SKYRIZI include: upper respiratory infections, fatigue, fungal skin infection, injection site reactions, headache.

**Monitoring information**
Physicians should test for tuberculosis at baseline and
monitor for signs and symptoms of tuberculosis thereafter (annual tuberculosis is usually performed, though not required by the FDA-approved label).99

**Tildrakizumab (Illumya®)**

Tildrakizumab is a human monoclonal antibody to the p19 component of IL-23 that has been approved for moderate-to-severe plaque psoriasis. The safety and efficacy of tildrakizumab 100 mg or 200mg administered at weeks 0,4 and every 12 weeks thereafter was assessed in a phase 3 trial [reSURFACE1] comparing it to placebo. At week 12, 62-64% of tildrakizumab-treated patients achieved PASI 75; 35% achieved PASI 90 and 14% achieved PASI 100.

**Dosing**

Tildrakizumab was used in 100 mg syringes administered as one or two injections subcutaneously at weeks 0,4 and every 12 weeks thereafter.

**Side Effects**

Mild to moderate injection-site reactions can occur. They are generally well-tolerated and can be treated symptomatically. They do not require discontinuation of treatment.

**Monitoring Information**

Physicians should test for Tuberculosis at baseline and monitor for signs and symptoms of tuberculosis thereafter (annual tuberculosis is usually performed, though not required by the FDA-approved label).

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**UNAPPROVED AGENTS**

**Hydroxyurea (Hydrea®)**

Hydroxyurea is an anti-metabolite that has been used to treat psoriasis for 30 years. It has moderate effectiveness as monotherapy, although about one-third of patients whose psoriasis improves develop bone marrow toxicity with leucopenia, thrombocytopenia or megaloblastic anemia.98 Although bone marrow suppression is usually mild and does not necessitate the discontinuation of therapy, it may occasionally be severe.

**Dosing**

- Initial dose: 500 mg PO BID
- If no response, increase by 500 mg daily increments every month, up to a maximum of 1.5-2.0 g/day.

**Side Effects**

- Cutaneous reactions may be seen in some patients.

- Long-term therapy may cause skin or leg ulcers.

- Macrocytosis is not clinically important.

**Clinical Pearls**

- It has a narrow therapeutic index.

- The drug is useful in combination therapy, and especially for recalcitrant palmoplantar psoriasis with acitretin.

- It is also of value in HIV-related psoriasis.

- After increasing dose, physicians should repeat CBC and platelet counts every 2-3 weeks. Once the dose is stable, CBC should be repeated every three months. These agents hold dosage if WBC is < 2,500 or platelet count is < 100,000.

**Mycophenolate Mofetil (CellCept®)**

Mycophenolate mofetil has been used to prevent organ transplant rejection and is effective in the treatment of several inflammatory or autoimmune skin disorders. In the 1970s, mycophenolate mofetil was investigated for the treatment of psoriasis with moderate improvements noted and some patients having long-term remissions. The side effects were tolerable.91-93

**Dosing**

- 500 mg PO 4 times/day based on clinical response.
- May be increased or reduced by 250 mg/day each month up to a maximum of 4.0 g/day.

**Side Effects**

- Patients may experience nausea, vomiting or diarrhea.
- Herpes zoster and herpes simplex occurred in more than 31% of patients in one study.92

**Clinical Pearls**

- It can be administered with CsA and is useful in maintaining clinical responses when tapering CsA.

- Since it is an immunosuppressive agent, patients should be followed to ensure that they do not develop opportunistic infections. It should not be given to patients with severe infections or untreated malignancies.
6-Thioguanine

6-Thioguanine is a purine analog that interferes with nucleic acid synthesis. It is an analog of the nucleic acid guanine and is closely related to mercaptopurine (Purinethol®). It is indicated for the treatment of acute nonlymphocytic leukemia and other neoplasms, but in a small study it was effective for psoriasis patients.

Dosing

- Starting dose: 80 to 100 mg PO twice weekly.
- Increase by 20 mg every 2-4 weeks.
- Maximum dose: 160 mg PO three times a week.

Side Effects

- It may cause bone marrow suppression.
- Patients may experience GI complaints, such as nausea and diarrhea.
- Elevation of LFTs is common.

Tofacitinib (Xeljanz®)

Tofacitinib is a JAK kinase inhibitor currently indicated for the treatment of rheumatoid and psoriatic arthritis. In patients with psoriatic arthritis, about half achieve ACR20 with a dose of 5mg twice a day. In two Phase III studies, it was effective in psoriasis patients. At a dose of 5mg twice a day, 40% of patients achieve PASI75; with a 10mg twice a day dose, 64% of patients achieve PASI75. Tofacitinib is not currently approved for the treatment of psoriasis.
CHAPTER 6 INSURANCE ADVOCACY

ACCESS TO CARE ASSISTANCE

Insurance challenges can be a barrier to appropriate patient care. The National Psoriasis Foundation’s Patient Navigation Center has the resources to help.

The Foundation’s Patient Navigation Center offers direct assistance for patients and medical professionals dealing with insurers. The Patient Navigation Center makes it easier to advocate for patients trying to navigate today’s managed health care system by providing steps to appeal insurance denials, sample letters from medical professionals on patients’ behalf and research citations to support appeals.

An NPF Patient Navigator can provide resources to help your patients work with insurance companies and access financial assistance for prescription costs.

After conducting an audit of more than a hundred health insurance plans nationwide, NPF continues to identify problematic policies that can be changed to improve access to treatment. The Foundation initiates dialogue and negotiations with insurers and works in partnership with health professionals to identify and implement more patient-centered policies. In fact, in one year alone, these efforts improved access to treatments for nearly 400,000 patients across the country with moderate to severe psoriasis. NPF’s advocacy department would like to hear from the medical community about policies that pose treatment barriers and about ways NPF can help in the appeals process.

Through state and federal legislative initiatives, the Foundation pursues its priorities to build greater federal investment in psoriasis research, improve access to treatments and accelerate toward a cure. By educating policymakers, influencing legislative action and increasing grassroots activity, NPF knows it is possible to achieve all three goals for the people who will benefit most: psoriatic disease patients and those who care for them.

For more information, contact the Patient Navigation Center:

- Email: education@psoriasis.org
- Phone: 800-723-9166 option 1
- On the web: psoriasis.org/navigationcenter

The Patient Navigation Center also offers one-on-one support to help your patients learn more about their disease and connect with others. Patient Navigators can share educational materials, answer disease-related questions and help patients find emotional support resources. All services are complimentary and available in multiple languages, including Spanish.

To request informational wallet cards to distribute to your patients, visit psoriasis.org/walletcards.

Additional patient resources can be found at psoriasis.org.
REFERENCES