Scrip
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Indication-Based Pricing Could Be Windfall For Interleukin Inhibitors

By Emily Hayes

EXPRESS SCRIPTS' PLAN TO REIMBURSE AT levels according to value of specific indications in inflammatory diseases will create more space for new entrants with proven value.

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Express Scripts Holding Co.'s implementation of indication-based pricing in inflammatory diseases could spur a big market shift toward anti-interleukin-17 drugs for psoriasis – **Novartis AG**'s *Cosentyx* in particular – at the expense of TNF-inhibitors. It also signals an important shift in reimbursement strategy with implications across other markets.

The pharmacy benefit manager announced plans on Sept. 8 to implement indication-specific pricing as part of its Inflammatory Conditions Care Value Plan, with rollout set for 2017. The plan also includes a broad rebate program for patients who drop out of therapy.

Indication-based pricing is a new approach to reimbursement that involves contracting for drugs for specific uses, rather than across all indications.

In the anti-inflammatory category, anti-tumor necrosis factor (TNF) drugs like **AbbVie Inc.**'s *Humira* (adalimumab), **Amgen Inc.**'s *Enbrel* (etanercept) and **Johnson & Johnson**'s *Remicade* (infliximab) are approved for a broad range of indications and have benefited from broad contracts, at the expense of new entrants, such as interleukin inhibitors, approved for a smaller number of conditions.

With TNF inhibitors in such a dominant position, in the past it has been very difficult for payers, PBMs and employers to convince physicians to switch stabilized patients from these drugs, commented Roger Longman, CEO of the reimbursement intelligence company Real Endpoints. Manufacturers have maintained this domination through rebate dollars and PBMs have found it difficult to ease themselves off the rebates to allow use of newer drugs, even where there are proven benefits over TNF biologics.

J&J's IL-12/IL-23 inhibitor *Stelara* (ustekinumab) has managed to pry its way in to the psoriasis/psoriatic arthritis market and produced worldwide sales of $2.5bn in 2015, but its market share could be a lot higher if the field was wide open.

During an American Academy of Dermatology meeting where data were presented showing superiority of new interleukin inhibitors over the standard of care, experts said that it was still unclear how the results would affect prescribing patterns, because decisions were often dictated by insurance coverage. *(Also see "New Interleukin Inhibitors May Give Stelara A Run For The Psoriasis Money" - Pink Sheet, 30 Mar, 2015.)*

Novartis' IL-17 inhibitor *Cosentyx* (secukinumab) launched last year and is off to a strong start. *(Also see "Does Novartis Need A Big Immuno-Oncology Deal? Jimenez Says No" - Scrip, 19 Jul, 2016.)***Eli Lilly & Co.**'s *Taltz* (ixekizumab) was approved in March. **AbbVie Inc.**, **UCB Group** and J&J have IL-17 inhibitors in Phase II for inflammatory diseases.

Express Scripts New Regime Promises To Shake Up Field

Starting in 2017, Express Scripts will be breaking up the inflammatory disease category in negotiations with drug manufacturers, for seven different indications: rheumatoid arthritis, psoriasis, psoriatic arthritis,

ankylosing spondylitis, juvenile idiopathic arthritis, ulcerative colitis and Crohn's disease.

Express Scripts says it will still be using a "blended" price at the drug level, regardless of indication, so a client still pays the same amount for each condition. But there are additional discounts and enhanced competition at the indication level. Medications will get formulary placement on the indication level, instead of the entire category of inflammatory conditions.

Indication-based pricing lays the groundwork for biosimilars, Express Scripts' Kautzner said.

This will allow smaller drugs that have only one or two indications to better compete with a drug that has all seven indications – leveling the playing field and helping to drive more competition, Adam Kautzner, VP of Express Scripts Drug Trend and Formulary Solutions, explained in an interview.

Payment will be tied to value, with higher rebates for indications where drugs don't work as well.

Indication-based pricing is part of a move toward value-based pricing, Longman commented. The first big area is inflammatory disease, but the model could make sense for any drug approved for multiple indications – the industry has already seen experiments in oncology demonstrating proof-of-concept, Longman noted.

Express Scriptsbegan contracting on an indication basis for cancer drugs earlier in 2016. *(Also see "Payer Briefs: Express Scripts Pricing Pilot; HHS Risk Adjustment; Value Frameworks" - Pink Sheet, 1 Apr, 2016.)* Rival PBM **CVS Health Corp.** is also planning to introduce indication-specific pricing in oncology. *(Also see "CVS Indication-Based Pricing For Cancer Drugs May Roll Out Later In 2016" - Pink Sheet, 4 Mar, 2016.)*

Datamonitor Healthcare analyst Astrid Kurniawan expects the model will be adopted by other commercial payers as well.

Biosimilars Will Boost Trend

The emergence of biosimilars will give payers more leverage in a number of therapeutic areas, including inflammatory diseases, Longman noted.

The TNF inhibitors represent one of the major areas for biosimilar development. **Sandoz Inc.**'s *Erelzi* (etancercept-szzs) still has some legal hurdles to clear, but the Enbrel biosimilar is expected to launch in October. *(Also see "FDA Biosimilar Policy Continues To Evolve With Approval Of Sandoz Erelzi" - Pink Sheet, 30 Aug, 2016.)***Pfizer Inc./Celltrion Inc.** also expect to launch *Inflectra* (infliximab-dyyb), a biosimilar version of Remicade, in October. *(Also see "Pfizer/Celltrion Prep For October Inflectra Launch" - Scrip, 23 Aug, 2016.)*

Kautzner said that indication-based pricing lays the groundwork for biosimilars, allowing Express Scripts to "slot them in at an indication level."

Inclusion as a preferred treatment will need to be in line with guidelines from the American College of Rheumatology and Express Scripts' Pharmacy and Therapeutics Committee will ensure that clinical value comes first, the exec said.

Manufacturers need to realize that the discounts may need to be very deep for biosimilars to compete, Kautzner said.

For new entrants, the new regime represents opportunity – at a price. Those with high-value products may be willing to deal more aggressively on pricing and rebates in order to win preferred status and gain market share, Longman said.

"Whereas before you could not break in, now you can," Longman predicted.

Kautzner notes that products need to be priced competitively and envisions that there will be broad access to a variety of preferred products, with a "large selection from the physician standpoint."

Cosentyx Well-Placed

Within the inflammatory category, there is likely to be big shift in psoriasis favor of interleukin inhibitors, with

Cosentyx particularly well placed to benefit, Datamonitor's Kurniawan expects.

Interleukin inhibitors have proven superior to Enbrel in head-to-head studies. Payers appreciate this difference in efficacy but pricing is still an important factor.

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Cosentyx is likely to have the upper hand over Taltz and Stelara, because it proved superior to Stelara in a head-to-head study, whereas Lilly's Taltz met the less rigorous standard of superiority against Enbrel. *(Also see "FDA OK's Lilly's Taltz; Rival To Novartis' Cosentyx " - Scrip, 22 Mar, 2016.)* However, the US market is very competitive on pricing and that upper hand could be diminished if Lilly offers a better price, the analyst explained.

As for Humira, the market implications are somewhat unclear. The drug is the market leader and is perceived as being more efficacious than Enbrel, but head-to-head data against Enbrel are not available, nor are head-to-head data for Humira against the interleukin inhibitors.

J&J has tested its IL-23 inhibitor guselkumab, one of three drugs in the class in Phase III for inflammatory diseases, successfully against Humira in psoriasis in a mid-stage study.

Novartis recently unveiled comparative efficacy data for Cosentyx against Humira in ankylosing spondylitis and plans to run head-to-head studies of the two drugs in ankylosing spondylitis and psoriatic arthritis *(Also see "New Data Bolsters Cosentyx In AS & PsA; Humira Head-To-Head Planned" - Scrip, 8 Jun, 2016.)*.

These smaller indications are now more in play, Kurniawan said, and head-to-head data will help sponsors make the value case.

How Sponsors Should Respond

Asked to comment on what manufacturers should be doing in response to the introduction of indication-based pricing, Express Scripts' Kautzner said that "they need to understand flexibility will be key."

Companies will need to have an understanding that other products with more competitive prices for a given indication may provide better care at a lower net cost and that just because a drug has multiple indications doesn't mean it has better overall value, Kautzner said.

Longman said that pharmas need to spend more time on determining value for each indication. A number of models are now available for measuring value, including Real Endpoints' RxScorecard. The Institute for Clinical and Economic Review plans to issue a value report on anti-inflammatory drug classes in October.

Indication-specific pricing will also allow pricing for subpopulations within a particular disease. For example, in oncology, PD-1 inhibitors work better in lung cancer patients with higher levels of PD-1 expression.

"Pharmas should be focusing a lot more attention on proving value in specific subpopulations in which they are uniquely advantaged" against the competition, Longman said.

Kautzner said that indication-specific pricing for subpopulations is not part of the new program but that many possibilities are open for the future. There is always opportunity to enhance these programs and go to greater depths if the market warrants it, he said.

"This is the first great step," Kautzner said.

The Great Rebate Plan

Express Scripts' Inflammatory Conditions Care Value Program also includes a plan to offer rebates to payers in cases where patients stop taking their biologics in the first 90 days on therapy.

One in four patients stops therapy after the first, second or third fill of a prescription, for a variety of reasons, Kautzner noted.

In the past, Express Scripts has partnered with a few manufacturers on a one-off basis for rebates related to early discontinuation of drugs, but notes that this is the first time the industry has ever seen refunds across a category of drugs.

Payers surveyed for Datamonitor's psoriatic arthritis and psoriasis market reports expressed concern about drugs that fail to demonstrate sustained effects for patients over time, so this offering is in line with demand, Kurniawan noted.

Payers are increasingly looking for evidence of sustained effects in real world settings, beyond standard measures used to assess skin clearance used in clinical trials, she added.

Manufacturers will need to think of more innovative ways to assess factors that contribute to increased adherence of drugs, such as dosing and ease-of-use, in order to differentiate their product from other biologics available, she said.

Going forward, PBMs and payers alike will be looking at these tangible and more economically relevant and real-world pertaining endpoints when they think about placing products in preferred tiers, she said.

The fact that this is being done on a broad scale, for an entire class of medications for multiple diseases, and that the inflammatory market is being split into indication-specific contracts means that manufacturers will really need to understand the nuances of each indication, including the factors that lead to non-compliance in specific indications, Kurniawan said.

"It will become more challenging for one product to win across all inflammatory markets, without showing demonstrated superiority in each indication segment," the analyst concluded.

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