AMCP Market Insights

Psoriasis Summit Webinar

May 8, 2018

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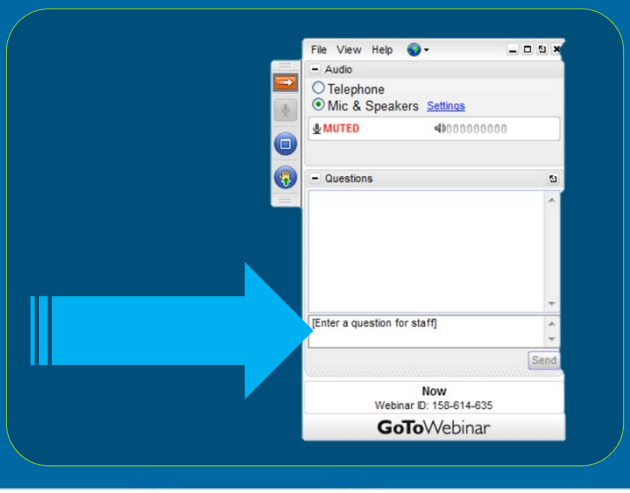
How to Ask Questions



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WELCOME

Terry Richardson, PharmD, BCACP
Director, Product Development, AMCP

Dana Regan
AMCP Market Insight Moderator
SVP, The Access Group

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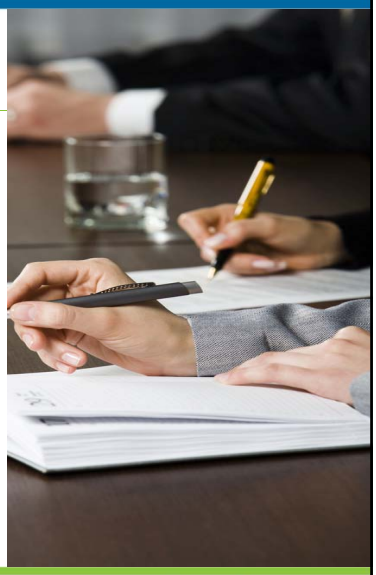
AMCP Market Insights

AMCP program designed to engage members on relevant topics

- Blinded format enables payers to participate in disease condition specific market research
- Multi-disciplinary market research enables manufacturers to gain clinical and payer guidance on specific topics
- Provides AMCP with strategic information regarding pipeline and member needs, gaps, etc.



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Disease Summit Platform

Disease Summits

Multi-disciplinary live meetings on a single disease state, not individual product

- Evening and full day session – First evening: disease state trends / pipeline – Full Day: Provider and Payer Panel discussions followed by workshops on key issues and challenges
- Sponsors may submit recommended speakers and questions for discussion and workshops
- Sponsors also sponsor dissemination of findings through JMCP outsert and AMCP webinar

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Objectives of Market Insights

01 Provide AMCP members relevant information regarding current and future treatments for psoriasis

02 Provide members information regarding category management of psoriasis treatment options

03 Identify impact of new entrants for treating psoriasis

04 Identify opportunities for payer/provider collaboration

Market Insights: Psoriasis Summit

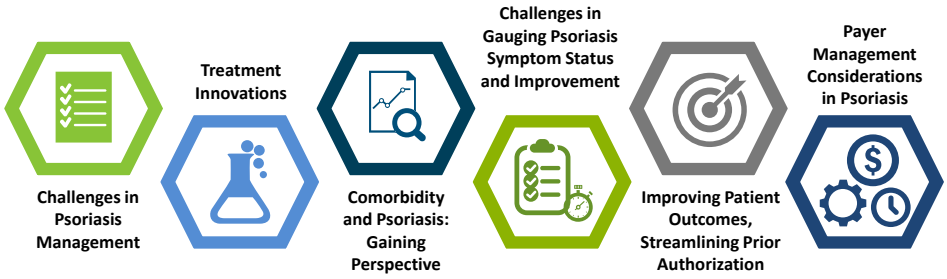
On December 14-15, 2017, an AMCP Market Insights Summit was held in Arlington, VA

13 Participants from around the US

- Medical directors
- Pharmacy directors/clinical pharmacists
- Key opinion leaders

Reviewed the marketplace but focused on the current state of management of psoriasis treatments, pipeline, challenges and solutions

Insights Gathering Process



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Diagnosis & Treatment Considerations Psoriasis

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Current Challenges

- Existing guidelines do not help clarify use of various approved biologics
- Frequently updates from professional societies (e.g., AAD) needed to keep up:
  - New medications
  - Biosimilar approvals
  - Changes in prescribing perspectives (i.e., comorbid disease and risk)

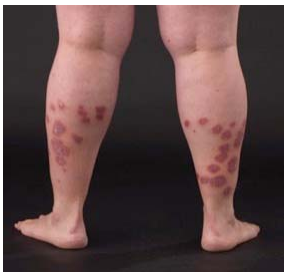
The standards of care in psoriasis management are changing

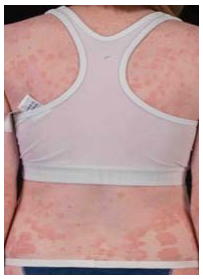
Measuring psoriasis severity/improvement

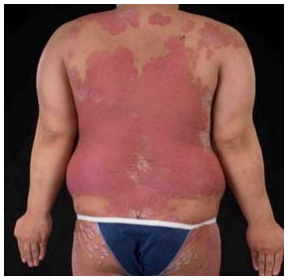
- Historically, PASI, BSA
- Since 1999 – PGA and PASI

- Good measures require
  - **TRUTH** (do they ***reflect true severity***?)
  - **DISCRIMINATION** (***can you tell*** mild from severe?)
  - **FEASIBILITY** (***can*** the provider do it?)

PASI, PGA vs BSA





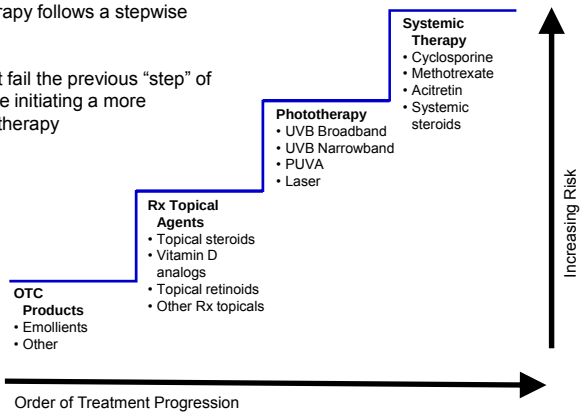


Mild-moderate	moderate	severe
PASI: 4.2	PASI: 10.8	PASI: 18.4
PGA: 2-3	PGA: 2-3	PGA: 3-4
BSA: 4%	BSA: 18%	BSA: 32%
BSAxPGA: 4x3=12	BSAxPGA: 18x2=36	BSAxPGA: 32x4=128

Traditional Treatment Paradigm

Process:

- Psoriasis therapy follows a stepwise progression
- Patients must fail the previous "step" of therapy before initiating a more "aggressive" therapy

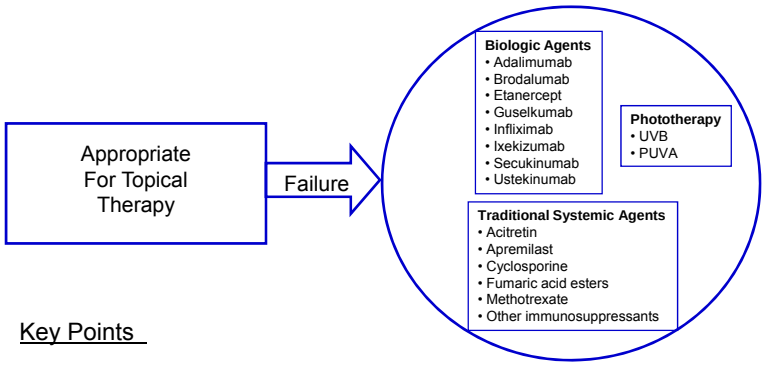


Shifts in Treatment

Traditional Thinking:
"Just a skin disease"

New Thinking:
"A systemic disease"

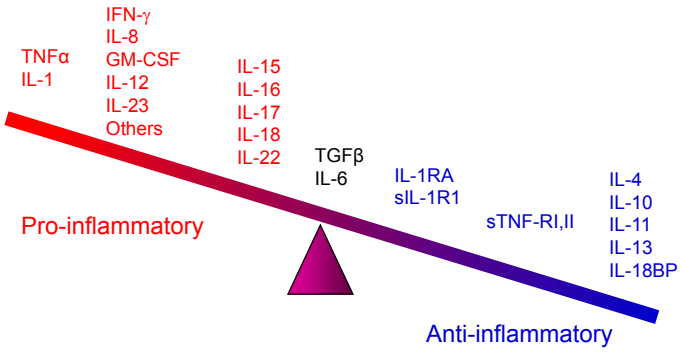
Emerging Treatment Paradigm



Key Points

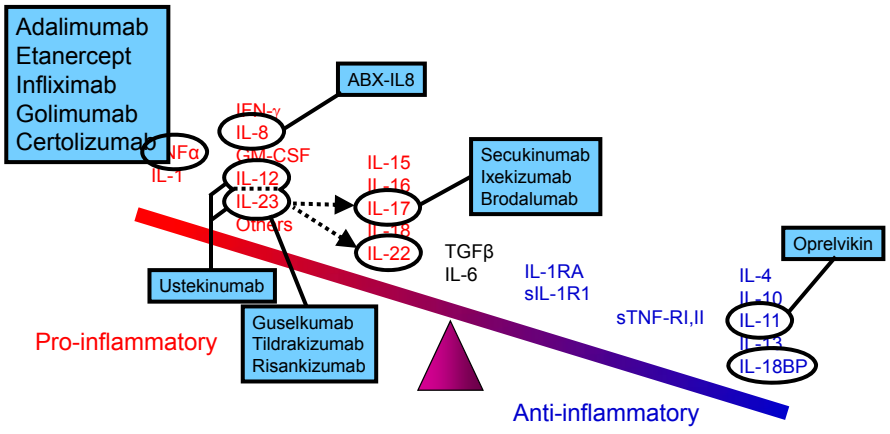
- Psoriasis treatment is not stepwise
- Choice of therapy depends on individual patient characteristics

Cytokines and Cytokine Inhibitors in Chronic Inflammation



Adapted from: Nickoloff BJ, Qin JZ, Nestle FO. Clin Rev Allergy Immunol. 2007 Oct;33(1-2):45-56.
Guttman-Yassky E, Krueger JG. Br J Dermatol. 2007 Dec;157(6):1103-15.
Lowes MA, Bowcock AM, Krueger JG. Nature. 2007 Feb 22;445(7130):866-73.

Cytokines and Cytokine Inhibitors in Chronic Inflammation



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Specialty medications approved to treat plaque psoriasis

Nonproprietary Name	Brand Name	Year Approved	Drug Class	Comments
Etanercept	Enbrel	1998	TNF-alpha inhibitor (FC Fusion Protein)	Only 50% of patients reach a PASI 75 response after 12 weeks, but also very effective for psoriatic arthritis; biosimilar approved in 2016 but not yet available TNF inhibitors are associated with reduced CV risk
Infliximab	Remicade	1998	TNF-alpha inhibitor	IV infusion, not attractive route; 80% reach PASI 75 by week 10; loses effectiveness after 1 yr; administered with MTX; **2 biosimilars now available (Inflectra and Renflexis)**
Adalimumab	Humira	2002	TNF-alpha inhibitor	Most commonly prescribed; 68% reach PASI 75 at wk 16; also effective in PsA (has widest range of indications as well); one of the better durations of effect for the biologic category
Apremilast	Otezla	2014	PDE-4 Inhibitor	An oral medication; approximately 30% reach PASI 75 at wk 12; may be most useful in patients with mild-to-moderate symptoms
Ustekinumab	Stelara	2009	Interleukin 12/23 inhibitor	Excellent duration of effect (5 yr); 67% reach PASI 75 by wk 16; excellent safety profile, but weight-based dosing is disadvantage
Secukinumab	Cosentyx	2015	Interleukin 17A inhibitor	80% reach PASI 75 by wk 12; 40% reach PASI 100. Head-to-head evidence vs. Stelara and Enbrel. Rapid improvement (in as little as 2 wk) noted anecdotally. Injection site reactions common
Ixekizumab	Taltz	2016	Interleukin 17A inhibitor	50% reached PASI 100 by wk 16. Injection site reactions common. Do not give in patients with IBD
Brodalumab	Siliq	2017	Interleukin 17 receptor A inhibitor	37% reached PASI 100 after 1 yr. 4 suicides in clinical trials (REMS program to address); only biologic that requires use of other available therapies first
Guselkumab	Tremfya	2017	Interleukin 23 inhibitor	75% received PASI 90/100 scores; good safety profile

Number Needed to Treat to Reach PASI Outcomes

Drug	NNT for PASI 75	NNT for PASI 90	NNT for PASI 100	Comment
Apremilast	3.6	--	--	ESTEEM 1[29]
Methotrexate	3.2	5.6	25	METOP[30]
Etanercept	2.2	4.8	23.3	50 mg BIW
Adalimumab	1.6	2.3	5.3	40 mg EOW
Ustekinumab	1.6	2.9	9.2	90 mg
Infliximab	1.4	2.2	4.1	5 mg/kg IV
Brodalumab	1.3	1.5	2.7	210 mg
Secukinumab	1.3	1.7	3.6	300 mg
Guselkumab	1.2	1.4	2.6	VOYAGE 1[31]
Ixekizumab	1.1	1.4	2.4	Uncover 2[32]

Note: Highlighting indicates the lowest NNT for each PASI improvement.
Sources: Craig Leonardi, M.D., St. Louis, MO; US FDA Package Inserts or Phase 3 Trials; NNT Calculator: http://clincalc.com/Stats/NNT.aspx?example.

The near-term specialty pipeline for psoriasis

- Certolizumab nearing approval for psoriasis indication
- Tildrakizumab is a humanized antibody targeting IL-23
- Risankizumab is an IL-23 inhibitor with recent phase 3 results
- Biosimilars approved for adalimumab, etanercept, and infliximab
  - Patent litigation delaying availability (adalimumab, etanercept)
  - Limited use in clinical practice for psoriasis (infliximab)

Comorbidities of Psoriasis

- Heart attack, stroke, CV death
- Metabolic syndrome (obesity, insulin resistance, cholesterol abnormalities, hypertension)
- Diabetes
- Psoriatic arthritis
- Mood disorders (anxiety, depression, suicide)
- Crohn's disease
- T cell lymphoma (rare)
- Decreased QoL

Gelfand JM, et al. *JAMA.* 2006; 296:1735 Gelfand JM et al. JID 2006; 126:2194-201 Langan SM, et al. *J Invest Derm.* 2012; 132:556. Kurd SK Arch Derm 2010;146:891-5 Armstrong AW, et al. *J Hypertens.* 2013; 31:433. Ma C, et al. *Br J Dermatol.* 2013; 168:486. Azfar RS, et al. *Arch Dermatol.* 2012; 148:995. Li W, et al. *Am J Epidemiol.* 2013; 175:402 Yeung H et al. JAMA Derm 2013;149:1173-9 Mehta NN, et al. *Eur. Heart J.* 2010; 31:1000 Najarian DJ and Gottlieb AB JAAD 2003;48:805-21

Biologic Selection Criteria for Patients With Other Comorbidities

- **Patients with PsO and PsA**
  - Adalimumab, etanercept, and infliximab
  - IL-17 inhibitors
  - Ustekinumab (esp, if PsO is severe and PsA is mild)
- **Patients with PsO and multiple sclerosis**
  - Ustekinumab (an IL-12/23 inhibitor)
  - IL-17 inhibitors
  - *Avoid all TNF inhibitors*
- **Patients with PsO and CHF**
  - Ustekinumab
  - IL-17 inhibitors
  - *Avoid all TNF inhibitors in NYHA class 3 or 4 CHF and use with caution in NYHA class 1 or 2 CHF*
- **Patients with PsO and IBD**
  - Adalimumab, infliximab, ustekinumab
  - Etanercept
  - *Use secukinumab and ixkizumab cautiously in patients with IBD. Avoid brodalimumab in patients with Crohn's disease*
- **Patients with PsO and Hep B**
  - Ustekinumab
  - IL-17 inhibitors
  - TNF inhibitors

Amin M, No DJ, Egeberg A, Wu JJ. Choosing first-line biologic treatment for moderate-to-severe psoriasis: What does the evidence say? Am J Clin Dermatol. 2018;19:1-13.

Challenges to Overcome

- Patient expectations and satisfaction
  - Outside of complete resolution, each patient's interpretation of successful treatment may vary
- Evidence-based guidelines need to be updated
  - Last AAD guidelines updates 10 years ago
  - Updates need to be made frequently, to reflect innovation in treatments
- What is the treatment target?
  - PASI 75 or 90
  - Symptom clearance is possible for most patients taking interleukin-17 or -23 inhibitors

PAYER MANAGEMENT

Payer Management

Review of payer approaches to management

- Indication based formulary
- Assessment of new products
- View into future

IDN approach to psoriasis protocols

Payer challenges and opportunities

Formulary Management of Psoriasis Medications

- P&T Committee review for safety/efficacy and therapeutic equivalence
  - Prior authorization criteria
- Formulary Committee review for cost considerations
  - AWP/WAC
  - Cost after manufacturer rebates

Commercial	Part D	Medicaid
• **Steps 1-2** – 2 of the following: • TNF1 • TNF 2 • IL antagonist • Oral	• **Ste** **wing:** • IL antagonist • Oral	• **Steps 1-2** – 2 of the following: • TNF 2 • IL antagonist • Oral

EXAMPLE

Prior Authorization Criteria: New Entrant

Therapeutic Designation: Equivalent

Prior Authorization – NEW

- **Indication:** Diagnosis of moderate to severe plaque psoriasis (per FDA approved indication)
  - BSA covering ≥10% (5% for Part D) OR psoriatic lesions affecting hands, feet, or genital area
  - Trial of (or candidate for) conventional agents: PUVA, UVB, acitretin, methotrexate
  - 18 years of age or older
  - Prescribed by or in consultation with a dermatologist
  - **Duration:** 6 months (initial), 12 months (renewal)
  - **Renewal:** PASI 50+ (Commercial only); physician attestation (Part D)
- **Step Therapy (in PA):** Trial of up to 2 preferred immunomodulator(s)
  - A. Up to 2 TNF blockers, **OR**
  - B. TNF blocker + non-TNF biologic (IL-antagonist), **OR**
  - C. TNF blocker + oral agent (PDE-4 inhibitor), **OR**
  - D. Up to 2 non-TNF immunomodulators

  *No more than 2 step agents for Part D
- **Quantity Limit (in PA):** per FDA approved dosing
- **Rationale:** per FDA labeling and aligned with other biologic guidelines

Planning for the Future

NEW TREATMENT OPTIONS

- New agents that are demonstrating higher efficacy don't have utilization that promotes price competition

BIOSIMILARS

- Biosimilars for adalimumab, etanercept have been approved by the FDA, but when will they come to market
- Anticipate price drop on these agents
  - Participants noted must be >20%
- Formulary positioning of TNFs:
  - Now vs the future?

PBM Ask of Clinicians

1. Help manage the Prescription Benefit from a cost perspective and use treatment progression before jumping to Biologics
2. Develop specific treatment algorithms that incorporate most effective therapy, outcomes and costs to treat
3. Utilize preferred products first, if appropriate, can save Rx Benefit dollars
4. Assess patient's progress and agree to change therapy if there is little improvement
5. Acknowledge when to stop therapy
6. Be aware of the Depression/Anxiety these Patients have with Psoriasis

Protocol Example – IDN Process

- Collaboration between Pharmacy, Device/Diagnostic, and Therapeutic Committee and employed Dermatologists
- Desire was to reconcile earlier demand for biological in treatment course and existing formulary management
- Approach:
  - Specific to Psoriasis, a clinical pathway was developed in consideration of our unique cost structure
    - Integrated Specialty Rx and Infusion Center with 340b pricing
  - Preferred formulary includes pathway
    - 1) TNF
    - 2) IL antagonist
    - 3) IL 23 options

IDN Example – PA Requirements

- Prior authorization occurs in medical groups and patients are referred to hospital services for ongoing management
  - Basic topical and oral therapies have no barrier to use
  - Phototherapy step edit, often in lieu of systemic oral therapy
  - Pictures of psoriasis must be taken during office visit and uploaded into EMR for second opinion on biologic initiation (auditing)

Workgroups Addressed Challenges and Potential Solutions

- Lack of Accepted Treatment Algorithms/Guidelines
- Assimilating Payer Coverage Concepts into New Guidelines
- Patient Variability in Presentation and Response
- Lack of Objective, Standardized, Clinical Practice Markers of Severity and Measures of Response
- Affordability of Drugs and Effect on Access: Patients
- Overall High Cost of Category
- Affordability of Drugs
- High-Deductible Plan Designs
- Lack of Accepted Treatment Limited Awareness of Drug Costs by Prescribers/Patients
- Coordination of PA and Lack of Documentation for the PA
- Alignment of Incentives/Contracting Restrictions
- Contracts Tied to Other Autoimmune Disease States
- Education Regarding Psoriasis Comorbidities and Patient Complexity
- Access to Specialists
- Value of Incremental Benefits (eg. PASI 90 vs. PASI 100)/Understanding Patient Expectations
- Investing in Biologic Therapies When Membership Duration Can Be Brief

A Summary of the Psoriasis Management Challenges

Lack of current treatment guidelines/treatment algorithms and integration of newer agents

Legacy contracts for auto-immune category

Lack of consensus on which disease severity assessment tool is most useful in practice

Lack of real-time provider/ payer engagement

Leading Recommendations: Guidelines

GUIDELINE RECOMMENDATIONS:

1. Define efficacy measures and treatment goals
   - PASI, BSA, PGA
   - Treat to Target
2. Define treatment algorithm based upon patient co-morbidities
3. Define treatment based upon current treatment post DMARD
   - Biologic naive
   - Biologic intolerant
   - Biologic treatment failure
4. Define time to effect
5. Define when to stop/switch treatment
6. Address patient tolerability and acceptance

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Leading Opportunities: Contracting

RE-EVALUATE CONTRACT

1. Pharma rebate structure impacts flexibility
2. Redefine Market Basket
   - Oral
   - New agents with limited indications
3. Indication/MOA based contracts
4. VBC/P4P approach
5. Ability to shift market share

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Leading Recommendation: Education

EDUCATION FOR PROVIDERS AND MEMBERS

1. Interface of cost information (e.g., First DataBank) with EMR, to illustrate the relative cost of medications ($$$ symbols), based on WAC and considering patient cost sharing based on plan policies
2. Utilize "relative cost symbols" in EMR; provide cost information to members
3. Provide clearer policy information to members as to what medical/pharmaceutical benefit interventions may count/not count towards the deductible

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Leading Recommendation: Real-time Communication

Provider Approach | **Payer Approach**

Treatment ineffective	Lack of adherence
Patient dosing needs	Dose creep
Efficacy established within 12-16 weeks	Re-assess annually

Payer and Provider collaboration can aid in optimal patient care

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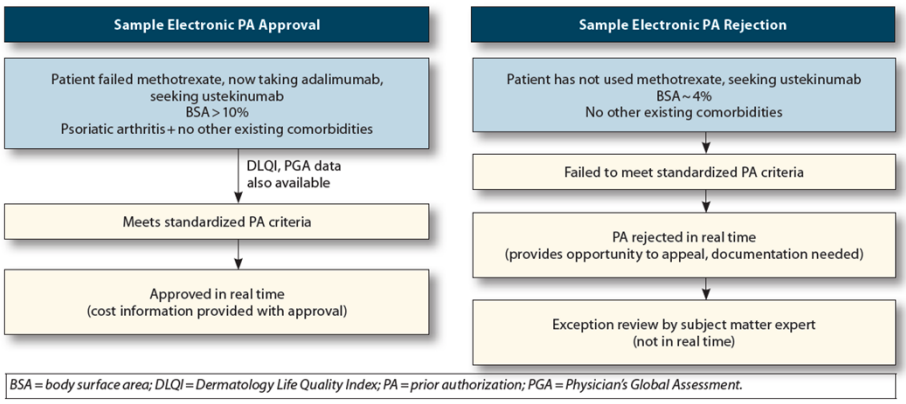
E-PA Process for Real Time Review

Figure 2. Simplified Algorithm for Potential Electronic PA to Evaluate a Nonpreferred Drug Choice in Psoriasis



BSA = body surface area; DLQI = Dermatology Life Quality Index; PA = prior authorization; PGA = Physician's Global Assessment.

Additional Challenges and Potential Solutions

Challenge	Solution
Access to Specialists	Greater use of telemedicine to gain access to specialists (but not yet covered by all plans in all geographic locations that could benefit most); need more consistent funding mechanisms to expand telemedicine use
Value of Incremental Benefits (eg. PASI 90 vs. PASI 100)/ Understanding Patient Expectations	• Better use of DLQI, tied to clinical ratings • Better understanding of which outcomes matter to patients • Educational efforts to raise provider awareness of analyses like NNT • Drug cost transparency

Market Insights: Psoriasis Summit

Market Insights Summary

- Double Blinded Summit Meeting
- Manufacturer Sponsored dissemination
  - Published outsert in JMCP
  - Webinar

MARKET INSIGHTS

Summit on Psoriasis

Findings from the AMCP Market Insights Program

Introduction

Psoriasis and Its Effect on Serious Complications: Mounting Evidence

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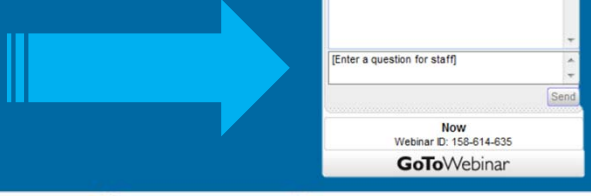
Reminder: How to Ask Questions



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