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Abilify wins approval battle, but long-acting war is just beginning

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Otsuka and Lundbeck have good reason to celebrate yesterday's US approval of a once-monthly form of the antipsychotic Abilify, but the war for market share between the long-acting atypicals is just beginning.

The war will be waged in a shifting landscape and on several fronts, perhaps most importantly against the long-acting versions of established atypicals that Johnson & Johnson already has on the market. There is also the threat to the franchise of generic forms of the short-acting Abilify blockbuster. And do not discount the joker in the pack, a once-monthly new molecular entity from Alkermes that is reaching the end of phase III studies.

US approval for Abilify Depot, now trademarked Abilify Maintena, came on the FDA's action date yesterday and followed a complete response letter last July, proving that this earlier delay, caused by problems with sterile water used for making the drug, was easily solvable.

From a franchise protection perspective then, the timing is good, setting the follow-up drug up for launch on March 18, more than a year before the expected expiry of key US patents on once-daily Abilify (*Event – Abilify Depot long-acting in more ways than one, January 28, 2013*). The purely economic lifecycle management considerations aside, Lundbeck also cites the prevention of relapses with the long-acting formulation as a patient benefit.

The Danish company has to some extent been vindicated for shelling out $200m up front in November 2011 for co-marketing rights to Abilify Maintena under a global CNS collaboration. Otsuka's partner for once-daily Abilify, Bristol-Myers Squibb, has no stake in the depot form, and in any case the deal between the companies has been winding down gradually since 2010.

Most lucrative franchise

But it will be no easy business defending what is Otsuka's most lucrative franchise, which at present is worth over $5bn but which, without the new formulation, would have seen sales fall off a cliff within two years. Even so, a formidable task lies ahead of Otsuka and Lundbeck; 2018 consensus sales forecasts for Abilify Maintena seem conservative at $920m, though no doubt upgrades are in the offing.

The long-acting atypicals market is currently controlled by J&J, whose twice-monthly Risperdal Consta sold $1.4bn last year. This had declined 10% from 2011, largely at the hands of J&J's once-monthly Invega Sustenna, which after four years on the market achieved 2012 sales of $796m and is expected to grow at a compounded annual growth rate of 16% over the next six years. Sales of Lilly's once-monthly Zyprexa Relprevv are presumed to be minimal.

Alkermes has so far played a supporting role, licensing the technology used to develop Consta and Sustenna to J&J. But it could soon come to the fore, thanks to its own aripiprazole lauroxil (formerly coded ALKS 9070), a prodrug of aripiprazole, Abilify's active ingredient, and currently in two phase III studies in over 1,000 patients.

The interesting thing about lauroxil is that it could become the first marketed long-acting atypical that is not simply a reformulation of an existing drug, although this makes the clinical trial burden that much harder. Alkermes insists that as an NME lauroxil should not infringe Abilify's IP, and hopes to file it in 2014; the project is not yet partnered.

Perhaps because of this last point consensus sales forecasts for the Alkermes drug are very restrained, not even reaching $25m in 2018, according to *EvaluatePharma*. Alkermes's prodrug might just prove to be similar enough to Abilify to pose a threat, but it is still too early to quantify just how big a threat that might be.

And in Otsuka and Lundbeck's favour is the fact once-daily Abilify was by a long way the most popular of the atypical antipsychotics. They will hope that the depot formulation ends up dominating too, even if it has come late to the party.

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