Evaluate Vantage

March 15, 2013

FDA cancer scrutiny casts shadow on diabetes drug development

Jonathan Gardner

The FDA's notice that it is looking at unpublished data on pancreatic cancer risk with use of incretin mimetic drugs casts a shadow over further development in two diabetes drug classes. The regulator's recommendation that patients now using DPP-IV inhibitors and GLP-1 agonists should continue doing so probably has no immediate effect on sales of such blockbusters as Merck & Co's Januvia and Novo Nordisk's Victoza.

However, for those drugmakers waiting in the wings – such as Zealand Pharma and Sanofi with Lyxumia or GlaxoSmithKline with albiglutide – the announcement portends closer scrutiny of safety data and the danger of extended approval timelines. And even for Novo, which is hoping for broader use of Victoza in obesity, the knowledge that other candidates have foundered on cancer signals could create new headaches (*Without delay, FDA sends Lorqess back for more work, October 25, 2010*).

More detail needed

The regulator's announcement yesterday was thin on detail – just that researchers had found signs of pancreatitis and pancreatic duct metaplasia, a pre-cancerous cellular change, in tissue taken from patients who had died of unspecified causes. The former was a well-known risk in both classes; the latter, however, was a new warning flag.

The agency has asked the unidentified researchers for their data, as well as an explanation of the methodology and the tissue samples in order to make its own evaluation. Thus it is far from certain that regulators will take any steps once they have completed their review.

But with a condition as widespread as type 2 diabetes – more than 25 million Americans are estimated to have developed it – the agency is rightly cautious, especially as GLP-1s and DPP-IVs are among the classes that patients progress to if blood sugar is not controlled on first-line metformin monotherapy. Even if a low risk were identified, there could be significant harm.

A solid link would be bad news for both marketed products and drugs in development. However, even as action is awaited from the FDA there is new risk introduced for drugs in development (see table).

Late-stage incretin mimetics in development					
					Annual sales ww ($m)
		Product	**Generic name**	**Company**	**2018**
GLP-1 agonists	**Filed**	Albiglutide	albiglutide	GlaxoSmithKline	352
		Lyxumia*	lixisenatide	Sanofi/Zealand Pharma	511
	Phase III	Dulaglutide	dulaglutide	Eli Lilly	668
		Semaglutide	semaglutide	Novo Nordisk	15
		ITCA 650	exenatide synthetic	Intarcia Therapeutics	-
DPP-IV inhibitors	**Phase III**	SYR-472	trelagliptin succinate	Takeda	9
		MK-3102	-	Merck & Co	242
		Tenelia	teneligliptin	Handok Pharmaceuticals	-
		CWP0403	anagliptin	JW Group	-

* *Lyxumia is approved in the European Union*

For example, the GLP-1 Lyxumia awaits an FDA approval decision later this year, and a demand for new safety data has the potential to lead to delay. That probably explains Zealand's share price movement, which after an initial 8% rise yesterday following year-end results fell back to no gain on the day. The share is down another 1% today to DKK86.50.

Elevated interest

It is no surprise that, with Victoza sales expected to reach $3.56bn in 2018, there is so much interest in the GLP-1 class. Indeed, obesity is expected to comprise 16% of that total, and with millions more obese people in the US, the risk is only enhanced.

Take GlaxoSmithKline, for example, which bought out Human Genome Sciences in part to obtain the total value of albiglutide (*Game of hardball wins Human Genome for Glaxo, July 17, 2012*). Another high-risk gamble is Intarcia Therapeutics. It raised $210m in a venture capital round and debt placement last year, the biggest of the year, to finance phase III trials of its ITCA 650, a tiny implant secreting the GLP-1 exenatide, the active ingredient in Bristol-Myers Squibb and AstraZeneca's Bydureon (*VC dollars rain onto Intarcia on diabetes implant hopes, November 19, 2012*).

The findings will be keenly awaited. After reviewing the data, the FDA clearly could decide that there is no risk. But with so much time and money invested in these drugs, not to mention the millions of patients using them, waiting must be the hardest part.

All data sourced to EvaluatePharma.

To contact the writer of this story email Jonathan Gardner in London at JonathanG@EPVantage.com or follow @JonEPVantage on Twitter

+81-(0)80-1164-4754