

Without payer support beta-amyloid tracers will languish



[Joanne Fagg](#)

Piramal Healthcare's purchase of Bayer's molecular imaging arm to secure the beta-amyloid tracer florbetaben F-18 shows that there remains robust hope that a diagnostic test for Alzheimer's disease will be a blockbuster. The Indian group boldly predicted a \$1.5bn market for the imaging agent, believing in its potential to identify the degenerative disease early and to assist in development of targeted treatments.

The trouble is that the theory has so far not received much support, as witnessed by the muted reaction to the US approval earlier this month for a related product, Eli Lilly's Amyvid. A declaration that the federal Medicare programme will not cover the compound limits its commercial potential – only the most bullish analysts are willing to forecast sales of more than \$100m in 2018. Thus a change of heart from payers or success with advanced therapies may be necessary for Piramal's optimism to be shared by the market.

Seeing plaque

A drug that can reverse the progression for Alzheimer's disease, or even delay it significantly, has the potential to be the next big thing in pharma, and a companion diagnostic to identify eligible patients would be an equally significant find. Thus in conjunction with drug developers those involved in imaging have been exploring the amyloid angle, the deposits of protein fragments on nerve cells in dementia patients, including Alzheimer's disease, that accumulate because of an inability to eliminate beta amyloid.

Amyvid and the Bayer compound, also known as AV1/ZK (BAY 94-9172), are similar compounds that cross the blood-brain barrier and then bind to beta-amyloid, making them visible on PET scans. A third related product is General Electric's [18F]Flutemetamol, which reported successful topline phase III data last week.

However, a diagnostic that has no companion drug does little to guide care, which is probably one consideration in Medicare's decision not to cover Amyvid. Its label specifically notes that a positive scan does not establish a diagnosis of Alzheimer's disease, which is currently identified by clinical tests but can only be confirmed with an autopsy.

An additional factor that could discourage use was the relatively high percentage of Amyvid scans of Alzheimer's patients with false positives, false negatives or that caused disagreement among readers about a positive diagnosis. Indeed, it was the need for a reader training programme that caused FDA to issue a complete response letter on its first pass more than a year ago.

Finally, requiring referral to a PET scan also discourages use; identifying a characteristic blood biomarker of patients failing to properly eliminate beta amyloid, for example, might hold more promise in that the test could be conducted in physicians' offices.

Beta amyloid diagnostic imaging agents

Status	Product	Generic Name	Company	Originator	Clinical Trial ID
Approved	Amyvid	florbetapir F-18	Eli Lilly	Avid Radiopharmaceuticals	NCT01447719 NCT00857415
Phase III	AV1/ZK (BAY 94-9172)	florbetaben F-18	Bayer/Eli Lilly	University of Pennsylvania	NCT01020838
	[18F]Flutemetamol	flutemetamol F-18	General Electric	University of Pittsburgh	NCT01053312 NCT01265394
Phase II	AZD4694	-	Navidea Biopharmaceuticals	AstraZeneca	NCT00991419
Phase I	MK-3328	-	Merck & Co	Merck & Co	NCT00954538 NCT01385033

Compensation wanted

In addition the cost, \$1,600, will put off many payers. Thus until Medicare, the US programme for the elderly most at risk for dementia causing conditions, covers Amyvid, its commercial promise is likely limited; given that many private payers take their cues from Medicare reimbursement policies, it is not likely to result in coverage outside the programme.

Thus, sales forecasts remain heavily risk adjusted – EvaluatePharma’s consensus is \$66m in 2018. That estimate gives it a net present value of \$198m, substantially less than the \$300m Lilly paid to acquire the agent when it bought Avid Radiopharmaceuticals ([Eli Lilly snaps up leading Alzheimer's diagnostic, November 8, 2010](#)).

So too with Piramal today, which closed a little more than 1% down today, at INR443.80, not a sign of faith from investors after hearing the company’s claim it had purchased a blockbuster diagnostic. Florabetaben sales forecasts stand at \$31m in 2018. The fact that the purchase price was not disclosed belies any claims that the market is worth \$1.5bn.

Forecasts for both compounds could change should early sales returns be more optimistic, or in the event that Amyvid receives European Union approval. But while the beta amyloid theory remains unproven and a treatment for Alzheimer's remains elusive, the success of this product will depend more on the skill of Lilly’s regulatory affairs team than its marketing unit.