Epilepsy: Key Metrics in the Nine Major Pharmaceutical Markets

Moderate Growth in the Epilepsy Market is Expected from 2012 to 2022

The global epilepsy market was valued at an estimated $4.2 billion in 2012. GlobalData expects the market to grow to $5.5 billion by 2022, with more than 50% of sales coming from the US.

Major drivers of market growth over this forecast period will include:

- Introduction of novel antiepileptic drugs (AEDs) with higher prices in the US and EU
- Introduction of the newer drugs into the Asian market, particularly in Japan
- Increasing access to epilepsy pharmacotherapy by the populations of India and China

Major barriers to the growth of the epilepsy market will include:

- A crowded marketplace, which currently comprises more than 20 AEDs, many of which are available in generic form, resulting in individual drugs struggling to distinguish themselves
- Concerns over decreasing healthcare costs as part of government austerity measures, which will impede market growth, particularly in Europe
- Generic erosion of branded drug sales following small-molecule patent and marketing exclusivity expiries, particularly affecting Vimpat (lacosamide) and Lyrica (pregabalin)
Companies Seek to Compete in a Crowded Epilepsy Market Through Novel Drug Development, Strategic Licensing and Acquisitions, and Expansion into New Markets

- Historically, the epilepsy market has been dominated by gamma-aminobutyric acid (GABA) modulators and sodium channel blockers. The major players in the market have been Pfizer, which markets the sodium channel blocker Dilantin (phenytoin); Abbott (North America) and Sanofi (outside North America), which market sodium valproate, which primarily modulates GABA; and Novartis, which markets the sodium channel blockers Tegretol (carbamazepine) and Trileptal (oxcarbazepine).

- However, the 2000s saw a shift in dominance in the epilepsy drug market with the launch of third-generation AEDs that focused on novel targets as well as improved tolerability and efficacy. UCB’s Keppra (levetiracetam) and GlaxoSmithKline’s (GSK’s) Lamictal (lamotrigine) grew rapidly to blockbuster status and have replaced the older gold standards in most western markets as first-line treatments. Even though both Keppra and Lamictal have faced declining sales following generic entry, UCB and GSK will maintain their dominance in the market by expanding their existing drugs into new markets, particularly in Asia, as well as by launching new AEDs, such as Vimpat and brivaracetam (BRV) from UCB and Trobalt/Potiga (retigabine/ezogabine) from GSK.
Eisai, a newcomer to the epilepsy market, is poised to become a key player during the forecast period through its offering of three AEDs acquired through licensing from other companies: Zonegran (zonisamide) from Elan, Zebinix (eslicarbazepine acetate) from Bial - Portela & CA, S.A., and Banzel/Inovelon (rufinamide) from Novartis, as well as its latest offering Fycompa (perampanel) which was developed in-house and has been recently approved in the US and EU.

Current strategies for growth in the face of steep generic erosion following patent expiration have included reformulation of pivotal products and strategic acquisitions or partnerships to expand pipeline and marketed product portfolios. The market entry strategy for new drugs is based on initially seeking approval for drugs as adjunctive therapies in the refractory partial-seizure population, the patient segment with the greatest unmet need.

Below figure provides an analysis of the company portfolio gap in epilepsy for the forecast period.
New Market Entrants Mainly Target the Unmet Needs of Refractory Epilepsy Patients and Improved Safety

- In the epilepsy drug market, the overall level of unmet needs is high. Despite numerous AEDs in the market, there is still an existing unmet need for the approximately 20% of patients with refractory epilepsy. More importantly, there is a lack of curative or disease-modifying drugs that will actually address the underlying mechanisms of epilepsy. In addition, the existing drugs are not well tolerated, which points to a need for drugs with better safety and side effect profiles.

- New drugs entering the epilepsy market, including the recently approved Trabalt/Potiga and Fycompa, have mainly focused on targeting refractory patients. Although there has been a marginal improvement in the number of refractory patients who achieve seizure freedom with the new AEDs, there is still a large population of these patients who could benefit from each novel AED that enters the market. In addition, new-generation AEDs, such as Keppra, and others in the pipeline, such as ganaxolone, are being developed to have fewer drug interactions and improved side effect profiles and overall safety. This addresses a major need in the AED market, since most of the older mainstay treatments, such as carbamazepine, valproate, and phenytoin, although effective, have very poor safety profiles and are not well tolerated.

Below figure provides a competitive assessment of the late-stage pipeline agents in development for epilepsy for the forecast period.

New Entrants Welcomed in the Market, but Face Stiff Uphill Climb to Gain Market Share

- By 2022, the AED market will be even more crowded, with almost 30 drugs. However, there will still be a ready market among the remaining refractory patients who are the first to be treated with any new drug entering the market. But from a commercial perspective, in order to launch a successful AED following the launches of drugs that are currently in the pipeline, the drug will need to show significant overall efficacy benefits compared with its competitors, while maintaining or improving on the safety and side effects profile of the current market leader, Keppra.
In addition, there are no existing or pipeline therapies for epilepsy that are truly antiepileptic in that they target the underlying disease and not just seizure symptoms. This is a prime need, which if addressed, would be revolutionary, both from a clinical perspective in terms of how patients with epilepsy are treated, as well as from a commercial perspective. Such a drug would be the first of its kind and would achieve unparalleled success in the market.

Therapies with Novel Mechanisms Will Revitalize the Antiepileptic Drug Landscape

- The epilepsy market has seen the approval and entry of two novel AEDs in the past two years: Trobalt and Fycompa. GSK's Trobalt, which launched in the EU in Q4 2011 and is anticipated to launch in the US as Potiga in 2013, is a first-in-class potassium channel opener. It is expected to be competitive on the market owing to its novel target, and to attain sales of $257m in 2022.

- Eisai’s Fycompa, which was approved in the EU and US in 2012, continues to enter the European market and is expected to enter the US market in 2013. It features a novel mechanism of action (MOA) as an aminohydroxymethylisoxazole propionic acid (AMPA) receptor antagonist, which will drive its uptake into the market. Unlike Trobalt/Potiga, Fycompa is currently in early Phase III trials in Japan, which means it is likely to enter the market in this country by 2017. Fycompa is thus expected to have higher peak sales than Trobalt/Potiga, at $526m in 2022.

- Brivaracetam from UCB is the only AED in Phase III development, and although it is a follow-on of Keppra, variations in its molecular structure make it more potent, and it possibly has a broader spectrum efficacy than its predecessor. For this reason, it is expected to be well received by physicians and compete for levetiracetam’s market share, increasing in sales to $583m in 2022.

What Do the Physicians Think?

- Overall physicians expressed a need for more AEDs and favorable opinions of those in pipeline development.

  “Among intractable epilepsy patients, any drug that helps treat an additional segment of them will be used, and because we don’t have a basis for using one or another, if it’s attractive, it will be used more.”

  [US] key opinion leader, November 2012

  “Brivaracetam is an interesting concept because it’s supposed to be “Super Keppra,” the follow-on from Keppra. The Phase II studies were very promising, but I think the Phase III were a bit of a disappointment; there might be some methodological issues in terms of some patient selection issues that they have come across. But I think that’s one of the more interesting of the new drugs that I’m really wanting to see in clinical practice, particularly if, as the Phase II studies suggested, that some patients who haven’t responded to levetiracetam are responders to this drug. So, I think that that’s going to be one drug to watch.”

  [EU] key opinion leader, November 2012
• However, with more than 20 existing AEDs, new ones currently entering the market, and more to come in the future, physicians are unsure of how all these drugs will fit in the treatment landscape, and lack a way to differentiate between them, particularly in terms of efficacy. Also, there are no predictive tools that would guide the choice of treatment from patient to patient.

“We have about 25 AEDs for focal (partial) epilepsy, but which one to choose? Upfront, it’s tough to say because we don’t have any tests to say, ‘this is the lamotrigine patient and this is the levetiracetam patient’.”

[EU] key opinion leader, October 2012

• In the future, physicians would like to see distinct new classes of AEDs that target different mechanisms, rather than more of the same drugs that currently dominate the market.

“Do we need the sixth or seventh sodium blocker? Do we need the tenth calcium channel modulator? I think we need new drugs, but more than that, I think we need new classes of drugs which address things differently.”

[EU] key opinion leader, October 2012

• Physicians believe that a better understanding of the disease mechanisms in epilepsy will be crucial to developing more effective treatments.

“I would not discourage the development of drugs, but I think we need to change the paradigm. But to change the paradigm, we need to understand things better, so we need a lot of basic research.”

[EU] key opinion leader, November 2012
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2 Introduction

2.1 Catalyst

The epilepsy market has been very dynamic since 2008, with several of the market-leading drugs losing patent protection and experiencing steep sales declines, particularly in the United States, including:

- UCB's Keppra (levetiracetam) (US patent expiry in 2008)
- GlaxoSmithKline's (GSK's) Lamictal (lamotrigine) (US patent expiry in 2008)

However, the decline in global sales of these products was buffered by their recent introduction into the Japanese market, as well as by a slower-than-expected uptake of generics for Keppra in Europe. Both of these former blockbuster drugs have also since been introduced to the market as extended-release formulations that hold exclusivity from generic competition during the forecast period. Levetiracetam (Keppra, Keppra XR, and generics) and lamotrigine (Lamictal, Lamictal XR, and generics) are predicted to remain key players in the clinical arena through the end of the forecast period in 2022, but will face stiff competition in market share from multiple new market entrants.

Since 2008, the epilepsy drug market has seen the approval and market entry of several major products, including:

- Eisai's Banzel/Inovelon (rufinamide)
- UCB's Vimpat (lacosamide)

And within the past two years:

- GSK's Trobalt/Potiga (retigabine/ezogabine) – launched in the EU in 2012; approved in the US in 2011
- Eisai's Fycompa (perampanel) – launched in the EU in 2012; approved in the US in October 2012

Of these new market entrants, Vimpat has experienced the most rapid uptake, providing competition for other sodium channel blockers, which represent the mainstay of epilepsy treatments in terms of mechanism of action (MOA). However, it is set to face patent expiry as soon as 2014, allowing the emergence of lacosamide generics, which will erode Vimpat sales. However, lacosamide as a whole (both Vimpat and generics) will continue gaining in market share during the forecast period, even after patent expiration.
Trobalt/Potiga, which is a potassium channel modulator; and Fycompa, which is an aminohydroxymethylisoxazole propionic acid (AMPA) receptor antagonist, are both new market entrants with novel first-in-class MOAs that offer patients, especially refractory patients, an alternative to the sodium and calcium channel blockers that have dominated the epilepsy treatment market in recent decades. Their safety and efficacy profiles, once tested in clinical practice, will determine their clinical position in the future treatment landscape and their significance as competitive market players.

The drivers for market growth will include the introduction of the newer drugs into the Asian market, particularly in Japan. India and China will also contribute to market growth as their populations obtain increasing access to epilepsy pharmacotherapy. The challenges will be the crowded marketplace, which currently comprises more than 20 antiepileptic drugs (AEDs), with individual drugs struggling to distinguish themselves, particularly in terms of efficacy.

2.2 Upcoming Related Reports

- GlobalData (2013). PharmaPoint: Migraine – Global Drug Forecast and Market Analysis to 2022

The drivers for market growth will include the introduction of the newer drugs into the Asian market, particularly in Japan.
11.8 About GlobalData

GlobalData is a leading global provider of business intelligence in the Healthcare industry. GlobalData provides its clients with up-to-date information and analysis on the latest developments in drug research, disease analysis, and clinical research and development. Our integrated business intelligence solutions include a range of interactive online databases, analytical tools, reports, and forecasts. Our analysis is supported by a 24/7 client support and analyst team.

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