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 fourth edition of *The Psoriasis and Psoriatic Arthritis Pocket Guide: Treatment Algorithms and Management Options*. The previous editions were well-received by dermatologists. Since the publication of the 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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EPIDEMIOLOGY
Psoriasis affects approximately 2.1 percent of U.S. adults, up to 7.5 million people, of whom about 25-30 percent 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.

Although there is evidence that 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. It costs more to treat the more severe form of the disease, which can lead to a lower quality of life. Psoriasis treatment costs add up to more than those of other lifelong illnesses, such as emphysema and epilepsy.

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, systemic or biologic therapy to adequately suppress the systemic, immunopathogenic process.

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

Physicians typically define the severity of psoriasis based on
their own judgment and by 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 percent BSA) are involved the emotional impact on the patient may be 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 percent 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 in psoriasis. 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.

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 percent of patients with mild and 60 percent of patients with moderate-to-severe psoriasis reported that it was a significant problem in their everyday life. The negative effect on physical, psychological and social dimensions of life can be greater than those from life-threatening illnesses such as myocardial infarction. (See Table 1-1.)

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 well-documented evidence shows an increase in depression and anxiety, with resulting personal behavior issues such 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, explaining their increased frequency among psoriasis patients.

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.

**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.
- Presence of psoriatic arthritis.

The decision to use systemic therapy requires a thorough discussion between the patient, the physician and the medical support staff. [See Table 1-2.] 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). Other treatment strategies (discussed in Chapter 3) employ combination, rotation and sequential therapies. Treating a chronic systemic immunologic disease such as psoriasis can be difficult for both patient and physician and this handbook facilitates 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.
In 2016 the National Psoriasis Foundation developed treatment target recommendations for those with severe psoriatic disease. After a rigorous, scientific Delphi process that involved 25 key opinion leaders, as well as practicing dermatologist and patient input, it was 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, for those who’ve not reached these target goals, it is recommended that they have a conversation with their provider where 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 present 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.
**Systemic Therapy Algorithm**

1. Does the psoriasis affect >3 percent body surface area (BSA)?
2. Is the patient disabled by the psoriasis?
3. Does the psoriasis have a significant impact on the patient’s quality of life?
4. Does the patient have psoriatic arthritis?

**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 a candidate for systemic treatment.

**YES TO ANY OF THE ABOVE.**

The patient is not a candidate for phototherapy or 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.
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 percent to 10 percent body involvement) and severe disease (>10 percent body involvement or <10 percent 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.
CHAPTER 2

ASSESSING A PSORIASIS PATIENT
CHAPTER 2 ASSESSING A PSORIASIS PATIENT

CLINICAL PRESENTATION

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

Chronic plaque-type disease is the most common form of psoriasis, present in 80 percent to 90 percent of patients. It is most often found on the elbows, knees, scalp, legs and sacrum.

Erythroderma, especially of recent onset, is often associated with psoriasis, but may be difficult to differentiate from other possible causes of erythrodermic or exfoliative dermatitis. Patients may present with systemic symptoms and abnormal laboratory values.

There are two types of pustular psoriasis. Patients with pustules localized to the palms and soles have palmoplantar psoriasis; patients with generalized pustulosis have the von Zumbusch form of psoriasis, usually in association with erythroderma.

Less common forms include guttate, characterized by numerous small, drop-like lesions frequently following a throat infection, and occurring most often in children; and inverse or intertriginous, which is a seborrhoeic-dermatitis-like form of psoriasis in which moist erythematous lesions appear in skin folds of the body (e.g., in the armpit, or under the breast, buttocks or genitals).

---

**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>
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.)

TABLE 2-2

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

Adapted from Menter and Weinstein17

DETERMINING DISEASE SEVERITY

The severity of psoriasis is determined by the extent and character of the lesions (measuring the percent 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.) Psoriasis affecting more than 10 percent of the body is generally severe. Psoriasis involving the palms and soles is often disabling and may be considered severe even if the rest of the body is not extensively involved.

ASSESSING A PATIENT

Psoriasis is traditionally classified as mild-to-moderate or as
moderate-to-severe. As shown in Table 2-3, about 65 percent of patients have mild disease as defined by body surface area involvement and about 35 percent have moderate-to-severe disease.\(^1\)-\(^3\) NPF defines moderate-to-severe disease not only in terms of BSA (>3 percent), but also includes patients with a BSA of <3 percent 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 percent) or extensive (BSA >3 percent). 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 2-3

<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>
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 percent of the body’s surface.

• Mild psoriasis: Affects up to 3 percent 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 percent to 10 percent 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 percent 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

Disease severity classifications serve as a reference point for the physical aspects of the disease, but not the emotional and social aspects. 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 [PQQL-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.

A copy of the KMPI instrument can be found on page 22. For additional copies, contact medevents@psoriasis.org.

**DEBILITATION COMPARES TO OTHER MAJOR DISEASES**

Research shows that 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.
**KOO-MENTER PSORIASIS INSTRUMENT**

### 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>
</tbody>
</table>
7. How much does your psoriasis impact your overall emotional well-being?
   | Not at All | Somewhat | Very Much |
   | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

8. Overall, to what extent does your psoriasis interfere with your capacity to enjoy life?
   | Not at All | Somewhat | Very Much |
   | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

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</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>10. Physical irritation?</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>11. Physical pain or soreness?</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>12. Choice of clothing to conceal psoriasis?</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

12-Item Psoriasis Quality of Life Questionnaire (PQOL-12), Copyright © 2002, 2003, Allergan Inc.

Total Quality-of-Life Score (1-120)
Medical staff to calculate
Physician Assessment

Name: ________________________________  Date: __________

Part 1: Total Quality-of-Life score (from part 1 of previous page)

Head
Anterior Trunk
Posterior Trunk
Right Leg
Left Leg
Both Arms
Genitalia

Part 2: Area of Involvement: percent BSA (body surface area)

Head
Anterior Trunk
Posterior Trunk
Right Leg
Left Leg
Both Arms
Genitalia

Head: up to 9 percent total BSA
Anterior Trunk: up to 18 percent
Posterior Trunk: Up to 18 percent
Right Leg: Up to 18 percent (includes buttock)
Left Leg: Up to 18 percent (includes buttock)

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

Total BSA Percent
**Part 2**
Using the figures below, place an ‘X’ on the parts of your body that currently have psoriasis

<table>
<thead>
<tr>
<th>front</th>
<th>back</th>
</tr>
</thead>
</table>

---

**Part 3**
Please answer the following questions by marking the appropriate checkbox

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
### KOO-MENTER PSORIASIS INSTRUMENT

**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>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Gluttate psoriasis?</td>
<td>YES</td>
<td>NO</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>YES</td>
<td>NO</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>YES</td>
<td>NO</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>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Substantial psychosocial or quality-of-life impact documented by patient Quality-of-Life self-assessment score of ≥50?</td>
<td>YES</td>
<td>NO</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>YES</td>
</tr>
<tr>
<td>Does the anatomical location or form of psoriasis (e.g., scalp, inverse, erythrodermic) preclude phototherapy?</td>
<td></td>
<td>YES</td>
</tr>
<tr>
<td>Does the patient have the dedication, time, stamina, or transportation for phototherapy?</td>
<td></td>
<td>YES</td>
</tr>
<tr>
<td>Has phototherapy, as monotherapy, failed in the past?</td>
<td></td>
<td>YES</td>
</tr>
<tr>
<td>Is phototherapy contraindicated (e.g., photosensitive drugs, history of multiple skin cancers)?</td>
<td></td>
<td>YES</td>
</tr>
</tbody>
</table>

In your clinical judgment, is phototherapy likely to yield substantial improvement to justify its use before systemic therapy? NO
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.

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
</table>

**Physician/Nurse comments**

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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 with a rheumatology/dermatology team that can diagnose psoriasis and psoriatic arthritis, and either treat or refer for care.

**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., 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 percent of respondents); frustration with ineffective treatments (90 percent); feeling unattractive (75 percent); depression (54 percent)

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

- 26 percent had to alter or stop their normal daily activities
- 40 percent chose clothing to cover up their condition
- 36 percent 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 size of the lesions helps determine the psoriasis type.
Plaque psoriasis is the most common type of psoriasis.  

- Diagnosed in 80 percent to 90 percent of patients.
- Characterized by sharply defined erythematosquamous 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 percent 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 percent 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, Sezary’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 percent 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 percent of patients develop it before age 60. Between 70 percent and 90 percent of patients are female; 10 percent to 25 percent 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.

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. About half of these patients have pain and are restricted in their daily activities because of nail changes.

• About 50 percent of all patients with psoriasis have fingernail involvement.

• Lesions can occur on mucosal membranes, including the geographic tongue in psoriasis patients.

Various factors that may trigger or exacerbate psoriasis are listed in Table 2-5.
PSORIATIC ARTHRITIS

- As many as 30 percent of patients with psoriasis of the joints, or psoriatic arthritis (PsA). It is characterized by inflammation and stiffness in the soft tissue around the joints. Joint stiffness in the morning or after inactivity is characteristic of inflammatory arthritis. There are five clinical subtypes of joint involvement, frequently involving 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 (Kavanaugh 2006).

- 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.

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.
Working with a rheumatology/dermatology team is essential for diagnosing and addressing the psoriasis and arthritis, plus these other diseases or comorbidities.

PsA treatment is complex because patients often have psoriasis along with inflammation in joints, spine, tendons and digits. Early interventions include treatment with non-steroidal anti-inflammatory agents (NSAIDs) along with physical therapy. Next are disease modifying anti-rheumatic agents (DMARDs), such as methotrexate (MTX), leflunomide or sulfasalazine. If these agents are not effective, biologic agents directed towards inhibition of tumor necrosis factor (TNF) are often prescribed because they can be effective for psoriasis and the various joint manifestations of PsA. A new oral drug, apremilast, was recently approved for PsA and is available for patients who do not respond to DMARDs. Ustekinumab, an anti-P40 antibody (inhibits both IL-12 and IL-23, which share the p40 subunit), is also effective for both psoriasis and PsA and is usually reserved for patients who cannot take anti-TNF agents or have shown lack of treatment response to

**TABLE 2-5**

<table>
<thead>
<tr>
<th>Triggers for Psoriasis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stress</strong></td>
</tr>
<tr>
<td><strong>Winter Weather</strong></td>
</tr>
<tr>
<td><strong>Physical trauma to the skin</strong></td>
</tr>
<tr>
<td><strong>Phototoxic reactions (solar, UVB, or PUVA induced)</strong></td>
</tr>
<tr>
<td><strong>Activation of local cellular immunity by allergens, infections and immunizations</strong></td>
</tr>
<tr>
<td><strong>Systemic immunological activation or alteration (e.g., hypersensitivity to a drug or other antigen)</strong></td>
</tr>
<tr>
<td><strong>Drugs (e.g., corticosteroids, lithium, antimalarials, beta-blockers, nonsteroidal anti-inflammatory drugs, angiotensin converting enzyme inhibitors)</strong></td>
</tr>
</tbody>
</table>

Adapted from Menter and Weinstein 17
these agents.20-22 The anti-IL-17 antagonists have also been demonstrated in clinical trials to have good efficacy in PsA.

**DIFFERENTIAL DIAGNOSIS**

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 discoid 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-standing 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.  
- 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. The scalp may show psoriasis-like changes.
- Patients with PRP are differentiated by having islands of unaffected skin (“skip areas”) surrounded by involved skin and 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.  

- An overlap syndrome with clinical features of both diseases.

### TABLE 2-6

<table>
<thead>
<tr>
<th>Type of Psoriasis</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chronic Plaque</strong></td>
<td>Eczema, PsEMA (combination of psoriasis and eczema), mycosis fungoides, patch or plaque stage CTCL, tinea corporis, Bowen’s disease, SCLE</td>
</tr>
<tr>
<td><strong>Guttate</strong></td>
<td>Secondary syphilis, psoriasiform, type tinea corporis, Sezary syndrome</td>
</tr>
<tr>
<td><strong>Erythrodermic</strong></td>
<td>PRP, eczema, SCLE, Sezary syndrome</td>
</tr>
<tr>
<td><strong>Pustular</strong></td>
<td>Eczema, PsEMA</td>
</tr>
<tr>
<td><strong>PSA</strong></td>
<td>Reactive Arthritis</td>
</tr>
</tbody>
</table>
Not widely accepted at present. It is not a recognized diagnosis.

**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 percent to 60 percent of patients.\(^{28}\)

- 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.

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 erythematos 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.

**COMORBIDITIES AND PSORIASIS**

There is growing recognition that psoriasis is a systemic inflammatory disease 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 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 2-7**

<table>
<thead>
<tr>
<th>Measurement Recommendation</th>
</tr>
</thead>
</table>

Blood pressure evaluated at least every 2 years; target <120/80 mmHg

Body mass index evaluated at least every 2 years; target <25 Kg/m²

Waist circumference evaluated least every 2 years; target
- <35 inches for women
- <40 inches for men

Pulse evaluated at least every 2 years

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 = < 200 mg/dL
- HDL = 50 mg/dL or higher
- LDL Optimal < 100 mg/dL

Near Optimal/Above Optimal 100 to 129 mg/dL
Borderline High 130 to 159 mg/dL
High 160 to 189 mg/dL
Very High 190 mg/dL and above

Fasting blood glucose evaluated at least every 5 years or every 2 years if risk factors are present; target <100 mg/dL

*AHA recommendations for cardiovascular risk factor screening (Kimball et al)*

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CHAPTER 3

CHOOSING A TREATMENT
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.

**TABLE 3-1**

<table>
<thead>
<tr>
<th><strong>Psoriasis Treatment Options</strong></th>
<th><strong>Topical Therapy</strong></th>
<th><strong>Phototherapy</strong></th>
<th><strong>Systemic Therapy</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topical Therapy</strong></td>
<td>Anthralin</td>
<td>Goeckerman (tar and UVB)</td>
<td>Retinoids</td>
</tr>
<tr>
<td><strong>Corticosteroid creams, lotions, ointments, gels, foams, shampoos, patches &amp; solutions</strong></td>
<td>Broad-band UVB</td>
<td>Methotrexate immune-modulating therapy</td>
<td></td>
</tr>
<tr>
<td><strong>Tars</strong></td>
<td>Tars</td>
<td>Narrow-band UVB</td>
<td>Other cytotoxic immune-modulating therapy</td>
</tr>
<tr>
<td><strong>Vitamin D</strong></td>
<td>Vitamin D</td>
<td>PUVA</td>
<td>Cyclosporine</td>
</tr>
</tbody>
</table>
| **Retinoid gel and creams**    | Retinoid gel and creams | Excimer laser | IL-17
|                                |                     |                 | TNF blockers
|                                |                     |                 | IL-12
|                                |                     |                 | IL-23
| **Topical immunomodulators**   | Topical immunomodulators | Phosphodiesterase 4 inhibitors | |
• Avoid adverse effects as much as possible.
• Improve the patient’s quality of life.

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.

• 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 not favored in PsA.
**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:**

- Allows 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.
- Allows the lowest possible effective doses to be used in an effort to minimize toxicity. For example, retinoid doses can be reduced to limit mucocutaneous toxicity and enhance tolerance.
- Allows the combination of a more potent, “less safe” agent for initial clearing with a “safer agent” for use in long-term control.
- 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 all of the new biologic and small molecule agents.
<table>
<thead>
<tr>
<th>Combination Therapy</th>
<th>Frequently Used Combinations</th>
<th>Combinations with Increased Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinoids and broad-band UVB</td>
<td>Hydroxyurea and methotrexate</td>
<td></td>
</tr>
<tr>
<td>Retinoids and narrow-band UVB</td>
<td>Bone marrow suppressants (e.g. hydroxyurea, methotrexate 6-thioguanine)</td>
<td></td>
</tr>
<tr>
<td>Retinoids and PUVA (Ultraviolet light A with the drug psoralen)</td>
<td>Drugs that increase cutaneous carcinogenicity (e.g. cyclosporine and PUVA)</td>
<td></td>
</tr>
<tr>
<td>Retinoids and methotrexate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retinoids and cyclosporine to decrease cyclosporine dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclosporine and methotrexate (low doses of both)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycophenolate mofetil and cyclosporine in order to taper off cyclosporine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral agents (methotrexate, retinoids, cyclosporine) with any biologic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytotoxics (e.g. methotrexate) and phototherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topicals and retinoids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate + TNF antagonists</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
• Table 3-2 lists frequently used combination therapies, and those to be used with caution.

• 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. (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...

<table>
<thead>
<tr>
<th>Rotational Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>PUVA</td>
</tr>
<tr>
<td>MTX</td>
</tr>
<tr>
<td>Acitretin</td>
</tr>
<tr>
<td>UVB +/- Tar</td>
</tr>
<tr>
<td>Immune Modulators  - Cyclosporine*</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.
phototherapy-induced skin changes) may be fully or partially reversed by discontinuing a drug or stopping therapy. • Retinoid mucocutaneous side effects are completely reversed when the drug is discontinued.

• As new forms of therapy become available, the circle of rotational therapies grows larger and the rotation intervals may change as knowledge about new treatments increases.

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. 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
# Table 3-4: Sequential Therapy Examples

<table>
<thead>
<tr>
<th>Phase</th>
<th>Topical</th>
<th>Traditional Systemic</th>
<th>Biologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>1-month for clearing</td>
<td>Cyclosporine initially 3-5 mg/kg/day for rapid improvement</td>
<td>Etanercept 50 mg s.c.</td>
</tr>
<tr>
<td></td>
<td>Calcipotriene or Calcitriol in combination with superpotent topical corticosteroid*, BID†</td>
<td></td>
<td>2x/week</td>
</tr>
<tr>
<td>Phase 2</td>
<td>Calcipotriene or Calcitriol BID on weekdays</td>
<td>Add acitretin 10-25 mg/day and gradually titrate upward to maximally tolerate dose. Then start tapering cyclosporine by 1 mg/kg/day each month</td>
<td>Etanercept 50 mg s.c.</td>
</tr>
<tr>
<td></td>
<td>Superpotent topical corticosteroid BID on weekends</td>
<td></td>
<td>1x/week</td>
</tr>
<tr>
<td>Phase 3</td>
<td>Maintenance</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Calcipotriene or Calcitriol BID, which may be tapered to once/day and discontinued if appropriate</td>
<td></td>
<td></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.
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.]

A more rapidly active conventional systemic agent such as cyclosporine has also been used as a sequential therapy with one of the biologic agents in order to take advantage of its rapid onset, but simultaneously limit the risks associated with long-term use. In general, however, the starting and then stopping of the biologic medications is not recommended given the increased risk of loss of efficacy. Therefore, it is recommended that these medications only be used if the plan is to continue them unless limited by toxicity or feasibility.

### TABLE 3-5

<table>
<thead>
<tr>
<th>Phase</th>
<th>Duration</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>Month 0-2</td>
<td>Cyclosporine</td>
</tr>
<tr>
<td>Phase 2A</td>
<td>Month 0-2</td>
<td>Oral retinoid or etanercept or adalimumab or apremilast</td>
</tr>
<tr>
<td>Phase 2B</td>
<td>Month 0-2</td>
<td>UVB/PUVA</td>
</tr>
<tr>
<td>Phase 3A</td>
<td>Month &gt;7</td>
<td>Cyclosporine</td>
</tr>
<tr>
<td>Phase 3B</td>
<td>Month &gt;7</td>
<td>Oral retinoid or etanercept or adalimumab or apremilast</td>
</tr>
<tr>
<td></td>
<td>(If needed)</td>
<td>UVB/PUVA</td>
</tr>
</tbody>
</table>
CHAPTER 4

TREATMENT ALGORITHMS FOR SPECIFIC PATIENT TYPES
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 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

If UVB phototherapy available, feasible, practical and suitable

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

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

- Adalimumab
- Apremilast
- Brodalumab
- Cyclosporine
- Etanercept
- Guselkumab
- Infliximab
- Ixekizumab
- Methotrexate
- PUVA
- Secukinumab
- Systemic retinoids
- Ustekinumab

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

If UVB phototherapy available, feasible, practical and suitable

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

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

- Adalimumab*
- Cyclosporine*
- Etanercept
- Guselkumab*
- Infliximab*
- Methotrexate*
- PUVA [dark skin]*
- Ustekinumab*

SECOND LINE

- Apremilast*
- Brodalumab*
- Ixekizumab*
- Secukinumab*

*Not approved for treatment of psoriasis in children.

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.
Women Trying To Become Pregnant with Chronic Plaque Psoriasis (>5 percent BSA), Without Psoriatic Arthritis

**FIRST LINE**

- Topical calcipotriene/calcitriol
- Topical corticosteroids
- Moisturizers and UVB phototherapy (NB and BB)
- Goeckerman

**SECOND LINE**

- Adalimumab
- Apremilast
- Brodalumab
- Cyclosporine
- Etanercept
- Guselkumab
- Infliximab
- Ixekizumab
- PUVA
- Secukinumab
- 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.
## Guttate Psoriasis (>5 percent BSA), Without Psoriatic Arthritis

<table>
<thead>
<tr>
<th>If UVB phototherapy available, feasible, practical and suitable</th>
<th>If UVB phototherapy unavailable, contraindicated, ineffective, or patient unable to comply</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FIRST LINE</strong></td>
<td><strong>FIRST LINE</strong></td>
</tr>
<tr>
<td>• UVB phototherapy (NB or BB)</td>
<td>• Apremilast</td>
</tr>
<tr>
<td></td>
<td>• Short course MTX or CsA</td>
</tr>
<tr>
<td><strong>SECOND LINE</strong></td>
<td><strong>SECOND LINE</strong></td>
</tr>
<tr>
<td>• Adalimumab</td>
<td>• Brodalumab</td>
</tr>
<tr>
<td>• Brodalumab</td>
<td>• Cyclosporine</td>
</tr>
<tr>
<td>• Etanercept</td>
<td>• Infliximab</td>
</tr>
<tr>
<td>• Guselkumab</td>
<td>• Ixekizumab</td>
</tr>
<tr>
<td>• Infliximab</td>
<td>• Secukinumab</td>
</tr>
<tr>
<td>• Ixekizumab</td>
<td>• Ustekinumab</td>
</tr>
</tbody>
</table>

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.
Erythrodermic Psoriasis in Males or Females Not of Childbearing Potential

**FIRST LINE**

- Cyclosporine
- Infliximab
- Ixekizumab
- Methotrexate
- Secukinumab
- Systemic Retinoids

**SECOND LINE**

- Adalimumab
- Brodalumab
- Etanercept
- Combinations: MTX and TNF, retinoids and TNF, retinoids and CsA, CsA and MTX
- Guselkumab
- 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

If UVB phototherapy available, feasible, practical and suitable

**FIRST LINE**

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

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

**FIRST LINE**

- Adalimumab
- Apremilast
- Brodalumab
- Cyclosporine [short term]
- Etanercept
- Gusekumab
- Infliximab
- Ixekizumab
- PUVA
- Systemic retinoids*
- Secukinumab
- Ustekinumab

**SECOND LINE**

- Combination therapies

*Liver studies should be monitored
**Hepatitis C 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

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

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

- Adalimumab*
- Etanercept*
- Infliximab*
- PUVA
- Systemic retinoids

**SECOND LINE**

- Apremilast
- Azathioprine**
- Brodalumab
- Cyclosporine**
- Combination therapies**
- Guselkumab
- Ixekizumab
- Secukinumab
- Ustekinumab

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

**Monitor viral load and consider antiviral prophylaxis

Prior treatment of Hepatitis C should be considered in patients with psoriasis.
Healthy Adults with Palmoplantar Psoriasis, Without Psoriatic Arthritis in Males or Females Not of Childbearing Potential

**FIRST LINE**
- Topical corticosteroids
- Topical calcipotriene/calcitriol
- Topical calcipotriene-steroid combination
- Topical tazarotene
- Keratolytics
- Moisturization

**SECOND LINE**
- Adalimumab
- Apremilast
- Brodalumab
- Cyclosporine
- Etanercept
- Gusetkumab
- Infliximab
- Ixekizumab
- Methotrexate
- PUVA/topical or systemic
- Secukinumab
- Systemic retinoids
- Targeted UVB phototherapy
- Ustekinumab

**THIRD LINE**
- CsA + MTX
- CsA + biologic
- MTX + biologic
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

If UVB phototherapy available, feasible, practical and suitable

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

**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

**SECOND LINE**

- Systemic retinoids

**THIRD LINE**

- Adalimumab
- Apremilast
- Brodalumab
- Cyclosporine
- Etanercept
- Guselkumab
- Hydroxyurea

- Infliximab
- Ixekizumab
- Methotrexate
- Secukinumab
- Ustekinumab
Pustular Psoriasis in Males or Females Not of Childbearing Potential

**FIRST LINE**

- Brodalumab
- Cyclosporine
- Guselkumab
- Infliximab
- Ixekizumab
- Methotrexate
- Secukinumab
- Systemic retinoids

**SECOND LINE**

- Adalimumab
- Apremilast
- Etanercept
- PUVA photochemotherapy
- Ustekinumab*

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

Rule out sepsis

Once stable, initiate maintenance with plaque psoriasis algorithm

*UC reports of TNF blocker & Ustekinumab-induced pustular psoriasis exist.
Hypertension 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
- **UVB phototherapy (NB or BB)**
  - UVB phototherapy alone
  - UVB phototherapy + systemic retinoids
  - UVB phototherapy + adjuvant topical agents
  - Goeckerman

### If UVB phototherapy unavailable, contraindicated, ineffective, or patient unable to comply
- **FIRST LINE**
  - Adalimumab
  - Apremilast
  - Brodalumab
  - Etanercept
  - Gusekumab
  - Infliximab
  - Ixekizumab
  - Methotrexate
  - PUVA
  - Secukinumab
  - Systemic retinoids
  - Ustekinumab

### SECOND LINE
- Combination therapies
  - MTX + biologic
  - Retinoid + biologic
  - Biologic + UVB phototherapy
  - Apremilast + UVB phototherapy
Healthy Elderly Patient with Chronic Plaque Psoriasis (>5 percent BSA), Without Psoriatic Arthritis

**If UVB phototherapy available, feasible, practical and suitable**
- UVB phototherapy (NB or BB)
  - UVB phototherapy alone
  - UVB phototherapy + systemic retinoids
  - UVB phototherapy + adjuvant topical agents
  - Goeckerman
  - PUVA

**First Line**
- Adalimumab
- Apremilast
- Brodalumab
- Etanercept
- Guselkumab
- Infliximab
- Ixekizumab
- Secukinumab
- Systemic retinoids*
- Ustekinumab

**Second Line**
- Methotrexate*

**Third Line**
- Cyclosporine*
  - MTX + CsA*
  - MTX + biologic*
  - CsA + biologic [short term only]*
  - Biologic + UVB phototherapy
  - Apremilast + UVB phototherapy

*When using these medications, screen for possible impairment of renal and/or hepatic function.
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><strong>FIRST LINE</strong></td>
<td><strong>FIRST LINE</strong></td>
</tr>
<tr>
<td>• Cosmetic treatment</td>
<td>• Intralesional steroids</td>
</tr>
<tr>
<td>• Topical steroids</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>SECOND LINE</strong></td>
</tr>
<tr>
<td></td>
<td>• Adalimumab</td>
</tr>
<tr>
<td></td>
<td>• Apremilast</td>
</tr>
<tr>
<td></td>
<td>• Brodalumab</td>
</tr>
<tr>
<td></td>
<td>• Etanercept</td>
</tr>
<tr>
<td></td>
<td>• Guselkumab</td>
</tr>
<tr>
<td></td>
<td>• Infliximab</td>
</tr>
<tr>
<td></td>
<td>• Ixekizumab</td>
</tr>
<tr>
<td></td>
<td>• Methotrexate</td>
</tr>
<tr>
<td></td>
<td>• PUVA</td>
</tr>
<tr>
<td></td>
<td>• Secukinumab</td>
</tr>
<tr>
<td></td>
<td>• Systemic retinoids</td>
</tr>
<tr>
<td></td>
<td>• Ustekinumab</td>
</tr>
</tbody>
</table>
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

**FIRST LINE**
- UVB phototherapy (NB or BB)
  - UVB phototherapy alone
  - UVB phototherapy + systemic retinoids
  - UVB phototherapy + adjuvant topical agents
  - Goeckerman
  - PUVA

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

**FIRST LINE**
- Adalimumab
- Apremilast
- Brodalumab
- Etanercept
- Guselkumab
- Infliximab
- Ixekizumab
- Methotrexate
- Secukinumab
- Systemic retinoids
- Ustekinumab

**SECOND LINE**
- Combination therapies
  - CsA + MTX
  - CsA + biologic
  - MTX + biologic
  - Biologic + systemic retinoid
  - 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

If UVB phototherapy available, feasible, practical and suitable

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

**SECOND LINE**

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

- Adalimumab
- Apremilast
- Brodalumab
- Etanercept
- Guselkumab
- Infliximab
- Ixekizumab
- Methotrexate
- Secukinumab

**THIRD LINE**

- Combination Therapies
  - MTX + biologic
  - Biologic + UVB phototherapy (only if absolutely necessary)
  - Apremilast + UVB phototherapy

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 (NB or BB)
  - UVB phototherapy alone
  - UVB phototherapy + systemic retinoids
  - UVB phototherapy + adjuvant topical agents
  - UVB phototherapy + short-term isotretinoin, if necessary*
  - Goeckerman

**First Line**
- Adalimumab
- Apremilast
- Brodalumab
- Cyclosporine
- Etanercept
- Guselkumab
- Infliximab
- Ixekizumab
- Methotrexate
- PUVA
- Secukinumab
- Ustekinumab

**Second Line**
- Combination Therapies
  - MTX + CsA
  - MTX + biologic
  - Isotretinoin (short term, if necessary)*
  - Biologic + UVB
  - 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.
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 tars
- Topical calcipotriene
- Topical tazarotene
- Anthralin

**SECOND LINE**

- Adalimumab
- Apremilast
- Brodalumab
- Cyclosporine
- Etanercept
- Guselkumab
- Infliximab
- Ixekizumab
- Methotrexate
- Secukinumab
- Systemic retinoids
- Targeted UVB phototherapy
- 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
- Conticosteroid injections into tendons, joints or sacroiliac joints

### Disease modifying anti-rheumatic agents (DMARDs)
- sulfasalazine
- Leflunomide
- Cyclosporine
- Hydroxychloroquine
- Methotrexate

### Biologic Agents

#### Anti-Tumor Necrosis Factor (TNF)
- Adalimumab
- Golimumab
- Etanercept
- Infliximab

#### Anti-Interleukin (IL) - 12,23 Antibody
- Ustekinumab

#### Anti-IL-17
- Secukinumab

### PDE4 Inhibitor
- Apremilast

### T cell Inhibitor
- Abatacept
CHAPTER 5

THERAPEUTIC TREATMENT OPTIONS AND THEIR SIDE EFFECT PROFILES
CHAPTER 5 THERAPEUTIC TREATMENT OPTIONS AND THEIR SIDE EFFECT PROFILES

The four types of therapies available for treating psoriasis are:

1. Topical therapies
2. Phototherapies
3. Systemic therapies
4. Biologic 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 severe psoriasis, they may be prescribed as adjunctive therapy along with systemic therapy or phototherapy.

Dosing
Topical corticosteroids are available in many different strengths, ranging from class 7 steroids such as 1 percent 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. 

36
Side Effects

- Suppression of the hypothalamic-pituitary-adrenal (HPA) axis may occur with medium-to-superpotent topical corticosteroids.\(^{37}\)
- 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.\(^{38}\) This drawback has led to the development of intermittent therapy, in which the superpotent topical steroid is only applied in pulses (e.g., on weekends).\(^{39}\)

Vitamin D Analogs: Calcipotriene, Cream and Scalp Solution, 0.005 percent (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. It does not have corticosteroid side effects. Calcipotriene combination therapy with a superpotent corticosteroid is superior to either agent alone.\(^{40}\)

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.\(^{41}\)

Dosing

Apply to affected area twice daily.\(^{41,42}\)

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.

- They should not be combined with salicylic acid or other acids, as these can inactivate vitamin D drugs.
- They should be used after phototherapy. 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 Products:** Calcipotriene/betamethasone dipropionate (Taclonex® ointment and suspension and Enstilar® foam)

Two fixed combination products are available. They are labeled for once daily use. Superiority of both to placebo and to the individual ingredients has been demonstrated. Its use on an as-needed basis has been studied for up to a year.

**Side Effects**
The side effects expected are based on the individual ingredients including topical steroids and calcipotriene as listed above.

**Coal Tar Preparations:** Psorent®, Scytera®

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.

**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. 37

**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 cream <1 percent is applied overnight. Anthralin 1 percent 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. 45, 46

**Side Effects**

- It stains skin, clothing and furniture. It releases anthralin as it melts at skin temperature; therefore the patient’s skin may be stained, but clothing and furniture may not be.
- It irritates skin. After anthralin is washed off, triamcinolone or other topical steroid may be applied to prevent or lessen irritation. 47

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

Tazarotene, a topical retinoid, does not produce the side effects of corticosteroids. Tazarotene topical cream is indicated for the treatment of stable-plaque psoriasis involving up to 20 percent of BSA. Combining tazarotene with corticosteroid therapy helps avoid irritant dermatitis and produces better results than corticosteroid monotherapy. 37

**Dosing**

Apply once a day, usually in the evening. 43

**Side Effects**

- Causes retinoid dermatitis at the site of application, especially with 0.1 percent 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, UV doses should be reduced by at least one-third to reduce burning.\(^\text{48, 49}\)
- Pregnancy category X: Retinoids should not be used by women who are or may become pregnant.\(^\text{43}\)

**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 percent crude coal tar and up to 10 percent 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-erythemadose (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**

- 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

- UVB plus low-dose acitretin: 10 to 30 mg/day (most often 25 mg QD or QOD with food) and lower doses of UVB.

**Side Effects**

- May cause increased photosensitivity and burning unless UVB dosing is individualized. If acitretin is added to a treatment that already includes UVB phototherapy, decrease the amount of UVB light should be decreased right away 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 may be an alternative.

- Salicylic acid blocks UVB.

- Combination therapy requires increased monitoring.

(See Table 5-1.)

**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.\(^{52,53}\) The efficacy of nbUVB is similar to that of PUVA in the initial clearing phase, but remissions are not as durable.

**Side Effects**

- Rarely causes burns but they could 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 percent 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) is an option for any patients with concerns about skin cancer risk or who want faster and more effective PUVA photochemotherapy.

Side Effects

• Squamous cell carcinoma (SCC): PUVA has been shown to increase SCC risk in Caucasians. This increase was not seen if the patient had less than 150 cumulative PUVA sessions. SCC risk was shown to be 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. 56

• Basal cell carcinoma (BCC): PUVA has been shown to increase 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.  

- 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).

**Clinical Pearls**

- No increase in skin cancer of any type in non-Caucasians.

- Patients should not use tanning beds. The combination of Oxsoralen and tanning beds can result in life-threatening burns. They 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. They should reduce the initial dose of UV, use smaller incremental doses and maximize the time period between the ingestion of photosensitizing drugs and phototherapy.

- For maintenance therapy, the frequency of PUVA phototherapy sessions can be less than once a week and sometimes as little as once a month due to a much longer duration of therapeutic effect than UVB phototherapy.
### TABLE 5-1

**Combination Therapy - Special Considerations for Monitoring**

<table>
<thead>
<tr>
<th>Current Therapy</th>
<th>Therapy Being Added</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MTX</strong></td>
<td><strong>CsA</strong></td>
</tr>
<tr>
<td><strong>MTX</strong></td>
<td>Monitor CBC &amp; renal function, electrolytes, Mg(^2); use lower doses of both drugs</td>
</tr>
<tr>
<td><strong>CsA</strong></td>
<td>Monitor CBC &amp; renal function, electrolytes, Mg(^2); use lower doses of both drugs</td>
</tr>
<tr>
<td><strong>Acitretin</strong></td>
<td>Monitor LFTs, lipids and CBC</td>
</tr>
<tr>
<td><strong>UVB</strong></td>
<td>Monitor for squamous cell carcinoma</td>
</tr>
<tr>
<td><strong>PUVA</strong></td>
<td>Monitor for squamous cell carcinoma</td>
</tr>
</tbody>
</table>

**Key:**
- MTX = Methotrexate
- CsA = Cyclosporine A
- CBC = Complete Blood Count
- LFT = Liver Function Test
SYSTEMIC THERAPIES

**Acitretin** *(Soriatane®)*

Acitretin is a synthetic retinoid that is effective for treating plaque, pustular, palmoplantar, guttate and erythrodermic psoriasis. Following an absolute drop in the psoriasis area, a severity index (PASI) score of 57 percent was observed by week 12. Seventy percent 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 it useful for maintenance therapy.

Although infrequent, symptoms related to bone changes or calcified ligaments or tendons may limit long-term use in selected patients. Published prospective studies on long-term, low-dose use of acitretin in psoriasis patients have all failed to demonstrate increased risk of hyperostosis such as bone spurs.

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.

In combination therapy, acitretin enhances efficacy and allows lower doses of each drug. The following applies to combination therapy including acitretin:

- Combination with PUVA or UVB light therapies enhances efficacy in plaque or guttate psoriasis and limits 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 as monotherapy to clear the psoriasis; acitretin is then added 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.

**TABLE 5-2**
Side Effects of Acitretin and Management Options

<table>
<thead>
<tr>
<th>Side Effects Requiring Therapy</th>
<th>Management Tips</th>
</tr>
</thead>
</table>
| **Headache**                  | • Eye exam; discontinue if papilledema  
|                               | • If severe, discontinue acetretin      |
| **Increased LFTs**            | • Often transient and reversible       |
|                               | • Ask if taking ASA, acetaminophen, alcohol |
|                               | • If LFT greater than 2.5x normal, decrease dose and re-check |
|                               | • Evaluate for other causes (e.g. hepatitis C) |
| **Pyogenic granulomas**       | • Lower dose                                |
| (frequently periungual)       | • Consider using steroid gels, silver nitrate, cryotherapy, C&D or surgical removal |
| **Bone changes* Hyperostosis [DISH syndrome]** | • If symptomatic, X-ray |
| **Osteoporosis**              | • Treat according to National Osteoporosis Guidelines |
| **Hyperlipidemia**            | • Check triglycerides [TG] at baseline; monitor every 2 to 4 weeks until stable, every 3 to 6 months after that. |
|                               | • TG>400 mg/dl; gemfibrozil [Lopid®] 600mg, BID |
|                               | • TG>700 mg/dl; discontinue acitretin, start lipid lowering drugs |
|                               | • Cholesterol>300 mg/dl; atorvastatin [Lipitor®] 10-80mg, fenofibrate [TriCor®] |

*Association with retinoids is questionable and subject to controversy, especially in low-dose combinations or maintenance therapy for psoriasis patients.*
### TABLE 5-2 CONTINUED

<table>
<thead>
<tr>
<th>Side Effects Requiring Therapy</th>
<th>Management Tips</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression †</td>
<td>Discontinue acitretin</td>
</tr>
<tr>
<td>Important drug interactions</td>
<td>Glibenclamide, ethanol, progestin contraceptives</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mucocutaneous Changes</th>
<th>Management Tips</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chelitis</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>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pregnancy Considerations</th>
<th>Management Tips</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female on acitretin</td>
<td>Category X, cannot use if pregnant or thinking of becoming pregnant</td>
</tr>
<tr>
<td>Partner of male on acitretin</td>
<td>No action, reassure female exposure to male semen not associated with birth defects</td>
</tr>
</tbody>
</table>

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

ASA = acetylsalicylic acid          DISH = diffuse idiopathic skeletal hypertosis
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”).
- It can be combined with almost any other treatment at lower doses to enhance efficacy.
- Women who may become pregnant should avoid alcohol because it facilitates the conversion of acitretin to etretinate.\textsuperscript{64-66}
- Lipid-lowering agents easily manage lipid changes.
- Hyperostosis data is contradictory and subject to controversy.\textsuperscript{67,68}
- Retinoid with phototherapy (acitretin-UV) is more effective, better tolerated and perhaps safer for long-term therapy than phototherapy alone.\textsuperscript{62} UVB and UVA doses can be lowered by about 50 percent and acitretin doses of 10 to 25 mg/day can be used.\textsuperscript{69} 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 percent 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.

Cyclosporine (Neoral®)

The immunosuppressant cyclosporine was introduced in the 1970s to prevent kidney transplant rejection. Since then, a microemulsion form of cyclosporine called Neoral® has been 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.
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 percent) occurred in 40 percent of those patients treated with methotrexate and 33 percent in the patients treated with cyclosporine. Partial remission (defined as a reduction in the baseline score of more than 75 percent) was achieved in 60 percent of the methotrexate-treated patients and 71 percent 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.\textsuperscript{70}

**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 percent, 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.\textsuperscript{71} 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.\textsuperscript{72,73} 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.\textsuperscript{74-76} 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: \textsuperscript{77}
  - Use cyclosporine for no longer than two years at a time.
  - Keep serum creatinine increase to <30 percent of the pretreatment baseline creatinine.
Table 5-3 details the side effects of cyclosporine, drug interactions and corresponding management options.

<table>
<thead>
<tr>
<th>Side Effects Requiring Therapy</th>
<th>Management Tips</th>
</tr>
</thead>
</table>
| Increased K⁺                  | • Discontinue K⁺-rich foods (e.g. bananas)  
  • Consider HCTZ (50mg, QOD); may reduce creatinine clearance  
  • K⁺ >5.5mEq/L, discontinue drug |
| Decreased Mg²⁺                | • Give OTC Mg⁺ supplements |
| Hypertension (DBP>90 mmHg)    | • Common, easily controlled; monitor weekly  
  • Use of calcium channel blockers nifedipine (Adalat®, Procardia®) and felodipine (Plendil®) may help limit nephrotoxicity  
  • No ACE inhibitors; may increase creatinine and decrease GFR  
  • No thiazide diuretics |
| Increased CrCl >30 percent    | • Reduce CsA dose |
| Drug Interactions             | • Some antibiotics, melphalan (alkeran®), antifungals, NSAIDS, cimetidine (Tagamet®), ranitidine (Zantac®), tacrolimus (Prograf®), calcium channel blockers, methylprednisolone, anticonvulsants and others |

Table 5-3 Continued
<table>
<thead>
<tr>
<th>Side Effects Not Requiring Tx</th>
<th>Management Tips</th>
</tr>
</thead>
<tbody>
<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></td>
</tr>
<tr>
<td>Increased uric acid</td>
<td>• Nothing unless symptomatic or has history of gout</td>
</tr>
</tbody>
</table>

HCTZ = hydrochlorothiazide
GFR = glomerular filtration rate
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).

  • Rotate therapy if possible.

  • 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 still one of the most effective therapies, particularly for psoriatic arthritis. 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

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, 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.\textsuperscript{78,79} 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

<table>
<thead>
<tr>
<th>Risk Factors for Liver Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
</tr>
<tr>
<td>• History of or current excessive alcohol abuse</td>
</tr>
<tr>
<td>• Abnormal liver function test</td>
</tr>
<tr>
<td>• History of liver disease, including chronic hepatitis</td>
</tr>
<tr>
<td><strong>Secondary</strong></td>
</tr>
<tr>
<td>• Diabetes mellitus</td>
</tr>
<tr>
<td>• Obesity</td>
</tr>
<tr>
<td>• Exposure to hepatotoxic drugs or chemicals</td>
</tr>
</tbody>
</table>
# Side Effects of Methotrexate and Management Options

<table>
<thead>
<tr>
<th>Side Effects Requiring Therapy</th>
<th>Management Tips</th>
</tr>
</thead>
</table>
| **Nausea** | • 1-5mg folic acid QD x6 days; do not give on day of MTX treatment due to possible reduction in efficacy  
• Decrease or divide MTX dose  
• Administer SQ or IM |
| **Aphthous stomatitis** | • Check CBC  
• Dose related and reversible, lower dose  
• Add topical TX  
• Folic acid, although it may reduce the efficacy  
• Leucovorin; do not give on day MTX is given |
| **Increased LFTs** | • Check LFTs 5-7 days after dose [see table 5-6: WHO Guidelines for Liver Toxicity]  
• Ask about alcohol, meds such as acetaminophen, ASA  
• Increased GGT and alkaline phosphatase not related to MTX  
• Consider liver biopsy [see Table 5 to 7: Liver Biopsy Findings] |
| **Bone marrow suppression (decreased Hct, megaloblastic anemia)** | • Monitor for drug interaction with NSAIDs, trimethoprim/sulfamethaxazole  
• Lower MTX dose if symptomatic  
• Folate, 5mg/day  
• Other medications should be avoided; however, if absolutely necessary, closely monitor for drug interaction with NSAIDs, trimethoprim/sulfamethaxazole |
| **Platelets** | • Any sudden and/or significant reduction in platelet count from pre-treatment level, repeat CBC and platelet count in 1 week and consider reducing dose |
## Side Effects of Methotrexate and Management Options

<table>
<thead>
<tr>
<th>Side Effects Requiring Therapy</th>
<th>Management Tips</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Platelets</strong></td>
<td>• Consider lowering dose and repeat platelet count more often</td>
</tr>
<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>• Consider lowering dose and repeat WBC more often</td>
</tr>
<tr>
<td>WBC 3,000 to normal</td>
<td>• Reduce dose or discontinue MTX</td>
</tr>
<tr>
<td>WBC &lt; 3,000</td>
<td>• Discontinue MTX</td>
</tr>
<tr>
<td>Pulmonary toxicity - acute pneumonia</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, phenotoin (Dilantin®), probencid (Benemid®), salicylates, and sulphonamides may raise free MTX levels; NSAIDs, phenylbutazone, probencid, salicylates, sulphonamids, 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>
</tbody>
</table>

WBC = White Blood Count
• 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

**WHO Guidelines for Liver Toxicity**

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

\[ ALT = \text{alanine aminotransferase} \quad \text{AST} = \text{aspartate aminotransferase} \]

### TABLE 5-7

**Liver Biopsy Findings**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (normal)</td>
<td>mild fatty infiltration, nuclear variability, portal hypertension</td>
<td>Continue MTX</td>
</tr>
<tr>
<td>II (moderate-severe)</td>
<td>fatty infiltration, nuclear variability, portal tract inflammation</td>
<td>Continue MTX; these changes are relatively common pre-therapy</td>
</tr>
<tr>
<td>IIIA (mild fibrosis)</td>
<td></td>
<td>May continue MTX; repeat biopsy in six months</td>
</tr>
<tr>
<td>IIIB (moderate-severe fibrosis)</td>
<td></td>
<td>Discontinue MTX</td>
</tr>
<tr>
<td>IV (cirrhosis)</td>
<td></td>
<td>Discontinue MTX</td>
</tr>
</tbody>
</table>
BIOLOGICS

Adalimumab (Humira®)

Adalimumab inhibits tumor necrosis factor-alpha (TNF-alpha), a key inflammatory cytokine. It is FDA-approved for psoriasis, psoriatic arthritis, rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, Crohn’s disease and ulcerative colitis and hidradenitis suppurativa. Adalimumab is a recombinant IgG1 monoclonal antibody that binds to TNF-alpha. Adalimumab also lyse surface TNF-expressing cells in vitro in the presence of complement. In the REVEAL 2008 clinical study 71 percent of patients achieved a PASI 75 at week 16. Of interest in this study, 240 patients were taken off treatment at week 33 and followed until week 52. Forty-five percent 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 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. 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.
• Patients generally tolerate injection site reaction and pain. Some agents are less irritating than others.

• 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.\(^8^2\)

• 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.

**Abatacept (Orencia®)**

Abatacept is a modified version of a protein normally produced by the body as a “checkpoint” in the immune system. It is believed to work by keeping a certain type of cells in the immune system from becoming activated. It is currently approved for use in rheumatoid arthritis and psoriatic arthritis and is being studied in psoriasis. In rheumatoid arthritis and psoriatic arthritis, abatacept can be given by an intravenous (IV) infusion or can be taken at home by injection, and can be used with or without other medications such as methotrexate.

**Brodalumab (Siliq®)**

Brodalumab is an interleukin-17 receptor antagonist that has been recently approved by the FDA for the treatment of moderate to severe plaque psoriasis. The medication has been shown to be 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.

**Cautions**

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 will require administration by a suitably trained dermatologist and via specialized pharmacies.

**Certolizumab pegol [Cimzia®]**

Certolizumab pegol (Cimzia®) is FDA-approved for treatment of psoriatic arthritis and has been tested for 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 200 mg in 1 ml 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.

• Concomitant methotrexate 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.

Etanercept (Enbrel®)

Etanercept is FDA-approved for treatment of adult and pediatric patients 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 percent of patients treated with 25 mg twice a week and 50 percent of patients treated with 50 mg twice a week had 75 percent improvement in PASI (PASI 75) after 12 weeks of treatment.83, 84

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 sites for injection (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 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. 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 percent of patients treated with 50 mg every four weeks and 45 percent of patients treated with 100 mg every four weeks achieved a 20 percent improvement in the American College of Rheumatology criteria (ACR20) response at week 14, compared to 9 percent of patients in the placebo control group.\(^{80}\) Patients in the same study with psoriasis affecting 3 percent or more of their body surface area were also evaluated for changes in the PASI score. At week 14, 40 percent of the patients receiving 50 mg and 58 percent of the patients receiving 100 mg of golimumab achieved a PASI 75 compared to 3 percent of the placebo-treated patients.\(^{85}\)

**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.\(^{86}\)

**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.

Guselkumab (Tremfya®)

Guselkumab is a human monoclonal antibody to the p19 component of IL-23 that is approved for psoriasis. The safety and efficacy of guselkumab 100 mg 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 is administered in 100 mg 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 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 percent of the 5 mg/kg group achieved a PASI 75 compared to 2 percent of the placebo group at week 10. At week 52, the PASI 75 rate was 59 percent. 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 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.
- 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

**Ixekizumab (Taltz®)**

Ixekizumab is an interleukin-17A inhibitor. It is a humanized IgG4 monoclonal antibody which acts by binding and neutralizing the IL17. 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), followed by 80 mg q 4 weeks thereafter.

**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 repeat annually thereafter. Hepatitis B and Hepatitis C screening is recommended prior to initiating therapy.

**Cautions**

Caution must be exercised in the setting of concurrent inflammatory bowel disease.\(^95,^96\)

**Secukinumab (Cosentyx®)**

Secukinumab is an interleukin-17A (IL-17) inhibitor. It is a recombinant, high-affinity, fully human immunoglobulin G1k monoclonal antibody that selectively binds and neutralizes interleukin-17A. It is currently approved for moderate to severe plaque psoriasis and psoriatic arthritis. In clinical trials, about 82 percent of the individuals taking 300 mg doses of Cosentyx experienced a PASI score of 75 percent after 12 weeks. About 72 percent 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 repeat annually thereafter. Hepatitis B and Hepatitis C screening is recommended prior to initiating therapy.

Cautions
Caution must be exercised in the setting of concurrent inflammatory bowel disease.\textsuperscript{95,96}

**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. It is approved for both psoriasis and psoriatic arthritis. 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. \textsuperscript{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 has been shown to be effective without any significant increase in side effects noted. \textsuperscript{89}

**Side Effects**

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

• Patients taking this medication do not appear to be at an increased risk of salmonella and mycobacterial infections; no increased risk of these infections has been identified in IL-12 or IL-23 genetically deficient patients. There has been one reported case of reversible posterior leukoencephalopathy syndrome (a non-infectious condition) that resolved with drug cessation.

• Pregnancy category B

**Clinical Pearls**

• Five years of safety data have shown no significant increase
SMALL MOLECULE

Apremilast (Otezla®)

Apremilast is a phosphodiesterase 4 (PDE4) inhibitor. It is currently approved for psoriasis and psoriatic arthritis. It is an oral, non-biologic therapy which selectively inhibits an enzyme called phosphodiesterase 4 (PDE4). PDE4 regulates the conversion of cAMP to AMP within the cell; the inhibition of this enzyme results in an increase in cAMP intracellularly which allows for the modulation of the network of pro-inflammatory and anti-inflammatory mediators within the cell.

In pivotal phase 3 studies it achieved an ACR 20 score of 41 percent at week 16 using the 30 mg twice daily oral dosage. Phase three studies in psoriasis are remarkable for a PASI 75 of 33.1 percent versus 5.3 percent 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

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

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

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. 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. 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 has proven effective in the treatment of several inflammatory or autoimmune skin disorders. In the 1970s, it 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 percent 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 a small study by Silvis and Levine showed it was effective in psoriasis patients. 94

**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.

These agents are currently being explored for treatment of psoriasis and psoriatic arthritis.

Tofacitinib (Xeljanz®)
Tofacitinib is a JAK kinase inhibitor currently indicated for the treatment of rheumatoid arthritis. In two Phase III studies, it was shown to be effective in psoriasis patients. It is under investigation for psoriatic arthritis. It is not currently approved for the treatment of psoriasis or psoriatic arthritis.

Tildrakizumab
Tildrakizumab is a human monoclonal antibody to the p19 component of IL-23 that has been tested for psoriasis and is not approved for 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 repeat annually thereafter. Hepatitis B and Hepatitis C screening is recommended prior to initiating therapy.
Once a patient’s psoriasis is adequately controlled, the therapeutic regimen used for clearing can be slowly tapered to the minimal effective dose, and perhaps combined with another agent. Alternatively, the patient can transition to a less-toxic therapy to maintain long-term control. In addition, a sequential or rotational schedule may help the patient maintain a state of remission.

Topical therapy, UVB and acitretin are the safest modalities for long-term use. TNF inhibitors, ixekizumab, ustekinumab, secukinumab and apremilast, also appear to be safe treatments for long-term use. They do not seem to contribute to the cumulative organ toxicity associated with methotrexate and cyclosporine. When possible, these safe choices should be used for the maintenance phase of therapy. In sequential or rotational strategy, the clinician’s expertise helps smooth the transition from one regimen to another, which is critical for overall therapeutic success. Table 6-1 contains details of several different transitions and combinations.
## Transitional Issues

<table>
<thead>
<tr>
<th>Drugs Being Added or Deleted</th>
<th>Issues During Transition</th>
<th>Therapy Time/Dose Limit</th>
</tr>
</thead>
</table>
| **Transitioning from MTX to acitretin (4-5 month period)** | • Use full doses of both and taper MTX as patients improve or  
• Taper MTX slowly (2.5mg every 4 weeks) while introducing acetretin  
• Monitor LFTs every week when starting combination treatment | MTX: rotate after cumulative dose of 3.5g in low-risk patients; 1.5g in high-risk patients or obtain liver biopsy  
Acitretin: no limit |
| **Transitioning MTX to CsA** | • Decrease MTX or discontinue abruptly; add CsA 2.5 to 5.0mg/kg/day  
• Increase frequency of CBC, PLT and creatinine monitoring | MTX: rotate 1.5g in high-risk patients or obtain liver biopsy  
CsA: 1-2 years of continuous treatment at a time |
| **Adding MTX or CsA to acitretin** | • Add full dose of MTX or CsA  
• With MTX: Monitor LFTs and CBC weekly at first  
• With CsA: monitor renal function and lipids weekly at first | MTX: rotate after 1.5g in high-risk patients or obtain liver biopsy  
CsA: 1-2 years of continuous treatment at a time |
### TABLE 6-1 CONTINUED

<table>
<thead>
<tr>
<th>Drugs Being Added or Deleted</th>
<th>Issues During Transition</th>
<th>Therapy Time/Dose Limit</th>
</tr>
</thead>
</table>
| Adding acitretin to phototherapy | • Decrease UVB or UVA dose by 50 percent  
• Use low-dose acitretin (25mg/day or every other day) | Acitretin and phototherapy; no limit |
| Adding TNF inhibitor systemic treatment | • Add the TNF inhibitor at the full/standard dose  
• Taper systemic treatment once adequate disease control is achieved | TNF inhibitors can be used in combination with other systemic treatments with no known time-limitations |
| Adding acitretin or methotrexate to TNF inhibitors | • Add the oral systemic medication using the normal dosing schedule  
• Once adequate disease control is achieved, the combination can be continued  
• Alternatively, the TNF inhibitor can be withdrawn or the dose of the oral systemic medication can be tapered | TNF inhibitors can be used in combination with oral psoriasis treatments with no known time-limitations |

PLT = platelets
CHAPTER 7 ACCESS TO CARE ASSISTANCE

INSURANCE ADVOCACY

Insurance challenges can be a barrier to appropriate patient care. The National Psoriasis Foundation has the resources to help. The Foundation’s advocacy department offers direct assistance for patients and medical professionals dealing with insurers. NPF 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.

NPF also provides resources to help patients work with insurance companies to improve treatment coverage and to access financial assistance with out-of-pocket 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: psoriasis patients and those who care for them.

For more information or to submit an insurance policy for investigation, contact NPF at 503-244-7404 or advocacy@psoriasis.org.

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


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