Finding ways to manage specialty pharmacy costs and ensuring patient access continues to be a critical concern of pharmacy executives in the payer environment. Biologics used for multiple indications (e.g., rheumatoid arthritis, psoriatic arthritis, psoriasis, inflammatory bowel disease) have been available for more than 15 years, and significant questions exist not only about the utility of the older agents but also the latest-generation biologics, and their appropriate place in treatment for any one of these autoimmune disorders. Several agents are in late-stage trials, and since the time of this meeting, a new biologic agent (ixekizumab) and a biosimilar medication (infliximab-dyyb) have been approved by the Food and Drug Administration, adding a new layer of complexity to the treatment and reimbursement of diseases like psoriasis.

On October 27, 2015, the Academy of Managed Care Pharmacy hosted its inaugural Market Insight Forum, which engaged members of the Academy (i.e., payers) in an environment of learning and discussion on the management and treatment of psoriasis. The objectives for this Market Insight Forum were to:

1. Provide attending AMCP members relevant information regarding current and future treatments for moderate-to-severe psoriasis
2. Provide members information regarding category management of psoriasis treatment options
3. Identify future member needs in the development of Phase 4 and health economic and outcomes research studies
4. Share best practices among AMCP members in the management of members with psoriasis

With this summary report, AMCP hopes to disseminate the key learnings of the Forum to other AMCP members and to other professionals involved in care, management, and policy decision making for psoriasis products.
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Psoriasis is a highly variable disease that presents in both limited areas of the body but also in widespread lesions. Patients may experience flare-ups of this chronic disease, manifested by a full range of mild, moderate, or severe symptoms.

Dr. Leonardi said that conventional treatments are prescribed in a manner that starts with over-the-counter medicines and move in a step-wise manner through phototherapy and systemic medications like retinoids, methotrexate, and cyclosporine, used alone, or tried in short, sequential courses. Topical medicines (e.g., calcipotriene, halobetasol, tazarotene) are often used concomitantly with systemic treatments, in a manner that optimizes efficacy but limits exposure to the well-known risks associated with both the systemic and topical agents (Figure 1).

Both patients and physicians are unsatisfied with conventional therapy, according to Dr. Leonardi—physicians, because the treatments have varying effectiveness and may require monitoring or other methods of risk avoidance; and patients, because these treatments may not work rapidly, have limited efficacy in a proportion of psoriasis patients, may not be well tolerated, and may be inconvenient to use.

In the last 20 years, the perspective on psoriasis has changed from that of a primary skin disorder to one of an immunologic disease. Many of the agents being used today and under investigation target individual immunologic cytokines, and there are a multitude of targets (Figure 2).

Conventional agents like methotrexate and cyclosporine address immunologic factors, but the first generation of biologics to target these anomalies were the T-cell inhibitors. Alefacept and efalizumab, Dr. Leonardi pointed out, like, were withdrawn from the market for lack of efficacy or serious adverse effects. The second-generation agents, however, were more accepted because of their effectiveness and relative safety profile. They comprised the TNF-alpha inhibitors, such as adalimumab, certolizumab, etanercept, infliximab, and golimumab. Subsequent third-generation agents targeted...
interleukins (IL):

- Ustekinumab targets interleukin-12 and -23.
- Secukinumab and ixekizumab are IL-17 targeted monoclonal antibodies
- Investigational medications guselkumab, tildrakizumab, and BI 655066 target interleukin-23 exclusively

Novel small-molecule medications have also been approved for use in psoriasis: apremilast, a PDE4 inhibitor, and tofacitinib, a JAK inhibitor.

With this degree in choice of therapies for moderate-to-severe psoriasis, it can be difficult to decide which may be most appropriate, based on efficacy and safety. All of the biologics used today are associated with at least some serious adverse effects, and clinicians should discuss these in detail with patients in determining the best treatment option. The Food and Drug Administration (FDA) historically used a Psoriasis Area and Severity Index (PASI) of 75, meaning that the intervention improves the score by 75% (after 12 wk) for its clinical trials. Dr. Leonardi showed evidence that PASI-75 scores do differ among modern psoriasis treatments, even among the TNF-alpha inhibitors (for which efficacy in other autoimmune disorders is deemed largely equivalent). Apremilast seems to achieve the lowest PASI-75 scores at 12 weeks (about one-third of patients achieved PASI-75), whereas secukinumab and ixekizumab, 2 IL-17 inhibitors (ixekizumab was approved by the FDA after the meeting, on March 22, 2016) achieve excellent PASI-75 scores (both in the 80% to 90% range). These IL-17 inhibitors also demonstrated excellent PASI-90 effectiveness—approximately 70% of the patients in phase 3 studies reached this milestone. Nearly 40% attained PASI-100 at 12 weeks with either IL-17 drug. Secukinumab is associated with serious but nonfatal infections in 6% of patients; mild-to-moderate adverse events were commonly reported. In patients taking ixekizumab, only 2% of patients experienced nonfatal serious adverse events, and 26% experienced any adverse event.

The investigational drugs guselkumab, tildrakizumab, and BI 655066 demonstrated PASI-75 scores in the 65% to 87% range, depending on dose, in phase 2 studies. Guselkumab also was associated with some serious infections and cardiovascular events.

One tool that is helpful in making coverage and treatment decisions is the calculation of number needed to treat (NNT)—the average number of patients who need to be treated to achieve one additional good outcome. Whereas the NNT figures to reach a PASI 75 outcome for older biologics are good, there is room for improvement, Dr. Leonardi emphasized, especially in attempting greater clearance. He stated that the newer treatments, like IL-17 biologic agents, are capable of obtaining PASI-90 or even PASI-100 scores in significant portions of patients. Table 1 demonstrates that on an NNT basis, the ability to reach 90% or even 100% clearance is now possible, even though as recently as the year 2000, this didn’t seem a realistic goal, said Dr. Leonardi. “It may be time to rethink our goals in psoriasis care,” he stated. Therefore, Dr. Leonardi believes that setting the clinical trial bar very high (i.e., PASI 90 or PASI 100) is appropriate based on our capabilities today.

He also pointed out that the stepwise progression in psoriasis treatment is being replaced with general paradigm that emphasizes topical therapy first, followed by any of the other available treatments, dependent on patient characteristics.

Table 1. Number Of Patients With Psoriasis Needed to Treat to Reach Various PASI Levels by Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>PASI 75</th>
<th>PASI 90</th>
<th>PASI 100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alefacept</td>
<td>6.3</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>6.0</td>
<td>43.5</td>
<td>—</td>
</tr>
<tr>
<td>Apremilast</td>
<td>3.6</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Efalizumab</td>
<td>2.7</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Etanercept</td>
<td>2.2</td>
<td>4.8</td>
<td>23.3</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>1.6</td>
<td>—</td>
<td>5.3</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>1.6</td>
<td>2.9</td>
<td>9.2</td>
</tr>
<tr>
<td>Infliximab</td>
<td>1.4</td>
<td>2.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>1.3</td>
<td>1.7</td>
<td>4.1</td>
</tr>
<tr>
<td>Ixekizumab</td>
<td>1.2</td>
<td>1.4</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Payers’ Comments. Although psoriasis is generally considered a disorder with moderate to severe clinical implications for the patient, it is not a high priority disease state for payers. They do not typically case manage patients with psoriasis, unless they have significant health resource utilization.

The participating AMCP members indicated that they have little reason to view the disease, or its treatments, differently than other autoimmune diseases. Some plans will separate psoriasis treatments as a separate formulary.
Focus on Psoriasis

category, but in this panel, this was not the norm. However, the attendees appreciated the fact that different agents have varying levels of efficacy in psoriasis, as compared with rheumatoid arthritis or other autoimmune disorders; this may be the basis for considering psoriasis separately. One pharmacist offered that the organization recently implemented an exclusive biologic contract for psoriasis treatment with ustekinumab based on its effectiveness in treating psoriasis.

They emphasized the value of the NNT data presented by Dr. Leonardi. This is accepted as a practical and convincing measure of the relative efficacy of this complex medication category. The payers in attendance found that the relationship between psoriasis and comorbidities, including cardiovascular disease, depression, and obesity/metabolic syndrome, is well founded. Although it would seem logical that improving a patient’s psoriasis symptoms would have a positive effect on depression and other comorbidities, available information to confirm this assumption seems limited.

Overall, the payers were impressed with the pipeline for psoriasis. They believed that they will offer physicians even more useful choices. From a plan view, the addition of the IL-17 inhibitors can be a challenge, as these products are relatively new and plans will have to develop a contract strategy as new products (e.g., the IL-23 inhibitors) are approved. Furthermore, they may have existing contracts with biologics manufacturers that cover all applicable autoimmune indications, meaning that step therapy may be required regardless of indication.

Defining Outcomes in Psoriasis

A report of a presentation by Kristina Callis Duffin MD, MS, Associate Professor, Dermatology, University of Utah, Salt Lake City, Utah

In many cases, payers will develop utilization management criteria based on FDA-approved indications and phase 3 trial data, which may not reflect real-world practice or physician experience. As a result, there can be a disconnect between physician diagnosis and assessment of psoriasis, and payers’ approach to coverage and utilization management of biologic therapies. This is also easy to understand from another standpoint, said Dr. Callis Duffin, because moderate-to-severe psoriasis has many phenotypic features, and patients often demonstrate overlapping phenotypes. The variability in lesion type, severity, location, comorbidities of the presenting patient, and patient preference must be considered in the choice of therapy—this is a true case of no-one-size-fits-all, commented Dr. Callis Duffin. Furthermore, the criteria for patient enrollment and outcomes in clinical trials of psoriasis medications often do not align with how community-based physicians evaluate patients and make treatment selections. For example, the inclusion criteria for clinical trials of most biologic agents to treat psoriasis include a body surface area (BSA) of ≥ 10%, and a PASI of ≥ 12 (PASI scores range from 0 to 72). These ratings are rarely used by community-based dermatologists, she emphasized. Also, clinical trials often exclude patients who have other major medical issues, she explained. Another important difference is that patient-reported outcomes play a role in nearly every clinical trial, but they play a very limited role in payer coverage decision making.

To expand on this disconnect, Dr. Callis Duffin stated that community-based dermatologists rarely use PASI or physician global assessment (PGA) scores in practice (although the PGA is sometimes preferred). “To perform the PASI, the investigator scores the plaque qualities and area for the head and neck, the upper extremities, the trunk (which includes the axillae and groin), and lower extremities, which includes the buttocks,” she said. Erythema, scale, and induration are each scored 0 to 4 for the area of the body being evaluated, then summed, then multiplied by an area score and a weighting multiplier. This allows weighting of the area involved; in other words, since the head and neck make up 10% of the total body area, its score makes up only 10% of the total PASI when it is multiplied by 0.1. Dr. Callis Duffin also pointed out that patients with severe psoriasis in specific areas (consider

Use topical therapy first, then any of the other available treatments, dependent on patient characteristics.
palmar-plantar disease, which may account for only 2% of the total BSA) are poorly represented in these assessments. She admitted that the PASI is time consuming and not clinically meaningful to most, and the PGA score is not considered accurate or to differentiate disease severity.

**AN ALTERNATIVE, STRAIGHTFORWARD OFFICE ASSESSMENT TOOL**

She suggested another option—the product of the PGA and the body surface area (PGA × BSA), may be a more practical and useful option for in-office assessment. In a study of the treatment of patients with apremilast, her team compared PGA × BSA to PASI and found good correlation for disease extent and severity (Figure 3).

Although quality of life and other patient-reported outcomes are not as important in coverage decisions by US payers, a useful way of measuring a patient’s quality of life would still be valuable in evaluating the holistic effect of therapy. Currently, the 16-item psoriasis symptom diary and the 8-item psoriasis symptom inventory are the key patient-reported outcomes scales used to measure local and global symptoms. In terms of quality of life, the 10-question dermatology quality-of-life index (DLQI) has shown to correlate with symptoms improvement, and the DLQI has been used in clinical trials as an outcome measure (e.g., percentage of patients achieving a “normative” DLQI score of 0 or 1), according to Dr. Callis Duffin. Not specific to psoriasis, the Short-Form 36 (SF-36) and EuroQol five-dimensional (EQ-5D) questionnaires have also been used. Several biologic therapies have been shown to improve not only PASI and PGA scores, but also patient-reported outcomes.

Productivity is another consideration that does not figure greatly into coverage decision making for payers but is of greater importance to employers. Productivity includes absenteeism, presenteeism, productivity loss, and overall impairment outside of work activities. Dr. Callis Duffin pointed to a placebo-controlled study of ixekizumab that yielded significant improvements in these measures of productivity.

In Dr. Callis Duffin’s practice, she processes as much information
as possible from the patient, and prints out a list of
treatment options (“not only what I think would be
their best options, but also is weighted to what I think
I can get them based on their insurance”). This process
involves weighing benefits, likelihood of clearance, risks,
monitoring, and costs. The goals are skin clearance,
sustainable improvement, convenient therapy, safety,
tolerability, and affordability.

She pointed out that the general knowledge of the
implications of treating psoriasis today are akin to that
decades ago with chronic disorders like hypertension and
diabetes: We have tools to improve disease status but we
don’t generally accept the importance of tight control.
In fact, Dr. Callis Duffin emphasized, tight control of
psoriasis turns out to be very important. Controlling this
autoimmune disease can prevent future joint destruction,
and treating psoriatic disease effectively (e.g., with
methotrexate and anti-TNF agents) reduces the risk of
cardiovascular disease. She recognized, however, that a
good algorithm for treating patients is still lacking, and
that patients who fail one anti-TNF inhibitor may well fail
another. Can we identify patients who will do better with
one biologic class versus another?

**Payers’ Comments.** The managed care professionals in
attendance acknowledged their awareness of psoriasis as
an autoimmune disorder, but were less up-to-date with the
effectiveness of currently available or pipeline products.
They also mentioned that it is challenging to measure
success or failure in psoriasis, since there is no way for
payers to directly monitor the patient.

One payer challenge is that without widely accepted and
utilized algorithms, prior authorization requirements are
defaulted to the clinical trial inclusion criteria. For example,
some patients with palmar-plantar psoriasis will have a BSA
< 10%, which would disqualify them under standard prior
authorization criteria from receiving biologic therapy, even
though it may be appropriate treatment. Physicians must
then write appeals, with photos, to convince the plan to
overturn the rejection.

Another issue related to the lack of guidelines is the
question of how long therapy with one biologic should
be tried before moving on to another agent of the same
class or to another category of biologic. This is particularly
important to plans who may have contracts where auto-
immune product use requires step therapy before newer
agents are available for use.

The managed care professionals also acknowledged the
correlation between efficacy and improved quality of life.
They expressed interest in the DLQI, and how these scores
improved reduction as well as PASI improvement, but

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**Tight control of psoriasis turns out to be very important. Controlling this autoimmune disease can prevent future joint destruction.**

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were less intrigued with other patient-reported outcomes
(such as productivity). They believed that patient-reported
outcomes may be more important in the context of the
physician office visit.

One outcomes measure that did not have much sway
with the attendees is data on presenteeism and absenteeism.
It is of limited interest to payers, but is of greater importance
to self-employed, union groups, and employers, who may see
the improvement in workplace productivity as a real value
of including these therapies on formulary. The pharmacists
noted a common issue among small employers: Although
the treatment may be effective, the cost of the biologic
exceeds the salary of many workers; in fact, disability may be
the lower-cost option for an employer.

A key topic among payers, across categories, is
the impact of biosimilars for biologic treatments. The
probability of biosimilar introductions (i.e., for anti-TNF
agents) raised the question of their effectiveness, their
similarity to the original branded (or reference) agent, and
when they might see cost savings through the utilization of
biosimilars (relative to rebates from original product). The
managed care professionals added that switching studies
between the reference and biosimilar product will play an
important role in helping to decide what is “appropriate
use”. Another issue related to biosimilars is how reference
manufacturers’ coupon programs and promotion activities
will be affected by their introduction. Whereas biosimilars
seem to be cost effective, there are many variables that
payers need to consider.●
A review of millions of patients with regard to Medicare and commercial formulary trends in the psoriasis indication revealed fairly consistent coverage information, said Dr. Palmgren. All six of the medications analyzed (secukinumab, etanercept, adalimumab, apremilast, infliximab, and ustekinumab) were generally covered by commercial plans and PBMs, ranging from 80% to 100% (adalimumab and etanercept were fully covered in this survey).

He noted that at the time of the meeting, secukinumab (with a psoriasis indication) had already garnered 35% access to plans (generally tier 3 in 3-tier plans), whereas adalimumab and etanercept were holding the preferred brand positions (39% for etanercept, 55% for adalimumab). Before accessing secukinumab, health plans commonly require a single step through either etanercept (Enbrel) or adalimumab (Humira). [Editor’s Note: at the time of the meeting, a large percentage of health plans and insurers likely had not yet evaluated secukinumab in their P&T Committees. This would account for the frequency of higher tier placement].

In stark comparison, Medicare part D and Medicare Advantage plans list all of these products mostly on tier 5, with adalimumab and etanercept sometimes being assigned to tier 4. He pointed out that he has begun to see 6 formulary tiers for some Medicare lives. The tier count is expanded through the use of 3 generic tiers (preferred, non-preferred, and "select" for high-cost generic injectables, for example), and 3 branded tiers. “People are still surprised when I tell them that some Medicare Advantage plans still use only 2 tiers,” he stated.

For commercial plans, said Dr. Palmgren, 5-tier formularies are still rare. He added that despite apremilast's lower efficacy rating in psoriasis, most plans still offer it, "perhaps because they consider it less expensive, and maybe it would be good to try first.”

Dr. Palmgren explained that due to the multiple autoimmune disease indications of several biologic agents, coverage of psoriasis is not usually regarded as separate for contracting purposes: It is commonly included in the market basket of other biologics. However, ustekinumab, a biologic whose sole indications are plaque psoriasis and psoriatic arthritis, some plans choose to separate the psoriasis biologic category, naming ustekinumab as the preferred agent.

If payers begin to consider psoriasis separate from other autoimmune categories, then it might sense to allow faster access than the double step edit allows.

Payers’ Comments. The payer participants noted that they may use a double step edit, because although autoimmune biologics/anti-TNF drugs may not be the most effective in psoriasis, the relatively benign nature of psoriasis means that 2 anti-TNF biologic step edit can be tried and be found to work well for some: “The additional time needed for 2 drug trials will not cause patients additional harm.” However, they believed that the approach to anti-TNF agents, “TNF cycling,” used in rheumatoid arthritis, may not really be appropriate in psoriasis, because unlike in the former, not all of the agents are equally efficacious in psoriasis. If, on the other hand, payers begin to consider psoriasis separate from other autoimmune categories because of the differential efficacy with the use of IL-17 products, for instance, then it might sense to allow faster access than the double step edit allows.

Both clinical presenters and payers discussed the possibility of limiting treatment options, such as allowing one TNF-alpha inhibitor, one other biologic, and an IL-17 agent instead of allowing open access to all products. The panel recommended a consensus approach between physicians and payers to define the parameters regarding treatment failure and time to switch.

With a competitive field of biologic agents to treat psoriasis, the pharmacists expressed interest in outcomes-based contracting, i.e., paying for anticipated positive outcomes or receiving rebates for medication failures.

The attendees acknowledged that the use of quantity limits for these agents is common, though these are not intended as restricting access. Rather, the use of quantity limits, they said, was mainly to ensure appropriate dosing, and reducing wastage in case patients could not tolerate the medicine.
Workshop Group Discussions

The pharmacist participants were divided into two workgroups to tackle individually questions regarding current and future treatments, as well as future studies in psoriasis that provide value to the payer.

Differentiation Among Products

When asked to what extent currently available agents (including the interleukin, TNF-alpha, and PDE-4 inhibitors) were meeting the goals of therapy, the two workgroups were in general agreement. Based on the evidence presented and their knowledge of the currently available drug categories, they believe that secukinumab, the IL-17A inhibitor, was rated highest, noting not only its general efficacy but the existence of long-term safety data. The product rated lowest was apremilast, the PDE-4 agent, on the basis of its limited efficacy in psoriasis, followed by etanercept, also based on a lower level of efficacy in psoriasis. Ratings for the other agents were positive but undifferentiated.

The payers also thought that, of the investigational medications, ixekizumab seemed to offer a great deal of potential, based on the evidence presented (including NNT calculations), for improving the care of patients with psoriasis.

Most Important Psoriasis Evaluation Criteria for Payers

The workshop groups were asked to rank by importance to payers a broad selection of clinical and economic outcomes associated with psoriasis care. Concordance was strongest between groups for reduction in symptoms, speed of onset, and route of administration and dosing being of lesser importance (Table 2) and of PASI 75, an estimate of number needed to treat, and cost of therapy being of greater importance. The greatest disagreement between the workgroups involved the PASI 100 ratings. One group considered this a critical differentiator. The other group acknowledged its importance but considered PASI 100 an unrealistic goal for the general population of patients.

The workshop groups were asked for recommendations as for phase 4 and observational studies they would like to see for approved products, investigational biologics, and psoriasis assessment scales. The workgroups based their recommendations on the types of data needed to make formulary decisions as well as the types of study endpoints that would be of most use to their organizations. Table 3 summarizes their responses, arranged by medications or assessment being evaluated, study type, and endpoints.

An overriding theme of these recommendations was the need for comparative-effectiveness studies (i.e., head-to-head evaluations). Several studies were requested to help plans and insurers better understand the relevance of the psoriasis assessments discussed, with a highlight on the possible use of the physicians...
Time to switch, duration of efficacy, and frequency of switches will help payers understand differences among treatment options.

global assessment × body surface area measure (presented by Dr. Callis-Duffin), tested in a real-world setting.

The workshop groups identified time to switch, duration of efficacy, and frequency of switches as important information that will help payers understand differences among treatment options. These endpoints are not frequently evaluated in clinical studies but they can provide valuable additional information regarding the utility of various therapies, and the data can sometimes be captured through claims. Furthermore, real-world information about patient discontinuations and switching can have implications for quantity limits and avoidance of drug wastage.
AMCP Market Insights

AMCP also offers a new program, Market Insights. This is a one day multi-disciplinary program integrating AMCP members with KOLs and practicing clinicians in the discussion regarding patient management of a disease state or condition. The focus of the program is to address the needs of AMCP members - disease and utilization management - such as psoriasis in this issue. This program provides the sponsor(s) the opportunity to provide education regarding current and pipeline treatments and understand the AMCP members’ approaches to category and disease management.

AMCP Market Insights is a blinded market research program, sponsored by AMCP corporate sponsors, (who also remain blinded to the participants), allowing an unbiased and objective approach to the content and program. Future programs are identified through AMCP member and corporate sponsor interest.

Please contact Charlie Dragovich at cdragovich@amcp.org for additional information regarding future Market Insights programs.