Psoriasis: Shaping the Future Through Advanced Therapeutic Strategies

The Payer’s Perspective

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Learning Objectives
Presentation Overview

• Psoriasis background and disease state review
• Comorbidities associated with psoriasis
• Guideline-based approaches to diagnosis and management of psoriasis
• Diagnosing and managing the patient with psoriasis
• Biologic treatments for psoriasis
• New and emerging treatments for psoriasis
• Payer approaches to psoriasis treatments

Psoriasis Disease State Review
Epidemiology

Psoriasis

- 7.5 million people afflicted
- Most common autoimmune disease in the U.S.
- Large unmet therapeutic need
- Patient survey (Lebwohl et al. 2014):
  - 46% feel that therapies worse than disease itself
  - 85% state that there is need for better therapies


Epidemiology

- Plaque psoriasis represents about 85-90% of the cases
- 2/3 of patients have mild to moderate disease
- 1/3 have more severe presentation

Distribution of psoriasis severity

- Severe: 8%
- Moderate: 25%
- Mild: 65%
- Mild*: 2%

*current phototherapy or systemic medication

Source: National Psoriasis Foundation (random sample of 278 adults with psoriasis)
Clinical Features

- Psoriasis can present at virtually any age.
- Most common age groups are 20-30 and 50-60 years.
- Plaque psoriasis is driven by inflammation and altered keratinocyte differentiation.

Papp, KA et al, *British J Dermatol* 2013 168(2) 412-421

Psoriasis has a Genetic Risk

First and second degree relatives
- One parent affected - 14%
- Both parents - 41%
- One sibling - 6%
- No parent or sibling affected - 2%
Making the Diagnosis

• Plaque psoriasis can usually be diagnosed by physical exam of the skin, nails, and scalp
• Rarely, as skin biopsy is needed
• Differential diagnosis considerations:
  o Lichen Planus
  o Pityriasis Rosea
  o Tinea Corporis
  o Seborrheic Dermatitis
• Labs and other diagnostics are usually not required except as a pre-requisite to biologic or immunosuppressive treatment.

Associated Co-morbidities

• Psoriasis patients are more likely to have associated co-morbidities including:
  o Cardiovascular disease
  o Psoriatic Arthritis
  o Depression
  o Obesity
  o Diabetes
  o Hypertension
  o Cancer
• 58% more likely to have a major cardiac event
• 43% more likely to have a CVA

National Psoriasis Foundation: https://www.psoriasis.org/about-psoriasis/related-conditions
Psoriasis Types

<table>
<thead>
<tr>
<th>Types of psoriasis</th>
<th>Scalp:</th>
<th>Guttate:</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Affects the scalp (other parts of the body may or may not be affected).</td>
<td>Affects trunk/forehead, face.</td>
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<tr>
<td></td>
<td>Affects 5% of people with psoriasis.</td>
<td>Text as red or scaly as plaque psoriasis and looks like ‘droplets’ on the skin.</td>
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<td>Smooth, dry and well-defined salmon-coloured patches.</td>
<td>Affects up to 10% of people with psoriasis.</td>
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<td></td>
<td>Not known how many people it affects.</td>
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<tr>
<td>Inverse:</td>
<td>Affects under the breast, groin, armpits and where the skin folds.</td>
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<tr>
<td>Erythrodermic:</td>
<td>Affects entire body surface.</td>
<td>Affects less than 1% of people with psoriasis.</td>
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<td></td>
<td>Involves whole body surface, which scales and itches.</td>
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<td></td>
<td>Affects 1%–5% of people with psoriasis.</td>
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<tr>
<td>Nails:</td>
<td>Affects fingernails, toenails.</td>
<td>Plaque:</td>
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<tr>
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<td>Nails may become pitted, discoloured, thickened and loose.</td>
<td>Affects knees, elbows, lower back, ears, scalp.</td>
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<td>Affects 10–50% of people with psoriasis.</td>
<td>Real plaques surrounded by white silvery scales, which can be itchy and sore.</td>
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Psoriasis Pathophysiology
Psoriasis is an Inflammatory Disease

Pathophysiology
Immunologic Factors

- Significant reduction in the number and percentage of CD4+ T cells in the peripheral blood, whereas they are found throughout the skin lesions.
- Dendritic cells present an unknown antigen to CD4+ cells within the skin, leading to T-cell activation.
- Fibroblasts have an increased proliferative activity and the capability to secrete increased amounts of IL-1, IL-6, and platelet-derived growth factors.
- Increased levels of leukotriene B4.

Role of Cytokines

- Interferon-gamma
- TNF-alpha
- IL-1, IL-2, IL-6, IL-8, IL-12, IL-15, IL-17 (A to F), IL-18, IL-19, IL-20, IL-21, IL-22, IL-23

Adapted from Goldsmith et al. Fitzpatrick's Dermatology in General Medicine. 8e, 2014, McGraw-Hill.
Psoriasis Treatments

Psoriasis Treatment Challenges

- Patients present with a broad spectrum of symptoms and severity
- A variety of treatment options are available and must be tailored to the patient needs

In general, psoriasis can be classified as:

- **Mild**: only a few patches, less than 3% of the skin surface.
- **Moderate**: 3% to 10% of the skin surface.
- **Severe**: more than 10% of the skin surface.

Goals of Therapy

- Gain initial rapid control of the disease
- Maintain the patient in long-term remission and avoid relapse
- Avoid adverse effects as much as possible
- Improve the patient’s quality of life

National Psoriasis Foundation:

Traditional Treatment

Traditional Treatment Paradigm

**Process:**
- Psoriasis therapy follows a stepwise progression
- Patients must fail the previous “step” of therapy before initiating a more “aggressive” therapy

**Systemic Therapy**
- Cyclosporine
- Methotrexate
- Soriatane
- Systemic steroids

**PhotoTherapy**
- UVB Broadband
- UVB Narrowband
- PUVA
- Laser

**Rx Topical Agents**
- Topical steroids
- Vitamin D analogs
- Topical retinoids
- Other Rx topicals

**OTC Products**
- Emollients
- Other

**Order of Treatment Progression**

PUVA = Psoralen + ultraviolet light A, UVB = Ultraviolet light B
Severity-based Treatment

Source: American Academy of Family Physicians
http://www.aafp.org/afp/2013/0501/p628.html

Non-Biologic Systemic Therapy

- Apremilast (first approved in March 2014 for treatment of active psoriatic arthritis)
- Phosphodiesterase-4 (PDE4) inhibitor that is specific for cAMP, resulting in increased intracellular cAMP levels
- Apremilast was approved for plaque psoriasis in September 2014

http://mauiderm.com/psoriasis-update-current-therapies/
Biologics for Psoriasis

- Biologics approved for treatment of psoriasis include
  - Etanercept
  - Adalimumab
  - Infliximab
  - Ustekinumab
  - Secukinumab
  - Ixekizumab

Etanercept (anti TNF)

- Indicated adults with chronic moderate to severe plaque psoriasis.
- Standard dosing:
  - Subcutaneous injection of 50 mg twice weekly for the initial three months of therapy
  - Followed by a 50 mg injection once weekly for maintenance therapy
Adalimumab (anti TNF)

- Indicated for treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy.
- Standard dosing for adults:
  - Initial subcutaneous injection of 80 mg
  - 40 mg given every other week, beginning one week after the initial dose.

Infliximab (anti TNF)

- Indicated for moderate to severe plaque psoriasis
- Standard dosing for infliximab for adults is intravenous infusion of 5 mg/kg at weeks 0, 2, and 6, followed by every eight weeks thereafter.
Ustekinumab (anti IL-12, 23)

- Indicated for moderate to severe plaque psoriasis
- Dosing of ustekinumab is weight-based.
- Standard dosing for ustekinumab for adults ≤100 kg is 45 mg given at weeks 0, 4, and every 12 weeks thereafter.
- A 90 mg dose given in the same regimen is recommended for adults who weigh more than 100 kg.

Secukinumab (anti IL-17A)

- Indicated for moderate to severe plaque psoriasis
- Initial dosing 300 mg. SC at weeks 0,1,2,3,4
- Maintenance at week 8 = 300 mg. monthly
- 150 mg. may be acceptable in some patients
- FIXTURE = superior to etanercept
- CLEAR = superior to ustekinumab
Ixekizumab (anti-IL 17A)

- Approved March 2016
- Indicated for moderate to severe plaque psoriasis
- Dosing:
  - Week 0: 160 mg SC (i.e., as two 80-mg injections), THEN
  - 80 mg SC q2wks at weeks 2, 4, 6, 8, 10, and 12, THEN
  - 80 mg SC q4wks
- UNCOVER 2, 3: superior to etanercept

Source: Griffiths et al., Lancet, Vol 386, No. 9993, p541–551, 8 August 2015

Treatment: Safety Considerations

- Do not start or continue anti-TNF therapy in patients with serious active infection; use caution in those at high risk of infection
- Screen all patients for infection with mycobacteria, human immunodeficiency virus (HIV), hepatitis B (HBV), and hepatitis C (HCV) before starting anti-TNF therapy
- Consider prophylactic vaccination for tuberculosis and HBV in high-risk patients before initiating anti-TNF therapy
Treatment: Safety Considerations

- In patients with HIV, HBV, or HCV, initiate anti-TNF therapy only in those with well-controlled disease
- Avoid anti-TNF treatment in patients with a current or previous history of malignancy,
  - Unless there is a high likelihood of cure or the malignancy was diagnosed and treated more than 10 years ago
- Regularly screen for skin cancers in patients who are receiving anti-TNF therapy
- Discontinue anti-TNF therapy prior to pregnancy
  - Restart anti-TNF treatment following the end of lactation or delivery if the mother is not breastfeeding
Payer Challenges

**Specialty Drug Management Is Posing Multiple Challenges for Health Plans**

- **Increased Utilization**
  - Specialty drug pipeline continues to grow
  - Increase in oral specialty drugs
  - New indications for existing therapies
  - Use of specialty drugs earlier in disease course

- **Clinical Guidelines**
  - Lack of widely accepted guidelines, resulting in variations in care
  - Lack of data demonstrating best practices in managing diseases

- **Outcomes Data**
  - Lack of data analyzing specialty drug utilization
  - Lack of comparative effectiveness data assessing efficacy, costs, outcomes, and safety

Reference: Health Strategies Group, Health Plan Pharmacy Management Trends March 2013

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**Payer Challenges**

- Treatment of inflammatory conditions including psoriasis is the largest category of specialty spending.
- According to ESI, inflammatory conditions was the most expensive specialty therapy class for the sixth year in a row.
- Per-member-per-year (PMPY) spend was $80.03 in 2014, up 25% from 2013.

**Medications for inflammatory conditions and multiple sclerosis topped specialty drug spending in 2014**

Payer Challenges

- It is still about the right therapy for the right patient while being fiscally responsible.

Management strategies include:
- Step therapy through non-biological immunomodifiers before biologicals.
- Prior authorization of biological agents
- Preferred biological agents
- Limited prescribing of biologicals to appropriate specialists
- Guideline-based management
- Managing site of service

Payer Challenges: Adherence to Therapy

Reasons for Medication Non-Adherence

https://rxoutcomesadviser.wordpress.com/author/healthoutcomesadviser/
Payer Challenges

Other payer strategies in 2015 and beyond:
- Newer benefit designs
- Multiple tiers of specialty benefit
- Consideration of the emerging biosimilar marketplace
- Specialty specific formularies
- Alignment of patient incentives

And things will get more complicated. . .

Payer Challenges—Biologic Pipeline

In the Pipeline (only a few)
- Briakinumab: an injectable anti-inflammatory (IL-12/-23 blocker).
- Brodalumab—IL-17 blocker
- AMG 827—IL-17 blocker
- Guselkumab—Anti IL-23p19
- Tildrakizumab—Anti IL-23p19
- BI655066—Anti IL-23
Questions