Treatment pearls for psoriasis and eczema

Mark Lebwohl, MD
Sol and Clara Kest Professor
And Chairman
Kimberly and Eric J. Waldman
Department of Dermatology
Icahn School of Medicine at Mount Sinai
• What do I do for the patient who has failed everything?
• Insurance won’t let my patient get the drug he/she needs. What can I do?
• How fast do psoriasis treatments work?
Adding Methotrexate to Etanercept Versus Etanercept Monotherapy in Adults with Moderate to Severe Plaque Psoriasis: Efficacy and Safety

A.B. Gottlieb, et al

Amer Acad of Derm 2012;
Figure 2,3,4.

PASI Improvements

*P < 0.05; †P < 0.01; ‡P < 0.0001; P-values for primary and secondary endpoints (PASI 50, PASI 75, and PASI 90 at weeks 12 and 24) adjusted based on a combination of sequential testing and Hommel procedures.

- Week 24 PASI 75 was significantly greater with etanercept + methotrexate compared with etanercept + placebo (77.3% vs 60.3%, P < 0.0001)
- Week 12 PASI 75 was significantly greater with etanercept + methotrexate compared with etanercept + placebo (70.2% vs 54.3%, P = 0.0112)
- PASI 50 and PASI 90 were also greater with etanercept + methotrexate than with etanercept + placebo at weeks 12 and 24
- Week 12 improvements were maintained through week 24 despite the reduction in etanercept dosage
Optimizing adalimumab treatment in psoriasis with concomitant methotrexate (OPTIMAP): study protocol for a pragmatic, single-blinded, investigator-initiated randomized controlled trial.

Busard C, et al.

Combination of adalimumab with traditional systemic antipsoriatic drugs - a report of 39 cases.

Philipp S, et al.

Effect of Infliximab Regimen and Immunosuppression on ATI Formation

Proportion of Patients With ATI* in ACCENT I Through Week 54

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Proportion of Patients (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodic Strategy</td>
<td>38</td>
<td>0.003</td>
</tr>
<tr>
<td>Maintenance q8w 5 mg/kg</td>
<td>11</td>
<td>0.42</td>
</tr>
<tr>
<td>Maintenance q8w 10 mg/kg</td>
<td>8</td>
<td>0.42</td>
</tr>
</tbody>
</table>

*442 patients with evaluable samples were assessed for ATIs

DOSAGE & INDICATIONS

For the treatment of moderate to severe plaque psoriasis in those patients who are candidates for phototherapy or systemic therapy.

Subcutaneous dosage

Adults
Dose is weight based. WEIGHT 100 kg OR LESS: 45 mg subcutaneously; repeat dose 4 weeks later. Then, give 45 mg subcutaneously every 12 weeks starting at week 16. WEIGHT MORE THAN 100 kg: 90 mg subcutaneously; repeat dose 4 weeks later. Then, give 90 mg subcutaneously every 12 weeks starting at week 16. A lower dose of 45 mg may be considered; however, greater efficacy is seen with a 90 mg dose.

For the treatment of active psoriatic arthritis with or without methotrexate.

Subcutaneous dosage

Adults
Most patients receive 45 mg subcutaneously initially and a repeat dose 4 weeks later, followed by 45 mg subcutaneously every 12 weeks. For patients who weigh more than 100 kg and have co-existent moderate-to-severe plaque psoriasis, give 90 mg subcutaneously initially; repeat dose 4 weeks later, then follow with 90 mg subcutaneously every 12 weeks.
2.2  Psoriatic Arthritis

For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, use the dosing and administration recommendations for plaque psoriasis [see Dosage and Administration (2.1)].

For other psoriatic arthritis patients, administer COSENTYX with or without a loading dosage by subcutaneous injection. The recommended dosage:

- With a loading dosage is 150 mg at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
- Without a loading dosage is 150 mg every 4 weeks
- If a patient continues to have active psoriatic arthritis, consider a dosage of 300 mg.

COSENTYX may be administered with or without methotrexate.
LY2439821, a humanized anti-interleukin-17 monoclonal antibody, in the treatment of patients with rheumatoid arthritis: A phase I randomized, double-blind, placebo-controlled, proof-of-concept study.

Genovese MC, et al

Ixeizumab used with MTX for RA
Combination use of ustekinumab with other systemic therapies: a retrospective study in a tertiary referral center.
Combination therapy of cyclosporine and anti-tumor necrosis factor α in psoriasis: A case series of 10 patients.

Cohen Barak E, Kerner M, Rozenman D, Ziv M.

Ixekizumab Package Insert

**Cyclosporine**: The formation of CYP450 enzymes may be altered by increased concentrations of cytokines during chronic inflammation. Thus, the formation of CYP450 enzymes could be normalized during ixekizumab administration. Clinically relevant drug interactions may occur with CYP450 substrates that have a narrow therapeutic index such as cyclosporine. If ixekizumab is initiated or discontinued in a patient taking cyclosporine, monitor cyclosporine concentrations; cyclosporine dose adjustments may be needed.

**Intranasal Influenza Vaccine**: Do not administer live vaccines to ixekizumab recipients. Before initiation of ixekizumab therapy, consider completion of all age appropriate vaccinations per current immunization guidelines. No data are available on the response to live or inactive vaccines in patients receiving Ixekizumab therapy.

Secukinumab Package Insert

### 7.3 CYP450 Substrates

A role for IL-17A in the regulation of CYP450 enzymes has not been reported. The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNFα, IFN) during chronic inflammation. Thus, COSENTKYX, an antagonist of IL-17A, could normalize the formation of CYP450 enzymes. Upon initiation or discontinuation of COSENTKYX in patients who are receiving concomitant CYP450 substrates, particularly those with a narrow therapeutic index, consider monitoring for therapeutic effect (e.g., for warfarin) or drug concentration (e.g., for cyclosporine) and consider dosage modification of the CYP450 substrate.
Biologic drugs and malignancy: A literature review examining the impact of concomitant immunosuppressive medications

Bernardo S, Harcharik S, Keeley B, Pan M, Lebwohl M
Biologics and Malignancy

- 64.8% of reports occurred in patients treated with other immunosuppressive medication

- Mtx, Azathioprine, Corticosteroids, 6MP

- 3.21x more deaths reported w/ combination Rx

Bernardo S, et al
Frequency of Monotherapy Versus Combination Therapy in Reported Cases of Infections Occurring in the Setting of Biologic Agents


Most opportunistic infections occur in patients who are also treated in combination with other immunosuppressive agents
Combining systemic retinoids with biologic agents for moderate to severe psoriasis.

Smith EC, Riddle C, Menter MA, Lebwohl M

Adalimumab plus narrowband ultraviolet B light phototherapy for the treatment of moderate to severe psoriasis.

Bagel J

Use of apremilast in combination with other therapies for treatment of chronic plaque psoriasis: A retrospective study.

AbuHilal M, Walsh S, Shear N.


- Effective
- Persistent benefit 8 w. p. stopping
- CsA side effects
Treatment of atopic eczema with oral mycophenolate mofetil.

• 10 patients
• 1 g/d x 1w
• 2 g/d x 11 w
• SCORAD ↓ 68%
Successful treatment of severe atopic dermatitis with methotrexate.
Balasubramaniam P, Ilchyshyn A. 
The use of azathioprine in severe adult atopic eczema.
Buckley DA, Baldwin P, Rogers S.

- 0.7-2.5 mg/kg/d. x 1 yr.
- 8/10 marked improvement
- 1 lymphoma
Combination Therapy for AD

Long-term Use of Systemic Treatments for Moderate-to-Severe Atopic Dermatitis in Adults: A Monocentric Retrospective Study.

Védie AL, et al

Data regarding systemic therapies in the management of atopic dermatitis are limited. The aim of this study was to provide evidence for the efficacy and tolerance of systemic immunosuppressive treatments for moderate-to-severe adult atopic dermatitis. A single-centre retrospective study was conducted. A total of 54 patients were prescribed systemic treatments between 2000 and 2014. Of these, 28 received methotrexate and 55.6% were considered as responders based on Physician's Global Assessment, 17 received azathioprine (37.5% responders), 43 received cyclosporin A (65.9% responders) and 7 received a combination therapy with methotrexate and azathioprine (57.1% responders). These treatments were well-tolerated overall and few adverse events required discontinuation of treatment. Combination therapy associating methotrexate and azathioprine appears to be a promising treatment for patients who fail to respond to conventional monotherapies.

PMID: 26925822 DOI: 10.2340/00015555-2389
Dupilumab Phase 2b Study: Mean Percent Change In EASI at Week 16 (LOCF†)

EASI: Eczema and Severity Index; LOCF: last observation carried forward; q2w: every 2 weeks; q4w: every 4 weeks.


†LOCF imputation method for missing data and patients who received rescue medications.
• What do I do for the patient who has failed everything?
• Insurance won’t let my patient get the drug he/she needs. What can I do?
• How fast do psoriasis treatments work?
National Psoriasis Foundation
Leah McCormick Howard
Health Policy Manager
Lhoward@psoriasis.org
(503) 546-5553
AAD Practice Management Center
Office of Access to Care and Treatment
Rachna Chaudhari

www.aad.org/priorauth
Prior Authorization Assistance Center

Reduce burden and improve access

The Academy has created several resources to reduce administrative burden and help your patients gain access to medications, including:

- Easily create prior-authorization letters to help your patients get the medication approvals they need from insurers.
- Practical tips to help you and your staff navigate prior authorization issues.
- COMING SOON! A help hotline for members. One-on-one help provided by the Academy's expert staff — complimentary for a limited time!

Prior authorization requires providers to obtain advance approval before performing a service to qualify for payment coverage. Prior authorization for medications usually involve brand-name products for which there is no generic equivalent, or a drug that a patient has taken for years but for which the insurance carrier now requires annual re-authorization.

Most physicians consider prior authorization to be an expensive and time-consuming process that questions their clinical judgment and siphons resources away from patient care. Even more concerning are the treatment delays and negative patient health outcomes that can be caused by prior authorization.

Common prior authorization drugs

In early 2016 the AAO sent surveys to a total of 208 AAO members and 300 Association of Dermatology Administrators & Managers (ADAM) members. Survey recipients were requested to forward the survey to those responsible for completing prior authorizations in their practices. A total of 72 AAO members and another 136 members of ADAM
Prior Authorization Letter Tool

Prior Authorization
Drug Denial Letter Template

Complete the following steps to create an individualized letter appealing a denial for a prescribed treatment for your patient.
Prior Authorization Letter Tool
Prior Authorization Letter Tool

Insurance Information

Name of medical director
Medical director

Insurance company name
Insurance company name

Insurance company address
Insurance company street address

Insurance company city, state, zip
City
State
Zip

PREVIOUS NEXT
Prior Authorization Letter Tool

**PATIENT INFORMATION**

Step 3 of 4

**Patient name**

Patient name

**Patient health insurance identification number**

Patient health insurance identification number

**Patient date of birth**

Patient date of birth

**Date of prior authorization**

Date of prior authorization

**I have previously prescribed this patient the following therapies**

- Name of medication
  - Start date
  - End date
- List reason for stopping medication

**ADD ITEM**

PREVIOUS NEXT
Prior Authorization Letter Tool

**TEMPLATE COMPLETE**

Click the button below to download your prior-authorization letter template.

[DOWNLOAD DOCUMENT]

[START OVER] [PREVIOUS] [NEXT]
Prior Authorization Letter Tool

2/16/2017

Mark G. Liebowitz, MD, FAPAD
S E 88th St
New York, NY 10029

Dr. Jon Doe
National Medical Director
BCBS
3234 Anywhere Lane
Chicago, IL 60607

Re: Denial of prior authorization for
Maggie Simpson 1234
02/12/2016

Dear Dr. Jon Doe,

I am contacting you as a board-certified dermatologist caring for Maggie Simpson with regard to the patient’s diagnosis of Psoriasis Vulgaris (L40.0).

I recently prescribed this patient Embedel, which required a prior authorization that was denied on 02/06/2017. The prior authorization was denied and the patient was unable to fill their prescription.

I have reviewed the patient’s diagnosis, case plan and clinical guidelines for treatment and provide a reason for the denial for Embedel.

When treating a patient with Psoriasis Vulgaris (L40.0) it is necessary to have access to the full spectrum of accepted treatments as patients may not be able to use one particular treatment due to lack of response, the potential for side effects or even an allergic reaction. It can become a serious safety issue for the patient if I am not able to prescribe a wide variety of treatments for this condition.

I have previously prescribed this patient the following therapies:

- Humira from 01/02/2017 to 02/01/2017. The patient had an adverse reaction to this medication, which included adverse reaction.

- I strongly believe Maggie Simpson needs access to Embedel. Embedel is not only an approved and effective treatment for psoriasis and psoriatic arthritis, but it has been shown in numerous studies to improve cardiovascular comorbidities of psoriasis.

My patient is not a good candidate for your suggested alternatives for the following reasons:

- Humira has been associated with an increase in malignancies, particularly skin cancers, and it’s therefore not an ideal therapy in patients with a history of malignancy, especially skin cancers.

- Humira has been associated with an increase in anti-nuclear antibodies and can cause drug-induced lupus.

Remicade is only available by intravenous infusion and is not a practical treatment for this patient because it requires visits to an infusion center that is not easily accessible to the patient. Remicade has been associated with an increase in malignancies, particularly skin cancers, and is therefore not an ideal therapy in patients with a history of malignancy, especially skin cancers. It has also been associated with respiratory tract cancers in smokers. Remicade has been associated with an increase in anti-nuclear antibodies and can cause drug-induced lupus.

Additionally, I request that you review the following evidence showing how this medication can be effectively utilized to treat Psoriasis Vulgaris (L40.0):


On behalf of Maggie Simpson, I would appreciate your prompt reconsideration of this denial. Please feel free to contact me at 1 847 240 1856 for any additional information you may require. I look forward to receiving your response and approval of coverage for this medication.

Sincerely,

Mark G. Liebowitz, MD, FAPAD
• What do I do for the patient who has failed everything?
• Insurance won’t let my patient get the drug he/she needs. What can I do?
• How fast do psoriasis treatments work?
PASI Score % Improvement

Mean % Improvement From Baseline
Placebo/ETNCPT25BIW
ETNCPT25QW
ETNCPT25BIW
ETNCPT50BIW

*P = 0.003 vs placebo
†P = 0.001 vs placebo
‡P < 0.0001 vs placebo
Mean Percentage PASI Improvement

† P<0.001 Adalimumab vs. methotrexate. Note: ITT: patients with missing PASI scores last observation carried forward

‡ p<0.02 Adalimumab vs placebo; *p<0.001 Adalimumab vs placebo

Presented in part at 15th Congress of the EADV, Oct. 4-8, 2006, Rhodes, Greece
Infliximab in Psoriasis (N=33)

Mean PASI Score Through Week 10

Mean Percent Improvement in PASI Through Week 40

PHOENIX 1

Mean Percent Improvement in PASI Through Week 40

- Placebo
- Placebo / Ustekinumab 45 mg
- Placebo / Ustekinumab 90 mg
- Ustekinumab 45 mg
- Ustekinumab 90 mg
300 mg Reduces Mean PASI by 50% at Week 3

Weeks of Treatment

% improvement in PASI score

Secukinumab 300 mg (n=323)
Secukinumab 150 mg (n=327)
Etanercept (n=323)
Secukinumab sustained high response rates through 52 Weeks

*Primary endpoint; grey arrows indicate peak response

![Graph showing PASI 75 response](image)

<table>
<thead>
<tr>
<th>Number of evaluable subjects</th>
<th>Responders (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEK 300 mg (n=323&lt;sup&gt;a&lt;/sup&gt;)</td>
<td>80, 90, 100</td>
</tr>
<tr>
<td>SEK 150 mg (n=327&lt;sup&gt;a&lt;/sup&gt;)</td>
<td>70, 80, 90</td>
</tr>
<tr>
<td>PBO (n=324&lt;sup&gt;a&lt;/sup&gt;)</td>
<td>60, 70, 80</td>
</tr>
</tbody>
</table>

<sup>a</sup>Number of evaluable subjects

Langley R, et al. EADV 2013: FC01.3.
PASI 75 Response Rates (NRI) by Visit During the Induction Phase

Adjusted p-values < .001 for comparisons between brodalumab groups against placebo at week 12
Adjusted p-value = .078 for comparison between brodalumab 210 mg against ustekinumab at week 12; nominal p-value < .001
Speed of Response, Ixekizumab
Induction Period (UNCOVER-1, -2, and -3)

ETN=Etanercept; IXE Q2W=80 mg of Ixekizumab Every 2 Weeks; IXE Q4W=80 mg of Ixekizumab Every 4 Weeks; MMRM=Mixed Effect Model Repeat Measurement; PASI=Psoriasis Area and Severity Index; PBO=Placebo.
Figure 2. Time Course of Clinical Responses as Measured by the Psoriasis Area-and-Severity Index (PASI) and Static Physician’s Global Assessment (sPGA) through 20 Weeks, According to Study Group.

Shown are the percentages of patients who had reduction in the PASI score by at least 75% (Panel A), at least 90% (Panel B), and 100% (Panel C), respectively. Panel D shows the percentage of patients who had an sPGA score of 0 (clear of disease) or 1 (minimal disease). Asterisks indicate significant differences ($P<0.05$) between each study group and placebo. Missing data were imputed by the last-observation-carried-forward method. Similar results were found with the use of nonresponse imputation (data not shown).