Event – Efficacy concerns likely to delay J&J’s Comfyde

Johnson & Johnson’s regulatory track record so far this year, a year in which the healthcare giant was slated to be the envy of its peers by bringing a raft of new products to the market, has been reasonably successful. FDA approval for potential blockbuster arthritis drug Simponi, and a follow-on antipsychotic product, Invega Sustenna, has helped offset some disappointment over delays and rejections of psoriasis drug Stelara and ovarian cancer therapy Yondelis.

Next week J&J should receive a decision from the FDA over a new epilepsy drug, Comfyde, which could become the third biggest selling anti-epileptic agent by 2014 if analysts’ sales forecasts of $500m are met. However, following mixed and slightly disappointing pivotal trial results, confidence in the approvability of the product on the data submitted so far is low, suggesting a complete response letter requesting further evidence is the most likely outcome.

Comfyde, known generically as carisbamate, was filed by J&J on October 24, 2008, for the treatment of partial onset seizures in patients 16 years of age and older. Given a standard 10-month review period, the FDA should reveal its response by August 24.

Although a J&J spokesperson confirmed to EP Vantage that the PDUFA date of August 24 remains the current expectation, the FDA’s track record of delaying or missing PDUFA dates suggests the timing of the regulator’s decision is still a little unpredictable.

Safety strong, efficacy weak

So far J&J has completed two phase III trials of Comfyde and the results have been mixed. Study 1 showed that a 400mg dose of the drug significantly reduced seizures compared to placebo, whereas Study 2 failed to demonstrate any difference between the 400mg, 200mg and placebo groups.

J&J has submitted the 400mg dose for approval by the FDA, but the failure of Study 2 and the fact that the 400mg dose appeared to be metabolised too quickly leaving suboptimal levels of the drug in the bloodstream, suggests the FDA will at the very least want to see more consistent evidence of the drug’s efficacy.

To this end, J&J may have already anticipated the FDA’s response by starting an additional phase III trial last year with much higher doses of 800mg and 1,200mg, the results from which are due next year. In addition, a comparative effectiveness study against two of the biggest epilepsy drugs which are now available generically, UCB’s Keppra and J&J’s own Topamax, was initiated two years ago and results are expected in 2011.

On the positive side, the increasingly safety conscious FDA is likely to be encouraged by Comfyde’s safety profile, with an adverse event rate similar to placebo and much lower than currently approved epilepsy drugs.

However, with more questions than answers over the drug’s efficacy, it seems likely the FDA will want to see the results of the additional trials, particularly the higher dose study, before granting final approval.

Although some analysts still expect approval and launch this year, a delay of around 12 months would not be surprising.

Tough market

The problem for Comfyde will be in carving out a decent share of an epilepsy market which is now subject to fierce generic competition following the sudden expiry of key patents for four of the top five biggest-selling blockbuster products within the last year (Therapeutic focus – Tough market for new wave of epilepsy drugs, April 23, 2009).

The challenge will therefore lie in proving to the FDA and physicians that Comfyde offers a distinct advantage.
over the existing generic and branded products. Whilst the drug’s superior safety profile is certainly one potential unique selling point, until the data is available to support the drug’s efficacy, Comfyde’s chances of regulatory and commercial success appear limited.