Teva Stands By Migraine Strategy After Ajovy Misses Boat On Express Scripts Deal

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by Emily Hayes | @emilykatehayes | emily.hayes@informa.com

Executive Summary

Agreement between Amgen/Novartis and Eli Lilly with Express Scripts on new migraine drugs could spur more demand by payers for simple, value-based outcomes deals.

Teva Pharmaceutical Industries Ltd. is defending the commercial strategy for its migraine drug *Ajovy* after Express Scripts Holding Co. excluded the drug from its formulary in favor of rival calcitonin gene-related peptide (CGRP) inhibitors – Amgen Inc./Novartis AG' *Aimovig* and Eli Lilly & Co.'s *Emgality* – with a new reimbursement program that includes a refund from sponsors if patients drop out of therapy in the first 90 days.

The pharmacy benefit manager (PBM) announced Oct. 17 that its new *SafeGuardRX Migraine Care Value* program – to be launched in the second quarter of 2019 – will give preference on its national formulary to Amgen/Novartis' Aimovig (erenumab-aooe) and Lilly's Emgality (galcanezumab-gnlm)

The news is a big blow for Ajovy (fremanezumab-vfrm), as Express Scripts covers 30% of commercially insured patients in the US. Granted, as ISI Evercore analyst Umer Raffat pointed out in an Oct. 17 note, only half of Express Scripts' covered lives are under plans that follow the company's preferred national formulary, while the other half are in plans with custom formularies.

Through Express Scripts' new program, the preferred CGRP inhibitors will be accessible to those who meet clinical guidelines for therapy with the class – coverage criteria mandate prior use of an acute medication, such as a triptan, and two older preventive medications.

Lilly has estimated that roughly 30m people in the US experience migraines and of these 10% use preventative therapies; this segment is its main focus with the launch of Emgality, which was approved by the US FDA on Sept. 27.

Announcing the new migraine program, Express Scripts said that it will "identify patients using high amounts of acute migraine treatments, and work with them and their physician to move them to an appropriate preventive treatment."

Best-In-Class Or First-In-Class: CGRP Inhibitors Line Up To Win The Migraine Market

By Mandy Jackson

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Amgen will be the first biopharma company to seek approval for a CGRP inhibitor when it submits a BLA for FDA approval later in the second quarter, but Alder, Lilly, Teva and Allergan are in the running for best-in-class status to treat unmet needs in migraine and other headache markets.

Those patients who clinically require Teva's product may use an exceptions process, because the company wants patients to have what they need, Express Scripts explained to *Scrip*. "However," it added, "there is parity across these medications, and it would be rare that a patient could not take a preferred product."

Will Quarterly Dosing Prevail In Competitive Market?

Teva is still stressing the differentiated dosing proposition for Ajovy, which may be taken monthly or quarterly, whereas the other two new CGRP products are only available in monthly regimens. (Also see "Is Quarterly Dosing For Teva's Ajovy Enough To Differentiate It From Other CGRP Inhibitors?" - Scrip, 17 Sep, 2018.)

"We are confident in the strategic decisions made when establishing the price for Ajovy, which is reasonable and appropriate for this therapy. While we are disappointed with the decision by Express Scripts Holding Co. (ESI) not to add an innovative product developed with flexible dosing options (quarterly, 675 mg and monthly, 225 mg) for the preventive treatment of migraine in adults to their national formulary, we have programs in place to ensure appropriate patients can access Ajovy," Teva told *Scrip*.

Following approval on Sept. 14, Ajovy was launched within a few days and prescription activity so far shows that many patients and physicians are choosing the option of quarterly dosing, the company said.

"For those living with this neurological disease, broad access allows patients and health care providers to choose the appropriate treatment option for the individual," Teva said.

Express Scripts' decision shows how tough the competitive proposition can be when there are new products from the same class with similar efficacy and safety launching at the same time.

The three CGRP inhibitors are all injectable monoclonal antibodies and were all approved in the last six months for prevention of chronic or episodic migraines and all have a list price of about $575 a month or $6,900 per year, which is much lower than the $10,000 to $12,000 annual price originally expected in the market and also lower than the $8,500 annual cost determined to provide value by the Institute for Clinical and Economic Review (ICER), a third party organization that makes cost-effectiveness assessments. (Also see "Amgen's Aimovig Aims To Capture As Many Migraine Patients As Possible With $6,900 Price" - Scrip, 17 May, 2018.)

"We understand the significant impact of migraine and felt it was important to bring Ajovy to the market at a wholesale acquisition cost (WAC) in line with the recommendation brought forward by the Institute of Clinical and Economic Review (ICER)," Teva said.

However, Express Scripts said in its statement that although the new CGRP inhibitors are priced in line with value-based assessments from ICER, they still cost a lot more than available preventative treatment "and require conscientious management" to ensure good outcomes.

"Given the drugs have far more similarities than differences, including comparable list prices, we (and the Street) had been expecting payers to step in following the recent approvals and steer their patients towards the one or two agents where payers were receiving the best deal," Leerink Swann's Vamil Divan said in an Oct. 17 note.

"Anyone following the biopharma industry and payer dynamics over the past few years should not be surprised that

this amount of differentiation was apparently not enough for the drug to gain any special consideration from Express Scripts," Divan added.

Simple Value-Based Outcomes Deal

The new program includes a value-based outcomes component, which is becoming more common, especially in categories where drugs in the same class appear to have similar efficacy and safety.

Express Scripts will offer “an early discontinuation reimbursement” to the plan sponsor if a patient discontinues treatment in the first 90 days.

"This industry-first program combines a comprehensive clinical care program to help patients achieve better outcomes and experience fewer migraines, while helping plan sponsors more affordably cover new, preventive therapy for their members," the company said.

Express Scripts said that the program for the CGRP inhibitors will also encourage adherence and appropriate use of the injectable therapies.

Chain Reaction To Come?

Past value-based reimbursement deals in other therapeutic areas include Amgen's agreement in 2017 with Harvard Pilgrim Health regarding use of the PCSK9 inhibitor/cholesterol drug *Repatha* (evolocumab), which included a refund for the cost of the drug for patients who had a heart attack or stroke while on treatment. (Also see "Amgen's Repatha Contract With Harvard Pilgrim Includes A Full Refund" - Pink Sheet, 3 May, 2017.)

Competitor Sanofi/Regeneron Pharmaceuticals Inc. secured a deal with Express Scripts this year to gain preferred access on the national formulary for the PCSK9 inhibitor *Praluent* (alirocumab) in exchange for a deeper discount. (Also see "Let's Make A Deal: Sanofi/Regeneron Extend A Hand On Praluent, Express Scripts Takes It" - Scrip, 1 May, 2018.)

Roger Longman, chairman of reimbursement intelligence company Real Endpoints, commented that the use of a simple, non-clinical endpoint like discontinuation from therapy differentiates the new agreement with Express Scripts and could spur demand by plans for similar deals in the future.

"This is a nonmedical measure of efficacy, a very simple, very straightforward, value-based agreement," Longman said.

Discontinuation of therapy could be used for any drug, regardless of whether there is a biomarker for efficacy.

"The only data you need is pharmacy data – did the patient continue to get a script?" Longman said.

The decision to have two preferred migraine products suggests that nobody was willing to provide enough discounting for a one-on-one deal, and it's unclear why Teva's Ajovy wasn't included in this type of an arrangement, though the company has been in a state of turmoil of late, Longman noted. Teva has been undergoing a major restructuring that involved layoffs of 25% of its workforce. (Also see "Schultz Swings The Cleaver At Teva, Cutting 25% Of The Workforce" - Scrip, 14 Dec, 2017.)

"My sense is they may not be able to react as quickly in these cases as they need to react," Longman said.

"While it remains unclear if other pharmacy benefit managers will follow suit, it appears that Teva may have lost in

the first battle to gain access for Ajovy in the extremely competitive CGRP-antagonist category," BTIG analyst Timothy Chiang said in an Oct. 17 note.

Chiang estimates that the gross-to-net discounts are in the range of 30% to 35%.

ISI Evercore analyst Umer Raffat said the rebate differential for the preferred drugs vs. Ajovy is unclear at the moment. Express Scripts' decision is "obviously not good news for Teva in 2018," but the company is offering up to 15 months of free drug for people who can't get insurance coverage and they may be able to get more favorable positioning in 2020, Raffat said.

Commercial Battle Only Just Beginning

The commercial battle is only beginning and clinical profiles may take a back seat to payer acceptance and product presentation, Leerink's Divan suggested.

In addition to the three approved drugs, Alder Biopharmaceuticals Inc.'s subcutaneous injectable eptinezumab, partnered with Teva, is in line for approval in early 2020 and Allergan PLC's oral CGRP antagonists ubrogepant and atogepant, which were in-licensed from Merck & Co. Inc. in 2015, are also nearing the market. (Also see "Allergan's Oral Drugs Overlooked In CGRP Inhibitor Development Race" - Scrip, 30 Sep, 2016.)

On Oct. 17, Allergan announced that it had completed two positive safety and tolerability studies of ubrogepant for acute treatment of migraine, one evaluating long-term use over one year and the other focusing on liver safety in healthy patients over eight weeks. Liver toxicity has been a stumbling block for CGRP antagonists in the past. (Also see "Allergan Touts Ubrogepant Phase III Success, But Liver Tox Concerns Overhang" - Scrip, 6 Feb, 2018.)

Allergan plans to file ubrogepant with the FDA in the first quarter of 2019 and expects that this will be the first oral CGRP receptor antagonist submitted in the US for the acute treatment of migraine with or without aura. (Also see "Allergan's Ubrogepant Succeeds In Second Acute Migraine Phase III Study" - Scrip, 27 Apr, 2018.)

The latest announcement reads quite positive going into regulatory review, though more details are needed regarding the liver safety results, Raffat said.

Atogepant is slated to enter Phase III in the first half of 2019. (Also see "Migraine Drug Atogepant Delivers Good News When Allergan Needs It Most" - Scrip, 11 Jun, 2018.)