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Migraine Market Update: CGRP Inhibitors Slowly Gain Ground

New Medicines For The Condition More Than Doubled This Year

by Mandy Jackson

The market for novel preventive and acute treatments grew from three anti-CGRP antibodies at the start of 2020 to four biologics and two oral drugs against CGRP plus a small molecule 5-HT1F inhibitor.

It appears that the COVID-19 pandemic largely has not had a big impact on sales of novel migraine therapies, except for the one new product that can't be administered by patients at home. In fact, with four new products launched since the beginning of 2020, overall sales of new migraine drugs – preventive therapies or acute treatments – increased 80.5% year-over-year in the second quarter.

Sales of the six calcitonin gene-related peptide (CGRP) inhibitors approved since 2018 totaled $253.3m in Q2 versus $140.3m for the three anti-CGRP antibodies on the market in the second quarter of 2019. (*See chart below.*) *Eli Lilly and Company* did not report sales for its serotonin (5-HT) 1F receptor agonist Reyvow (lasmiditan), which launched in January at the same time that *Allergan plc* (now part of *AbbVie Inc.*) launched the first-ever oral CGRP inhibitor Ubrelvy (ubrogepant). (Also see "*Lilly, Allergan Beat Biohaven To Acute Migraine Market With Reyvow, Ubrelvy Launches*" - Scrip, 31 Jan, 2020.)

Reyvow, Ubrelvy and *Biohaven Pharmaceutical Holding Company Ltd.*'s oral CGRP inhibitor Nurtec ODT (rimegepant) – approved in February and launched in March – are indicated for acute treatment to stop a migraine attack when it happens. (Also see "*Biohaven's Oral CGRP Inhibitor Nurtec ODT Approved In The US For Acute Migraine*" - Scrip, 27 Feb, 2020.) Biohaven hopes to expand Nurtec's label to migraine prevention after showing earlier this year that the drug reduced monthly migraine days versus placebo in a Phase III clinical trial. (Also see "*Biohaven's Nurtec May Be First Migraine Drug For Acute Treatment And Prevention*" - Scrip, 30 Mar, 2020.)

Amgen, Inc.'s Aimovig (erenumab) followed by *Teva Pharmaceutical Industries Ltd.*'s Ajovy (fremanezumab) and Lilly's Emgality (galcanezumab) were approved in 2018 for prevention of episodic migraine (14 headaches or fewer per month) and chronic migraine (15 or more headaches per month). All three subcutaneous injections are administered monthly, but Ajovy also is approved as a quarterly treatment. The US Food and Drug Administration approved a second quarterly preventive treatment option – *H. Lundbeck A/S*'s CGRP inhibitor Vyepti (eptinezumab), administered by intravenous infusion – at the end of February and Lundbeck launched the product in April. (Also see "*Pricing Could Help Lundbeck's Vyepti In Slow-Growing CGRP Market*" - Scrip, 26 Feb, 2020.)

Sales growth has been slow for the first three biologics despite the fact that millions of people in the US and other markets experience migraine attacks, characterized by severe headaches that may be accompanied by nausea, vomiting and sensitivity to lights and sounds.

The anti-CGRP antibodies are competing with generic oral drugs used off-label for decades for migraine prevention – including antihypertensive medicines, anticonvulsants and antidepressants – and AbbVie's blockbuster Botox (onabotulinumtoxinA). Botox may be best known as a wrinkle reducer, but a larger percentage of its sales come from therapeutic indications and mostly from its use in chronic migraine prevention.

Market Snapshot: Migraine Prevention Therapies' Slow Road To Blockbuster Status

By Mandy Jackson

23 Jan 2020

Aimovig, Emgality and Ajovy have been on the market for more than a year, but are still far from blockbusters even though millions of patients are eligible for treatment – and at least one new competitor is coming.

Read the full article here

The primary competition for the two oral CGRP inhibitors and Lilly's 5-HT1F receptor agonist are generic triptans. The mostly oral drugs were the last big class of medicines approved for acute migraine treatment and companies continue to develop new triptan formulations to capitalize on the still-frequent use of this drug class to end migraine attacks. (Also see "*Market Snapshot: Three Acute Migraine Launches Are First In Over 20 Years*" - Scrip, 27 Jan, 2020.)

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Sales Of First-To-Market Aimovig Grew In Q2

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Amgen reported $98m in second quarter sales of Aimovig, which was up 18% year-over-year from $83m in the second quarter of 2019. The increase was driven by 45% volume growth, offset partially by lower net selling price as the company negotiated with payers to make the first-to-market product accessible to more patients. (Also see "*Amgen's Aimovig Aims To Capture As Many Migraine Patients As Possible With $6,900 Price*" - Scrip, 17 May, 2018.)

"Aimovig sales grew 18% YoY and 38% QoQ and beat our forecast by 18% but was in line with consensus," SVB Leerink analyst George Porges said in a 29 July note. Porges expects sales to decline from $306m in 2019 to $286m in 2020 but grow to $547m in 2024.

Aimovig had a 48% share of total prescriptions (TRx) in the CGRP class during the quarter and exited June with a 41% share of new-to-brand prescriptions (NBRx) even as new prescriptions for CGRP inhibitors were impacted by the COVID-19 pandemic, which has kept patients from visiting doctors as they seek to avoid exposure to the novel coronavirus.

Amgen, Teva and Lilly all provided substantial amounts of their migraine prevention products for free in the US during the two years following their launches to get patients started on therapy while they waited for payers to cover the medicines' costs. However, Amgen said in its second-quarter earnings report that it was continuing to transition patients from free to paid product and improve reimbursement. The company has had to discount Aimovig's list price considerably to obtain coverage, but pricing is expected to be relatively stable for the rest of 2020.

"Modelling the launch of Aimovig has remained challenging, with a 38% decline in revenue in the first quarter despite 8% script growth," William Blair analyst Matt Phipps said in a 29 July note. "Similarly, the 38% revenue growth off the back of 17% unit growth in the second quarter compared to the first suggests continued challenges in predicting revenue growth for the product, though hopefully stable net selling price through the remainder of the year could reduce the lumpiness observed to date."

Phipps predicted $947m in 2023 sales of Aimovig despite increasing competition in the migraine space.

Executive vice president of global commercial operations Murdo Gordon said during Amgen's earnings call that he didn't view oral CGRP inhibitors as competitors, but as add-on therapies, since they are approved to treat migraines that break through preventive treatments. In fact, he noted, the oral drugs have helped raise awareness of the CGRP class overall and Aimovig in particular.

Amgen Has Relatively Smooth Sailing In Q2 Despite COVID-19 Headwinds

By Mandy Jackson

29 Jul 2020

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Amgen intends to broaden its promotions of Aimovig, which primarily is marketed to neurologists and headache specialists, to a greater number of primary care physicians. Gordon noted that primary care is an important market, since neurologists have big backlogs of patients waiting for treatment and limited capacity to treat them in a timely manner, especially with current COVID-19 precautions.

Amgen reported a 6% year-over-year increase in second quarter sales despite pandemic-related declines for several drugs as newer product gains and Otezla righted a rocky ship.

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Teva's Ajovy Still Struggling To Catch Up

Teva's Ajovy was the second CGRP inhibitor approved in the US, just weeks ahead of Lilly's Emgality in October 2018, but its sales significantly lag its competitors, largely because the product launched as a pre-filled syringe rather than in an easy-to-use autoinjector. An Ajovy autoinjector was approved in January of this year and launched in April; the company believes its sales are improving as a result.

Teva president and CEO Kåre Schultz said during the company's 5 August earnings call that "since we got the autoinjector, the NBRx share has continued to grow significantly per month and per week, and I can tell you here that the July numbers are even higher than the June numbers."

Ajovy sales totaled $39m in the second quarter, including $34m in North America and $5m in Europe, up 62.5% from $24m during the same period in 2019 with just $1m in sales outside of North America. Teva has forecast $250m in Ajovy sales for 2020, which is 2.5 times more than the 2019 total of $96m.

Ajovy's NBRx share of the CGRP inhibitor market in the US was greater than 20% and its TRx share reached about 16.5% as of 3 July, Teva reported. Schultz noted that about 40% of NBRx and 50% of TRx prescriptions in the second quarter were for the autoinjector. The company submitted the biologic for approval in Japan during July and has obtained reimbursement for Ajovy in 16 countries.

Lilly's Emgality Sales Gain On Aimovig

Lilly has made an aggressive marketing push to keep up with its biggest competitor Amgen in the CGRP drug class, resulting in a narrowing of the gap between Emgality and Aimovig sales. Emgality also has the distinction of being approved in the US for the prevention of episodic cluster headaches in addition to episodic and chronic migraine.

Lilly reported $87.4m in second quarter Emgality sales, which was up 154.8% year-over-year

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from $34.3m in the second quarter of 2019 – more than double the growth in the overall injectable CGRP inhibitor market despite the COVID-19 impact the company felt across its portfolio.

The gap between Emgality and Aimovig sales narrowed to $10.6m in Q2 from $48.7m in the year-ago period. Lilly noted that Emgality had an almost 38% share of new CGRP inhibitor prescriptions in the second quarter of this year and its share of total prescriptions increased by 17 percentage points.

Lilly Points To Six-Month Growth Instead Of Pandemic Impacted Q2

By Joseph Haas

30 Jul 2020

Lilly argues the overall trend is positive, although the second quarter was down. Trial successes with Verzenio, Trulicity, Jardiance and mirikizumab offer additional growth potential.

Read the full article here

Lilly Bio-Medicines president Patrik Jonsson said during the company's 30 July earnings call that "we continue to remain very confident in the future of Emgality and aiming for a market leadership in the preventive market. And we see also a strong market leadership, particularly in primary care, where we've expanded our effort in 2020."

"If we look upon the Reyvow launch, I think it's fair to say that we are not pleased with the performance so far, but we need to have in mind that we had approximately one month in the marketplace prior to we were hit by COVID-19," Jonsson continued. "And we made a conscious decision to actually pull back from our promotional efforts, both in the field as well as in terms of ceasing promotion overall."

Virtual promotional activities have started, however, "and we remain very confident in the molecule, taking into account that it's the only one that actually can offer a strong relief from the most painful physical symptoms as well as the most bothersome symptoms associated with migraine. And we know that there's a huge opportunity. Out of the 6 million people being treated in the US today, 35% to 40% of those are not responding to the triptans." (Also see "*Lilly Expands Migraine Franchise With Reyvow Approval*" - Scrip, 11 Oct, 2019.)

Ubrelvy Sales Hit Double Digits, Botox Holds Market Share

Many AbbVie products were impacted by COVID-19-related reluctance for patients to visits their doctors during the second quarter, but the oral CGRP inhibitor Ubrelvy generated $22m during its first full quarter on the market versus $13m during the last two months of the first quarter.

CEO Richard Gonzalez noted during the company's 31 July earnings call that sales of Ubrelvy and other new migraine therapies did not significantly cut into physician-administered Botox, which generally maintained its position despite reduced doctor visits during the pandemic.

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"Our migraine portfolio is anchored with Botox Therapeutic, which had revenues of roughly $300m to AbbVie in the second quarter," Gonzalez said. "Despite multiple new competitive entrants, Botox Therapeutic has largely retained its total treated patient base – a testament to its efficacy, safety and brand recognition."

While Botox sales declined by about 20% versus what Allergan reported in the second quarter of 2019, he noted that injections of the product are on the rise again as patients return to doctors for treatment across the product's aesthetic and therapeutic indications.

AbbVie Says Botox Business Recovering But Allergan Drags Down Q2 Financials

By Joseph Haas

31 Jul 2020

AbbVie reported revenue growth during the second quarter, with products like Rinvoq and Skyrizi leading the charge. But Allergan, despite growth for Vraylar and Ubrelvy, pushed down overall performance.

Read the full article here

AbbVie could have a second migraine prophylaxis on the market in 2021, after its second oral CGRP inhibitor atogepant recently succeeded in the Phase III ADVANCE clinical trial in the prevention of episodic and chronic migraine. (Also see "*Pipeline Watch: Phase III Starts With AL001, Beremagene Geperpavec And Relacorilant*" - Scrip, 3 Aug, 2020.) The company plans to file atogepant for regulatory approvals early next year. (Also see "*Combined AbbVie/Allergan Makes Earnings Debut*" - Scrip, 29 Jul, 2020.)

Biohaven Nearly Hits Double Digits With Nurtec

Ubrelvy had a month or so head start versus Biohaven's early March launch of its oral CGRP inhibitor for Nurtec, which brought in $9.7m during the second quarter. However, Nurtec for migraine prevention is likely to beat atogepant to the US market by several months.

The company plans to submit a supplemental new drug application (sNDA) to the US FDA during the second half of 2020, which means Nurtec could be approved as the first CGRP inhibitor for migraine prevention as well as acute migraine treatment during the first half of 2021.

SVB Leerink analyst Marc Goodman, in a 10 August note, forecast $255m in Nurtec sales for 2021 based on the drug's existing acute migraine treatment indication alone and $440m in sales in 2022.

Wedbush analyst Laura Chico forecast $17m in third-quarter 2020 sales and $22m in fourt-quarter sales in a 10 August note.

Biohaven claimed that its drug led in new-to-brand prescriptions during the second quarter of

2020 with a 52.6% NBRx share of the oral CGRP inhibitor market after 16 weeks of sales, which outpaced expectations.

The company highlighted its ability to launch a new drug through virtual meetings with prescribers as the COVID-19 pandemic keeps sales representatives from meeting with doctors in person. It also noted the impact of its direct-to-consumer marketing efforts featuring reality TV star Khloe Kardashian; AbbVie's celebrity endorser for Ubrelvy is tennis star Serena Williams.

Biotechs Face Daunting Launch Environment Going It Alone

By Jessica Merrill

10 Aug 2020
Several small biotechs are launching new drugs independently in a launch environment that now presents unexpected challenges caused by COVID-19.

Read the full article here

Reimbursement for Nurtec prescriptions also has grown rapidly during the early days of the drug's launch, Biohaven CEO Vlad Coric told the company's 10 August earnings call.

"We now have widespread insurance coverage with our managed market teams achieving 141 million covered lives, representing approximately 83% of covered commercial lives," Coric said. "This level of coverage is often the goal that is set for a full year after launch, never mind after one quarter."

Submissions for regulatory approvals outside the US are ongoing with a submission in the EU planned for early 2021. Biohaven also is expanding its migraine franchise with the development of zavegepant, an intranasally administered CGRP inhibitor that is expected to move into Phase III testing this year.

Lundbeck's Vyepti Disappoints In Partial Quarter

Lundbeck acquired its I.V. CGRP inhibitor through the acquisition of *Alder Biopharmaceuticals, Inc.* for up to $1.95bn and is under pressure to deliver a big return on its investment. (Also see "*Lundbeck CEO: Alder Buy Will Boost Pipeline*" - Scrip, 16 Sep, 2019.) However, sales of DKK14m ($2.2m) fell short in the second quarter as the COVID-19 pandemic kept patients from visiting infusion centers for treatment with Vyepti.

The company said its sales representatives reached just 10% of the top targeted prescribers after Vyepti's launch in April and about 30% of the top 20 accounts. However, negotiations with payers resulted in reimbursement

Lundbeck's Vyepti Launch In US Disappoints In First Half

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agreements with commercial health plans that cover more than 100m patient lives. Also, the Centers for Medicare and Medicaid Services issued a permanent J-code effective 1 October enabling coverage by the US government's health plans.

Lundbeck also is looking to expand Vyepti's use to additional patients. It expects results in the third quarter of 2020 from the Phase III RELIEF study testing the infused treatment in the acute treatment of migraine. The company also plans to start a Phase III study in the prevention of cluster headaches in the fourth quarter of this year.

By John Davis

13 Aug 2020

The coronavirus pandemic held back sales of Lundbeck's newest product, Vyepti, in the US during the first half, but the company spent less than expected on SG&A because of COVID-19, and increased investments in marketing infrastructure and restructuring R&D.

Read the full article here

In addition, Vyepti has been submitted for approvals in the prevention of migraine headaches in seven ex-US markets. A Phase IIIb study to support a filing in the EU was initiated in June; approval there is targeted for late 2021.

"We continue to forecast $600m worldwide peak Vyepti sales, assuming it captures a relatively niche 10%-15% market share to treat migraine," Jefferies analyst Peter Wolford said in a 28 August note. "We envisage commercial challenges ahead as the fourth injectable drug targeting calcitonin gene-related peptide (anti-CGRP) to market, and it could be difficult to differentiate against big pharma muscle, in our view, notably with infrequent quarterly but I.V. dosing."

Morningstar analysts said in a 13 August note that they expect peak Vyepti sales of DKK4bn ($636m).