AbbVie's Orilissa, Myovant's relugolix both expected to face similar payer scrutiny in uterine fibroids as the former has in endometriosis, experts say

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- Physicians using Orilissa longer than labeled, and additional documentation required by payers
- Results from payer pushback have been mixed for Orilissa in endo pain

The reimbursement experience physicians are having with **AbbVie's** (NYSE:ABBV) Orilissa (elagolix) in endometriosis-related pain is likely to spill over to **Myovant Sciences'** (NYSE:MYOV) relugolix and both drugs' use to control menstrual bleeding in uterine fibroids if approved, noted physicians and reimbursement experts.

To prescribe Orilissa beyond the specified limit on its label, a physician letter stating the need and the drug's effectiveness has been required, experts said. While interviewed physicians expected access after such a process, it was not a uniform experience for all doctors, they noted.

Insurance coverage is a major obstacle for Orilissa's adoption, one analyst noted, adding AbbVie has stated approximately 70% of patients taking Orilissa have access to the drug through their insurance plans and the rest are offered the drug for free.

The challenge of proving adequate evidence for the reimbursement of prolonged gonadotropin-releasing hormone (GnRH) antagonist treatments like Orilissa and relugolix will likely extend to other indications like uterine fibroids, said experts. This may be even more obvious since treatment is driven by patients, and endometriosis-related symptoms are more distressing than those in uterine fibroids, two experts noted.

AbbVie plans to file a New Drug Application (NDA) for Orilissa to address menstrual bleeding with uterine fibroids in mid-2019 based on topline data from two trials, according to a 14 November 2018 announcement. Myovant announced data from one trial in May, and plans an NDA in 4Q pending positive results from a second Phase III trial, as per a 14 May press release. **ObsEva** (NASDAQ:OBSV) also has a Phase III GnRH antagonist, linzagolix, with results expected in mid-2019. As a likely third-to-market asset, the impact of ObsEva's efforts to differentiate linzagolix from Orilissa and relugolix by offering dosing flexibility remains unclear, this news service reported on 31 January.

Individual analysts estimated revenues for Orilissa, relugolix and linzagolix to be USD 1.58bn in 2027, USD 1bn in 2028 and USD 992.6m in 2028, respectively, for endometriosis-related pain. Sales for their use to address bleeding with uterine fibroids are anticipated to be USD 985m in 2027, USD 700m in 2028 and USD 600m in 2028, respectively. The market caps for AbbVie, Myovant and ObsEva are USD 107.83bn,

USD 785m and USD 489m, respectively. Orilissa was approved for endometriosis-related pain in June 2018 and launched at a list price of USD 10,000 per year.

AbbVie and Myovant did not respond to a request for comment.

Extrapolation of Orilissa experience across women's health

Initial reimbursement challenges with Orilissa use for endometriosis-related pain will likely carry over to Orilissa's and relugolix's use in patients with uterine fibroids, noted Dr Richard Stefanacci, chief medical director, Managed Markets, Eversana, Pennsylvania. Since long-term evidence is lacking in women's health, these drugs will likely face the same issues with payers requiring additional information to cover using the drugs for longer than what is noted on their labels, said R. Brett McQueen, PhD, assistant professor, Center for Pharmaceutical Outcomes Research, University of Colorado Anschutz Medical Campus.

It is quite common to consider prescribing Orilissa beyond the time period approved, given the lack of new and effective treatment options, said interviewed experts. Orilissa is indicated at either 150mg once daily for two years or 200mg twice daily for up to six months. The relugolix Phase III program is testing the drug for six months of use.

However, in both uterine fibroids and endometriosis, the need for therapy is dictated by the patient, unlike in blood pressure medications where test data drives treatment, said Stefanacci. It will be surprising if the drugs are very successful in treating bleeding associated with uterine fibroids where symptoms are not as debilitating as those in endometriosis, since symptomatically women deal better with fibroids than endometriosis, said Dr Charles Ascher-Walsh, director of Gynecology, Urogynecology, MIS Mount Sinai School of Medicine, New York. Moreover, the side-effect tradeoff is clearer for endometriosis compared to uterine fibroids, he noted.

However, Dr Tatiana Burnett, consultant, Department of Obstetrics and Gynecology, Mayo Clinic, Rochester, disagreed about whether women are more likely to seek care for endometriosis-related pain as opposed to heavy menstrual bleeding related to fibroids. Even women with endometriosis have an average eight-year delay from symptoms to diagnosis, some of which is due to the normalization of symptoms either by family, friends or physicians, she added.

The prevalence of endometriosis is probably underestimated given its poor diagnosis history, so as more drugs become available, it could have a major impact on healthcare budgets, said McQueen. Gynecologists are familiar with identifying symptoms, but drug approvals and advertisements may result in more patients speaking out about their symptoms, said Ascher-Walsh.

Payer pushback over Orilissa in endometriosis-related pain

The reimbursement experience for Orilissa in endometriosis-related pain, including the need for prior authorization or outcomes-based contracts, has been variable depending on an individual patient's insurance, said Burnett and Ascher-Walsh. While she has not been denied coverage for her patients, Burnett noted she has heard about rejections from her colleagues.

Although it is not straightforward, insurance companies can be convinced to pay for Orilissa with a letter from the physician, said Ascher-Walsh, based on his experience. In general, physicians will need to write an appeal based on the literature to support continued use, and the vast majority of written appeals are successful, agreed Stefanacci.

Based on its approved label, Orilissa is under the cost-effectiveness threshold the Institute for Clinical and Economic Review (ICER) used in its analysis, said McQueen, who was part of the ICER report group that published its findings in August 2018. However, during the ICER panel, gynecologists said they would continue treatment for longer periods of time if it worked, and that is where the cost-effectiveness estimate dropped, he added.

An AbbVie-sponsored analysis looked at Orilissa treatment for up to two years and found it to be cost effective, noted Scott Johnson, PhD, a health economist who worked on this analysis and principal, Medicus Economics, Boston. The analysis compared Orilissa to Lupron (leuprolide acetate) instead of placebo, as done by ICER. Lupron is indicated for the management of endometriosis, including pain relief and reduction of endometriotic lesions.

The AbbVie analysis indicated if a plan covers Lupron, it should also cover Orilissa, said Johnson. US payers are increasingly using cost-effectiveness analyses, which is partly driven by the need for value-based plan designs, he added. Payers may explore outcomes-based contracts to allow continued access to the drug if effective, said McQueen and Johnson. Such contracts would involve financial rebates where the manufacturer is required to pay back the cost of the drug if the patient does not respond, said McQueen.

Nonetheless, long-term use also comes with safety questions like the higher risk of bone mineral density loss, said Burnett. However, the one to two year time period used to determine cost effectiveness may be inadequate to capture any adverse event changes, noted Johnson.

While Orilissa is currently the only approved GnRH antagonist, relugolix is in two Phase III studies for patients with endometriosis-related pain, with completion dates in December. As more drugs get approved for endometriosis-related pain, companies may provide additional rebates to retain a drug's position on a formulary tier, but list prices would be unlikely to change, said McQueen. Factors like bone loss leading to fractures would be a consideration for providers and payers alike, but any differentiation between multiple drugs on that front will have to be significant, and it will not be substantial if it is a class effect or based on just one trial, noted Stefanacci.

by Manasi Vaidya in New York

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