DEFY THE LAWS OF PSORIASIS

RESULTS WITH JUST A FEW DOSES
- With **just 2 doses** at Week 12, 64% and 61% achieved PASI 75 (reSURFACE 1 and reSURFACE 2, respectively) vs placebo: 6% and 6% (reSURFACE 1 and reSURFACE 2, respectively).
- With **just 3 doses** at Week 28, 74% and 70% achieved PASI 75 (reSURFACE 1 and reSURFACE 2, respectively).

RESULTS THROUGH WEEK 64
- **Based on PASI 75 responders at Week 28 (reSURFACE 1)**
  - 84% maintained PASI 75* vs 22% placebo

LIGHTEN THE BURDEN OF FREQUENT DOSING
- **ILUMYA™ is dosed at Weeks 0, 4, and every 12 weeks thereafter**

DURABLE SAFETY PROFILE
- **Through Week 64**, the frequency of adverse reactions was similar to that during the placebo-controlled period of the trial, and no new adverse reactions were identified.

*These endpoints were considered “other” secondary endpoints in reSURFACE 1 and 2. All results based on the recommended 100 mg dose of ILUMYA™.

PASI=Psoriasis Area and Severity Index; PGA=Physician Global Assessment.

reSURFACE 1 and 2 were Phase 3, double-blind, placebo-controlled trials of ILUMYA™ given at Weeks 0, 4, and every 12 weeks thereafter. Patients in reSURFACE 1 (N=463) and reSURFACE 2 (N=463) with moderate-to-severe plaque psoriasis who were candidates for phototherapy or systemic therapy were randomized to ILUMYA™ 100 mg or placebo. At Week 28, patients in reSURFACE 1 initially randomized to ILUMYA™ who achieved at least PASI 75 were re-randomized to either continue initial treatment or to receive placebo up to 64 weeks. The co-primary endpoints of both trials were: 1) the proportion of subjects who achieved at least PASI 75 and 2) the proportion of subjects with a PGA 0 or 1 and at least a 2 point improvement, both at Week 12. Other evaluated outcomes included PASI 90/100 at Week 12 and PASI 75 at Week 28. reSURFACE 1 also measured maintenance of efficacy in responders up to Week 64.

INDICATION
ILUMYA™ (tildrakizumab-asmn) is indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
ILUMYA™ is contraindicated in patients with a previous serious hypersensitivity reaction to tildrakizumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Hypersensitivity
Cases of angioedema and urticaria occurred in ILUMYA™-treated subjects in clinical trials. If a serious allergic reaction occurs, discontinue ILUMYA™ immediately and initiate appropriate therapy.
Infections
ILUMYA™ may increase the risk of infection. Treatment with ILUMYA™ should not be initiated in patients with a clinically important active infection until the infection resolves or is adequately treated. Consider the risks and benefits of treatment prior to prescribing ILUMYA™ in patients with a chronic infection or a history of recurrent infection. Instruct patients receiving ILUMYA™ to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection, or is not responding to standard therapy, closely monitor and consider discontinuation of ILUMYA™ until the infection resolves.

Pretreatment Evaluation for Tuberculosis
Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with ILUMYA™. Do not administer ILUMYA™ to patients with active TB infection. Initiate treatment of latent TB prior to administering ILUMYA™. Consider anti-TB therapy prior to initiation of ILUMYA™ in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving ILUMYA™ should be monitored closely for signs and symptoms of active TB during and after treatment.

Immunizations
Prior to initiating therapy with ILUMYA™, consider completion of all age-appropriate immunizations according to current immunization guidelines. Patients treated with ILUMYA™ should not receive live vaccines.

Adverse Reactions
The most common (≥1%) adverse reactions associated with ILUMYA™ treatment that were more frequent than in the placebo group are upper respiratory infections, injection-site reactions, and diarrhea.

Please see brief summary of Full Prescribing Information on next page or visit ILUMYAPRO.com
**WARNINGS AND PRECAUTIONS**

**Hypersensitivity:** Cases of angioedema and urticaria occurred in ILUMYA-treated subjects in clinical trials. If a serious hypersensitivity reaction occurs, discontinue ILUMYA immediately and initiate appropriate therapy (see Adverse Reactions).

**Infections:** ILUMYA may increase the risk of infection. Although infections were slightly more common in the ILUMYA group (23%), the difference in frequency of infections between the ILUMYA group and the placebo group was less than 1% during the placebo-controlled period. However, subjects with active infections or a history of recurrent infections were not included in clinical trials. Upper respiratory infections occurred more frequently in the ILUMYA group than in the placebo group (see Adverse Reactions).

The rates of treated infections for the ILUMYA group and the placebo group were ≤0.3%. Treatment with ILUMYA should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated.

In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing ILUMYA. Instruct patients to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection or is not responding to standard therapy, monitor the infection and consider discontinuation of ILUMYA until the infection resolves (see Adverse Reactions).

**Pretreatment Evaluation for Tuberculosis:** Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with ILUMYA. Initiate treatment of latent TB prior to administration of ILUMYA. For patients with TB infection, a small increase in the rate of serious adverse events during therapy is expected. ILUMYA should not be initiated in patients with active tuberculosis. Monitor these patients for TB clinical response (see Adverse Reactions). Initiate anti-TB therapy prior to initiation of ILUMYA in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Do not administer ILUMYA to patients with active TB infection.

**Immunizations:** Prior to initiating therapy with ILUMYA, consider completion of all age-appropriate immunizations according to current immunization guidelines. Avoid the use of live vaccines in patients treated with ILUMYA. No data are available on the response to live or inactivated vaccines.

**ADVERSE REACTIONS**

**The following serious adverse reactions are discussed elsewhere in the labeling:**

- **Hypersensitivity Reactions** (see Warnings and Precautions)
- **Infections** (see Warnings and Precautions)

**Clinical Trial Experience**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In clinical trials, a total of 1949 subjects with plaque psoriasis were treated with ILUMYA, of which 1083 subjects were treated with ILUMYA 100 mg. Of these, 672 subjects were exposed for at least 12 months, 587 for 18 months, and 469 for 24 months.

Data from three placebo-controlled trials (Trials 1, 2, and 3) in 705 subjects (mean age 46 years, 71% males, 81% white) were pooled to evaluate the safety of ILUMYA. In the ILUMYA group, of which 1083 subjects were treated with ILUMYA 100 mg. Of these, 672 subjects were exposed for at least 12 months, 587 for 18 months, and 469 for 24 months.

In the placebo-controlled period of Trials 1, 2, and 3 in the 100 mg group, adverse events occurred in 48.2% of subjects in the ILUMYA group compared to 53.8% of subjects in the placebo group. The rates of serious adverse events were 1.4% in the ILUMYA group and 1.7% in the placebo group.

Table 1 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the ILUMYA group than in the placebo group.

**Table 1: Adverse Reactions Occurring in ≥2% of Subjects in the ILUMYA Group and More Frequently than in the Placebo Group in the Plaque Psoriasis Trials 1, 2, and 3**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>ILUMYA 100 mg (N=705) N (%)</th>
<th>Placebo (N=355) N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Upper respiratory infections</strong></td>
<td>98 (14)</td>
<td>41 (12)</td>
</tr>
<tr>
<td><strong>Injection site reactions</strong></td>
<td>24 (3)</td>
<td>7 (2)</td>
</tr>
<tr>
<td><strong>Diarrhea</strong></td>
<td>13 (2)</td>
<td>5 (1)</td>
</tr>
</tbody>
</table>

* Upper respiratory infections include nasopharyngitis, upper respiratory tract infection, viral upper respiratory tract infection, and pharyngitis.
† Injection site reactions include injection site urticaria, pruritus, pain, reaction, erythema, inflammation, edema, swelling, bruising, hematoma, and hemorrage.

During the placebo-controlled period of Trials 1, 2, and 3, adverse reactions that occurred at rates less than 1% but greater than 0.1% in the ILUMYA group and at a higher rate than in the placebo group included dizziness and pain in extremity.

**Specific Adverse Reactions**

**Hypersensitivity**

Cases of angioedema and urticaria occurred in ILUMYA-treated subjects in clinical trials (see Warnings and Precautions).

**Infections**

Infections were slightly more common in the ILUMYA group. The difference in frequency of infections between the ILUMYA group (23%) and the placebo group was less than 1% during the placebo-controlled period. The most common (≥1%) infections were upper respiratory infections. The rates of severe infections for the ILUMYA group and the placebo group were ≤0.3%.

**Safety Through Week 52/64**

Through Week 52 (Trials 1 and 3) and Week 64 (Trial 2), no new adverse reactions were identified with ILUMYA use and the frequency of the adverse reactions was similar to that observed during the placebo-controlled period.

**Immunogenicity**

As with all therapeutic proteins there is the potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of samples, and patient status. The presence of antibodies is not believed to have any clinical significance. For these reasons, comparison of incidence of antibodies to tildrakizumab in the studies described below with the incidences of antibodies in other studies or to other products may be misleading.

Up to Week 64, approximately 6.5% of subjects treated with ILUMYA 100 mg developed antibodies to tildrakizumab. Of the subjects who developed antibodies to tildrakizumab, approximately 40–45% (25.1% of all subjects receiving ILUMYA) had antibodies that were classified as neutralizing. Development of neutralizing antibodies to tildrakizumab was associated with lower serum tildrakizumab concentrations and reduced efficacy.

**DATA INTERACTIONS**

Avoid use of live vaccines in patients treated with ILUMYA (see Warnings and Precautions).

**USE IN SPECIFIC POPULATIONS**

**Pregnancy:** Risk Summary

Limited available data with ILUMYA use in pregnant women are insufficient to inform a drug associated risk of adverse developmental outcomes. Human IgG is known to cross the placental barrier; however, ILUMYA may be transferred from the mother to the fetus. An embryofetal developmental study conducted with tildrakizumab in pregnant monkeys revealed no treatment-related effects on the developing fetus. Administration of tildrakizumab to monkeys during organogenesis resulted in no major adverse effects on fetal development.

**Contraindications**

ILUMYA is contraindicated in patients with a previous serious hypersensitivity reaction to tildrakizumab or to any of the excipients (see Warnings and Precautions).

**INDICATIONS AND USAGE**

**PLR-00015**

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PLR-00015

RX ONLY
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Regulatory Guidance on Biosimilar Development, Plus a Look at the Biosimilar Pipeline

**Eighteen biosimilars have** been licensed by the Food and Drug Administration (FDA) since 2015, seven of which have launched. When submitting a biosimilar to the FDA, manufacturers must show the following:

- Biosimilarity to reference product
- Same mechanism(s) of action (if known)
- Condition(s) for use (i.e., indications) were previously approved for reference product
- Same route, dosage form, and strength
- Manufacturing facility meets standards to ensure safety, purity, and potency

During a presentation at the AMCP Annual Meeting, **Jennifer M. Day, PharmD**, coordinator of emerging therapeutics strategy program at Kaiser Permanente in Downey, California, discussed regulatory and utilization updates for U.S. biosimilars. Former FDA Commissioner Scott Gottlieb, MD, said the agency is focused on advancing policies that make the process of biosimilar development more efficient. The key areas of focus include:

- Improving the efficiency of the biosimilar and interchangeable product development and approval process
- Maximizing scientific and regulatory clarity for the biosimilar product development community
- Supporting market competition by reducing gaming of FDA requirements or other attempts to unfairly delay competition
- Developing effective communications to improve understanding of biosimilars among patients, clinicians, and payers

Since last year, the FDA has released several guidance documents for biosimilars, including information on labeling, licensing, and nonproprietary naming. And since 2013, 45 states and Puerto Rico have passed substitution laws for switching to a biosimilar. They include:

- Must first be FDA-approved as “interchangeable”
- Prescriber may prevent with “no substitutions” on prescription
- Almost all require RPh communication to prescriber
- Many require RPh to retain records
- Many require patients be informed

Per the Bipartisan Budget Act of 2018, biosimilars can be included in coverage gap manufacturer discount program within Medicare Part D. A policy change from the Centers for Medicare & Medicaid Services resulted in lower cost-sharing for low-income Medicare Part D beneficiaries and promotes medication adherence and biosimilar utilization.

Dr. Day then discussed U.S. biosimilar uptake patterns. Filgrastim-sndz launched in September 2015 and currently holds 44.3% of the filgrastim market share,

**Barriers persist surrounding the uptake of biosimilars. Some of the key areas that need improvement are education for clinicians and patients, improved informational materials, interchangeability requirements, health care and public acceptance of these agents, and the ‘nocebo’ effect.**
according to January 2019 IMS Health data. However, in another drug class, despite having two infliximab biosimilar products available, the reference product, Remicade®, continues to hold 93% of the market share.

Barriers persist surrounding the uptake of biosimilars. Some of the key areas that need improvement are education for clinicians and patients, improved informational materials, interchangeability requirements, health care and public acceptance of these agents, and the “nocebo” effect. Other barriers include new competition from reformulated therapies, long-term contracts and rebates for reference products, skinny labels and off-label use of drugs, and patent litigation and settlements for reference products.

She said that in the next 10 years, the market could see biosimilars become available for aflibercept, alemtuzumab, certolizumab pegol, denosumab, eculizumab, golimumab, natalizumab, omalizumab, onabotulinumtoxinA, pantumumab, ranibizumab, tocilizumab, and ustekinumab.

Dr. Day concluded by noting a statistic from the RAND Corporation: “We estimate that biosimilars will lead to a reduction of $54 billion in direct spending on biologic drugs from 2017 to 2026 (range $24 to $150 billion).”


How to Address the Drug Coupon Challenge

The number of drugs with copay cards has soared in the past 10 years, from 75 drugs in 2009 to 700 drugs in 2015. These direct-to-consumer funding programs include manufacturer-provided patient assistance programs (PAPs) and charitable PAPs.

During a presentation at the AMCP Annual Meeting, Josh Golden, area senior vice president of Solid Benefit Guidance in Atlanta, Georgia, and Manual Jayabalan, PharmD, MBA, clinical pharmacist account manager of Magellan Rx Management in Canton, Michigan, discussed different direct-to-consumer payment and management options for payers.

POSTER

Nonadherence, Switching Still a Problem When Treating Psoriasis

Many patients with moderate-to-severe psoriasis are treated with biologics; however, a study found that adherence rates for these treatments were low, and patients were nonpersistent with treatment. The results of the study were presented at the AMCP Annual Meeting during a poster session titled “Biologic and Apremilast Treatment Patterns in Moderate-to-Severe Plaque Psoriasis.”

Researchers queried the IBM® MarketScan® Commercial and Medicare Supplemental databases to identify adult patients with psoriasis who were newly initiating secukinumab, ixekizumab, adalimumab, ustekinumab, etanercept, or apremilast between January 1, 2015, and August 31, 2018. Eligible patients had not previously received the index agent and had no evidence of cancer or HIV over the 12-month pre-index period. Patients also had continuous medical and pharmacy benefits over the 12-month pre-index and 24-month post-index periods.

Over 12-, 18-, and 24-month follow-up periods, the researchers assessed:

- Adherence (proportion of days covered ≥0.8)
- Nonpersistence (no refill within pre-defined gaps for each therapy)
- Discontinuation (no claim for any study medication after a treatment gap)
- Switching (subsequent claim of the index medication after a treatment gap)
- Reinitiation (initiation of a biologic, apremilast, or other systemic medications that is different from the index medication after a treatment gap)

A total of 7,773 patients were included. Over the 24-month follow-up period, adherence to treatment ranged from 21% for etanercept to 33% for secukinumab. Nonpersistence rates ranged from 58% with ustekinumab to 87% with etanercept. Discontinuation rates ranged from 38% with ustekinumab to 51% with adalimumab. Switching rates ranged from 17% with apremilast to 42% with etanercept. Reinitiation rates ranged from 19% with secukinumab to 44% with etanercept. Similar trends were observed for the 12- and 18-month post-index periods, and outcomes were worse with prolonged follow-up.

“Despite many new self-administered therapies with frequent dosing coming to market, there is still a need for new therapies that could offer better adherence through long-term control in an office setting,” the researchers concluded.

The study is limited by its use of a population with commercial or private Medicare supplemental coverage, limiting the generalizability of the outcomes. The study also relied on information from a database, which could have errors.

The study was sponsored by Sun Pharmaceutical Industries, Inc.

Copay cards typically reduce copayment to a specified dollar amount that have monthly or annual caps. These can be distributed in various ways (print, electronic, debit card, and electronic systems for prescribing physicians); however, coupons are prohibited for federal-funded plans, such as Medicare and Medicaid.

The speakers discussed different stakeholder perspectives on these copay cards. For patients, coupons and cards can lower out-of-pocket costs, particularly at a time when cost-sharing is shifting more of the financial responsibility to patients. Patients often learn about coupons from the prescriber or dispensing pharmacy, or directly from the manufacturer.

For manufacturers, multiple studies have shown that coupons increase treatment adherence. In addition, coupons can protect drug market share from competitors. There are also tax advantages for manufacturers, particularly for programs that are managed by charitable foundations.

For plan sponsors, reactions to coupons vary based on the drug and class. Coupons can encourage the use of more expensive brand name products, thus increasing overall costs, as coupons can increase brand drug sales by 60%. These coupons eliminate the financial barriers to off-label or inappropriate use of a product, but they can subvert plan design strategy and undermine formulary tier decisions. Coupons can also contribute to drug cost inflation, as pharmaceutical companies must recover the costs of these cards through wholesale price. Brand drugs with coupons have been shown to have 12% to 13% annual price growth, while drugs without coupons had 7% to 8% annual price growth, according to a report from CNN.

The speakers then laid out the “copay conundrum”: Specialty drugs drive up benefit costs, leading plan sponsors to increase deductibles and coinsurance. Manufacturers then offer coupons to insured patients, and plan sponsors adopt management programs, so manufacturers offer debit cards. For plan sponsors, formulary exclusions, benefit design, and utilization management may need to be employed to manage this situation.

The speakers then discussed accumulator adjustment programs, which “back-out” the value of indirect funding for specialty drugs. Most solutions are automated within the adjudication platform, and these programs are frequently offered at no charge to plan sponsors. Uptake of this solution is increasing, as many pharmacy benefit managers saw a significant increase in program participation in 2018 and 2019. There are challenges to these programs, however, including that they are not feasible in the retail setting and self-filing is difficult. In addition, industry-sponsored debit cards may sidestep these programs. Patients may also be exposed to a midyear cost spike if the coupon value is exhausted (called the “coupon cliff”).

Variable copay programs can also be implemented to maximize the use of available direct-to-consumer funding. Thus, copays may be scaled by product or “tiered” for groups of products. However, uptake of this solution is slow.


Session Puts a Spotlight on Health Care Disruptors and Innovators

Despite its rising level of health care spending, the United States lags behind other countries in many outcomes and quality measures. Much of the U.S. health care costs includes major administrative functions and infrastructure that bring little or no value to the system, some contend.

During a presentation at the AMCP Annual Meeting, Jorge Font, MPH, senior vice president of Precision for Value, LLC, in Sugar Land, Texas, and Elizabeth Oyekan, PharmD, FCSHP, CPHQ, senior director of quality and population health solutions at Precision for Value, LLC, in Centennial, Colorado, discussed innovative and disruptive companies and services that will likely change the health care landscape in the coming decade.

Value-based care has become a key focus in health care, and while preliminary outcomes for disease-specific conditions have shown good results, questions remain as to the overall impact. Thus, more progress is needed, particularly in areas where spending remains high.

The speakers noted that there are different archetypes for health care disruption and innovation:

- Care delivery disruptors
- Technology and big data enablers
- Personalized care enhancers
- Cost trends and access facilitators
They then gave examples for each of these categories: The CVS/Aetna merger is a care delivery disruptor that may reduce cost of care through scale and site of care and integrate data. An example of the technology and big data enablers is health care blockchain, which helps manage clinical trials data and electronic medical records, while maintaining regulatory compliance. Data cannot be changed without leaving a mark, and the complex coded data is highly secure. United Healthcare, Quest, Humana, and Multiplan are participating in a pilot to keep provider directories accurate, while IBM Canada, Kalibrate, and Boehringer Ingelheim are using a blockchain app to complete medical histories in hospitals.

The Amazon, J.P. Morgan Chase & Co., and Berkshire Hathaway Inc., Health Transformation Alliance is an example of access facilitators. These corporations are seeking to create a health system that reduces costs and increases supply chain efficiency, transparency, and consumerism by incorporating innovative technology, operating in a not-for-profit structure, and creating consumer-focused solutions to encourage competition and transparency. Use of biomarkers in cancer is an example of personalized care enhancers. A more personalized approach to cancer diagnosis and care can reduce unnecessary therapies, toxicities, and adverse events, as well as maximize response to and durability of treatment.

Finally, an example of legislative and performance drivers is Medicaid’s use of social determinants of health, including genetics, behavior, and social and environmental factors. This includes addressing housing and community development, job creation, exercise, and education, as well as identifying public health patterns. The Centers for Medicare & Medicaid Services is working with communities to expand their geographic reach, access, and success to provide more cost-effective care.

The speakers concluded by discussing strategies for keeping up with disruptors and innovators: Establish a culture and process for rapid implementation of new endeavors; focus on quality, access, and affordability; pursue partnerships; invest in data analytics and health information technology; and focus on improving access and convenience.

Necessity drives innovation, and there is currently a profound need to improve the efficiency, quality, and cost of the health care system, the speakers concluded.

On the Horizon: The Specialty Pharmacy Pipeline

Specialty medications represent about 1.5% to 2.5% of prescriptions but comprise approximately 50% of total prescription costs. The average cost of a specialty drug is approximately $4,000, and specialty cost inflation has run between 11% of 15%. According to a study, 55% of employer respondents rated drug costs as their top concern, and 71% said they do not feel that the current prices of orphan drugs are sustainable.

During a presentation at the AMCP Annual Meeting, Susan Trieu, PharmD, director of enterprise specialty clinical solutions at MedImpact Healthcare Systems, Inc., in Southlake, Texas, gave an overview of the specialty pharmacy pipeline.

Dr. Trieu said that when considering the budget impact, the following components are important:

- Population
  - What does this new agent offer?
- Market share
  - Will prescribers and patients want the new treatment?
- Are there other viable treatment options that payers will require first?
- Treatment cost
  - Is there anything else to treat this condition?

Other factors to consider include the line of business (commercial, Medicare, Medicaid), size of the plan, whether it’s a genetic disease, regional differences, the need for centers of excellence, and medical versus pharmacy costs.

She then discussed some specialty drugs in the pipeline. An investigational chimeric antigen receptor T-cell therapy, bb2121, is in development for the treatment of relapsed/refractory multiple myeloma. In a phase I study of heavily pretreated patients, there was a 95.5%
overall response rate in the 22 patients who received the highest dose, including a 50% complete response rate. The median progression-free survival was 11.8 months. Many patients (63%) experienced cytokine release syndrome, and 33% of patients experienced neurotoxicity. If approved, this drug may launch in 2020.

Risdiplam is an investigational oral agent for the treatment of spinal muscular atrophy (SMA). In the phase II/III FIREFISH study that included patients with type 1 SMA, 95% (n=20/21) were event-free at 10.5 months. In the phase II/III SUNFISH study that included patients with type 2 and 3 SMA, 63% of patients (n=19/30) had improvement of three or more points in motor function measure at 12 months. No patients have discontinued treatment due to adverse events (AEs). In the FIREFISH trial, 10 patients (48%) had at least one serious AE, and two patients died due to disease progression. In the SUNFISH trial, six patients (11.8%) had at least one serious AE. The sponsors plan on filing 2H in 2020.

Valoctocogene roxaparvovec is an adeno-associated virus-factor VIII vector gene therapy in development for the treatment of adults with severe hemophilia A with no inhibitors. In a phase I/II trial of nine adult patients, the high-dose cohort (n=7) saw increased factor VIII levels, which was maintained one year after infusion. The high-dose cohort had an annualized bleeding rate that decreased from 16 events to one event after the gene transfer. No patients developed inhibitors to factor VIII or thrombosis. Seven patients experienced an increase in alanine aminotransferase levels with resolution. The manufacturer plans to file via accelerated approval this year or next year.

Specialty spend will continue to increase due to a very active pipeline, Dr. Trieu concluded, noting that the impact on payers will vary based on the size of the treatable population and plan.


Best Practices for Navigating Preapproval Information Exchange

Preapproval information exchange is the communication between biopharmaceutical companies and population health decision-makers on topics such as phase III clinical trial data, pharmacoeconomic data, and patient-reported outcomes prior to a product’s approval and launch. This communication can provide benefits to both payers and manufacturers, as plans can more accurately forecast formularies and manufacturers can provide factual, accurate, and nonmisleading information on products or indications that are not yet approved, according to Elisabeth Brisley, MPH, legislative analyst at AMCP, who delivered a presentation on the topic at the AMCP Annual Meeting, along with Amy Duhig, PhD, vice president of consulting services at Xcenda, LLC, in Palm Harbor, Florida, and Sheila M. Thomas, PharmD, global head of patient insights and engagement strategy at Sanofi, Inc, in Bridgewater, New Jersey.

Dr. Duhig discussed the findings of a survey of 47 U.S. payers to gauge their opinion on preapproval information exchange. The survey included 30 questions, and respondents included payers from managed care organizations (66%) and pharmacy benefit managers (26%). More than half (57%) were part of regional plans, and many (62%) were pharmacy directors. Combined, the respondents covered 203 million lives.

The researchers found that the most important types of preapproval information were product pricing information (89%), study results (77%), possible timelines for Food and Drug Administration (FDA) approval/clearance/licensure (77%), and indication information (74%). Some respondents (40%) said the frequency of this type of information has increased, but most (68%) said the quality of the information has remained the same.

Payers reported some gaps in the communication, including topics such as plans for further trials/subgroup analyses, pricing, place in therapy, other indications in pursuit, health resource utilization/outcomes data, dosage strength/product size, and more. Approximately half of those who perceived a proactive information gap said that formulary decision-making could be improved if this gap were closed. Many respondents said the preferred timing of proactive information is six months prior to approval. A majority (93%) said their preferred source of this information is a medical science liaison.

Dr. Thomas then provided outcomes from a survey of 41 U.S. manufacturers to gauge their opinion on preapproval information exchange. The survey included 10 questions, and respondents were from small- to large-sized companies, most (56%) of which conducted health economics and outcomes research. Respondents were split when asked if there was a process in place to deal with preapproval information exchange materials: 37% said yes, while 39% said no, but a process was under development. Most
said they shared information through an account manager (67%) and health economic outcome liaison (60%).

She then discussed best practices for delivering a credible message: “The focus should not be on who but should be on the what and ensuring appropriate skills and competencies of individuals delivering the information.” Dr. Thomas’ tips include:

- Know your audience
- Desirable skills and competencies are similar pre- and post-approval
- Job title will likely vary based on size and structure of manufacturer
- May require a team of individuals with complementary areas of expertise
- Labels of “promotional” versus “nonpromotional” personnel should not limit the ability to communicate
- Individuals should be trained to communicate at the top of their scope of practice

Dr. Thomas said that it is important to stay educated on the latest FDA Final Guidance surrounding this type of communication. Firms should develop and implement a robust internal training plan for communicating this type of material and provide timely updates when information has changed. Lastly, flexibility is a necessity.


How to Manage Generics When They Become Too Costly

There is insufficient competition in the generic drug marketplace, and market consolidation has led to price increases. Because of a lack of appropriate alternatives for these therapies, generic drugs may be expensive. However, shifting utilization to lower-cost alternatives can produce considerable plan savings.

During a presentation at the AMCP Annual Meeting, Sara Carruth, PharmD, manager of health economics and outcomes at MedImpact Healthcare Systems, Inc., in San Diego, California, and Alan Lukazewski, RPh, CDE, CGP, director of clinical pharmacy at NeuGen Health in Madison, Wisconsin, discussed strategies for managing this expense and successfully transitioning patients to lower-cost alternatives.

To manage high-cost generics, payers can increase member cost-sharing for these agents, creating an incentive to switch to lower-cost alternatives. Payers should identify clinically relevant, lower-cost therapies and engage in multichannel communication with the member, prescriber, and pharmacy to discuss alternatives.

When comparing alternatives, plans should consider total drug spend, cost per unit, cost per claim, cost per 30-day supply, and change in cost. To identify lower-cost alternatives, rank the generic drugs by total cost or total plan paid at formulation level and filter for those meeting the pre-defined cost threshold. Then, examine other drugs in the therapeutic class and indication; the costs should also be verified at the individual strength level, as this can differ and may not result in cost savings. However, once a change is made, the dynamic nature of the generic marketplace requires continuous monitoring of prices and costs.

Members may not be interested in switching medications: In a survey published in the American Journal of Managed Care, 53.6% of members self-reported that they would rather pay the higher copay of a nonformulary status prescription.
medication, while 26.0% said they switched to a mediation on formulary. However, a copay differential can be a management strategy. According to MedImpact data, a greater proportion of members switched to a lower-cost alternatives when there was a larger copay differential.

Utilization management strategies, such as uptiering, step therapy, and benefit exclusion, along with communication outreach can also help move members to lower-cost alternative treatments. Future directions for communication of these changes can include real-time prescriber notification of lower-cost alternatives through e-prescribing, outreach through text message and outbound calls, and optimizing member cost-sharing incentives.


**Specialty Drug Growth Continues: A Look at the Pipeline**

**Key Specialty Pharmaceuticals** market trends include increased competition along with cancer and orphan drug development, according to Aimee Tharaldson, PharmD, senior clinical consultant of emerging therapeutics at Express Scripts in Woodbury, Minnesota, who gave a presentation at the AMCP Annual Meeting.

In the past four years, a number of specialty drug generic options have been approved, representing $14 billion in overall U.S. spending opportunities, with the potential for $24 billion in expected specialty generics in the next five years. Through 2023, 71 specialty therapy patents will expire, representing a $55 billion market opportunity. In addition, the biosimilar market keeps growing, as seven more agents are projected to be approved this year. There has also been extensive oncology drug development over the past seven years, with 2017 and 2018 seeing increasing growth after a slowdown in 2016.

The orphan drug pipeline, however, is experiencing extensive growth, as these agents represent more than half (53%) of the current specialty pharmacy pipeline. Food and Drug Administration approvals for the agents continue to grow in comparison with traditional drugs. In quarter one of 2019, four specialty drugs have already been approved: caplacizumab-yhdp (for acquired thrombotic thrombocytopenic purpura), turoctocog alfa pegol (for hemophilia A), esketamine (for depression), and brexanolone (for depression).

Dr. Tharaldson then provided an extensive look at projected approvals for the top specialty pharmaceutical drug classes.

Inflammatory conditions are the leading therapy class based on per-member, per-year spending ($153 billion). The pipeline includes:

- Risankizumab, an interleukin (IL)-23 inhibitor for psoriasis (expected 2019)
- Upadacitinib, a JAK-1 inhibitor for rheumatoid arthritis (RA; 2019)
- Ustekinumab, an IL-12 and -23 inhibitor for ulcerative colitis (2019)
- Bimekizumab, an IL-17A and -17F inhibitor for psoriasis (2020)
- Filgotinib, a JAK-1 inhibitor for RA, ulcerative colitis, and Crohn's disease (2020)

Various multiple sclerosis (MS) medications are in development, including:

- Cladribine, a nucleoside analog that depletes B and T lymphocytes for relapsing MS (RMS; 2019)
• Siponimod, a sphingosine 1-phosphate receptor modulator for secondary progressing MS (2019)

• Diroximel fumarate, a monomethyl fumarate prodrug for RMS (2019)

• Ozanimod, a sphingosine 1-phosphate receptor modulator for RMS (2019)

• Dimethyl fumarate, a monomethyl fumarate prodrug for RMS (2020)

A number of oncology products are in development and are projected to be approved before the end of the year, including:

• Erdafitinib for urothelial cancer

• Quizartinib for acute myeloid leukemia

• Selinexor for multiple myeloma

• Pexidartinib for tenosynovial giant cell tumor

• Entrectinib for NTRK-fusion+ solid tumors

• Polatuzumab for diffuse large B-cell lymphoma

• Darolutamide for prostate cancer

• Fedratinib for myelofibrosis

In addition, four new HIV medications are expected to be approved within the next two years, including dolutegravir/lamivudine, cabotegravir/rilpivirine, fostemsavir, and lereronlimab (PRO-140).

The nonalcoholic steatohepatitis pipeline for 2020 and beyond is extensive as well, with 11 phase II and phase III drugs pending approval. This is particularly important, as current treatment options are limited; most recommendations for treatment are focused on weight, diet, and exercise. However, these new treatment options come with many unknowns, including a steep projected price of $3,000 to $70,000 per year. It remains to be determined which patients will be prescribed the medications and which will remain on a diet and exercise-focused regimen.

There are nine medications pending approval for Alzheimer’s disease, which are projected for approval in 2021 to 2024 and beyond. The hemophilia market has seven medications in the pipeline, which could result in approvals between 2020 and 2022. Lastly, Dr. Tharaldson discussed some unique pipeline drugs, including:

• Romosozumab for postmenopausal osteoporosis

• Onasemnogene for spinal muscular atrophy

• Bremelanotide for hypoactive sexual desire disorder

• Celiprolol for vascular Ehlers-Danlos syndrome

• Tafamidis for transthyretin cardiomyopathy

• Afamelanotide for erythropoietic protoporphyria

• Fenfluramine for Dravet syndrome

• Golodirsen for Duchenne muscular dystrophy

Real-Time Benefit Checks May Improve Medication Adherence, Reduce Patient Costs

Providers often have a limited knowledge of a specific patient’s insurance coverage when prescribing medications, and a real-time benefit check program may be a solution for this. Real-time benefit checks can provide information on coverage (quantity limits, prior authorization, step therapy), channel options (retail, mail order, specialty), patient payment details, and alternative drugs based on the patient’s plan formulary.

During a presentation at the AMCP Annual Meeting, Jacqueline Hager, BS, product manager at Surescripts in Minneapolis, Minnesota, and Roger G. Pinsonneault, RPh, vice president of product innovation at Gemini Health in Alpharetta, Georgia, discussed different options and implementation strategies for real-time prescription benefit check programs.
This program uses a standard format to exchange data between providers and pharmacy claim processors in real time. Providers, prescribers, or the pharmacy originate a request from their practice management system. The pharmacy claim processor adjudicates the requests and communicates a response in real time. The practice management software receives the response and presents the details in the provider’s workflow.

The proposed Medicare Part D rule for 2020 seeks to make revisions to the Medicare Advantage program (Part C) and Prescription Drug Benefit Program (Part D) regulations to support health and drug plans’ negotiation for lower drug prices and reduce out-of-pocket costs for enrollees. A real-time benefits tool can provide patient-specific cost-sharing information within the prescriber’s electronic health record. Providers can identify a patient’s specific benefit plan and assess utilization management tools that are included.

According to the Medicare guidance, these tools “should not be used by providers to evaluate alternatives for drugs prior to discussing whether the patient intends to self-pay for the prescribed drugs. Health care providers ... should ensure that individuals are aware that information about services or treatment, such as a future prescription, may be disclosed to the plan by the tool and effectuate the individual’s disclosure restriction request by refraining to use the tool in instances in which the patient intends to self-pay in full.”

According to research presented from Surescripts, the average savings per prescription with the use of a real-time benefit check can range from $21 for cardiology to $228 for psychiatry. The speakers gave an example of the use of this program in action: The prescriber selects 90 capsules of cariprazine—an antipsychotic used to treat schizophrenia or bipolar disorder—at a patient’s preferred pharmacy. The real-time benefit check notification prescribes that the medication will cost the patient $1,775.84 but that it is available through their pharmacy benefit manager’s mail order pharmacy for just $125. The prescriber then sends the prescription to the mail or pharmacy for added savings for the patient.

When engaging with a real-time benefit check program, employ a team-based approach to discuss costs with the patient. Establish a process to document cost concerns that the entire team can reference, and train your team to have financial conversations with the patient, the speakers concluded.

Study Finds Tildrakizumab May Decrease Cardiometabolic Symptoms in Patients With Psoriasis

Patients with psoriasis have a higher prevalence of cardiometabolic risk factors associated with metabolic syndrome, including major adverse cardiovascular events, obesity, hypertension, and diabetes. Researchers assessed the impact of tildrakizumab on cardiometabolic factors in patients with psoriasis with and without metabolic syndrome.

The study found that changes in cardiometabolic disease risk factors following treatment with tildrakizumab were generally consistent regardless of metabolic syndrome status. The results of the study were presented at the AMCP Annual Meeting during a poster session titled “The Effect of Tildrakizumab on Cardiometabolic Risk Factors in Psoriasis by Metabolic Syndrome Status: Post Hoc Analysis of 2 Phase 3 Trials (reSURFACE 1 and reSURFACE 2).”

The post-hoc analysis included data from two phase III, double-blind, randomized, controlled studies: reSURFACE 1 and reSURFACE 2. The trials included adults with moderate-to-severe chronic plaque psoriasis who continuously received tildrakizumab 100 mg (n=369) or 200 mg (n=330) at weeks zero and four, as well as every 12 weeks thereafter to week 64 (reSURFACE 1) or week 52 (reSURFACE 2). Among the patients, 79 (21.4%) in the 100 mg group and 67 (20.3%) in the 200 mg group had metabolic syndrome. Baseline demographics and disease characteristics were similar; however, patients with metabolic syndrome had higher median baseline weight, body mass index, and prevalence of cardiovascular disease and diabetes.

Following continuous treatment with tildrakizumab 100 mg or 200 mg, mean changes and mean percentage changes from baseline in cardiometabolic disease risk factors were generally consistent regardless of metabolic syndrome status. In the tildrakizumab 100 mg group, patients with metabolic syndrome experienced clinically relevant numerical decreases in fasting glucose, triglycerides, and systolic blood pressure. Similarly, patients with metabolic syndrome in the tildrakizumab 200 mg group experienced numerical decreases in systolic and diastolic blood pressure readings.

Targeted, prospective studies may provide further understanding of these findings, the researchers noted.

The study was sponsored by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc, and Sun Pharmaceutical Industries, Inc.
