Evaluate Vantage

February 20, 2015

$200bn a year for new cholesterol drugs? Try again, payers

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The expected premiere later this year of the novel lipid-lowering agents alirocumab and evolocumab will be expensive for healthcare systems. And now payers have begun sounding alarm bells over pricetags assumed to be in the $10,000 range, and warning of annual bills that could amount to hundreds of billions of dollars from one drug class alone.

The scenario confronting payers will be different than with the last pricey launch, the hepatitis C drug Sovaldi, as many millions more people have high cholesterol and will take the drugs for years rather than months. That cost-driving force will be tempered by the existence of effective, cheaper drugs that are not used optimally, which should allow health insurers to use management techniques like step therapy to steer patients away from the more expensive offerings.

Eye-popping

Worries over the costs of Sanofi and Regeneron Pharmaceuticals' alirocumab and Amgen's evolocumab, which could be launched within weeks of each other later this year, were brought to the fore this week by executives from the pharmacy benefit manager CVS Caremark. In a blog post on the respected policy journal *Health Affairs*, they predicted eye-popping bills that could come due from these two new PCSK9 projects – citing as much as $200bn a year in the US.

Importantly, the CVS executives outlined possible utilisation management responses to limit spiking costs, requiring evidence of muscle inflammation or liver damage for patients claiming intolerance to cheaper statins like Lipitor; for those complaining of muscle pain multiple courses of statins will be tested to determine whether they are the cause. A greater unknown is how PBMs can improve statin uptake and achievement of higher dosing (*Payer demands threaten rosy PCSK9 forecasts, September 11, 2014*).

But forecasting hundreds of billions in annual costs could be a case of rhetoric getting ahead of reality, as the usually bullish sellside analysts come nowhere close to such a figure in five-year forecasts. Even accounting for peak worldwide sales, the equity analysts come well short of even $100bn a year. Combining the greatest analyst forecasts of peak sales for alirocomab ($5.2bn from Bank of America Merrill Lynch), evolocumab ($4.3bn from Leerink) and Pfizer project bococizumab ($2bn) only gets to $11.5bn a year.

Certain patients seem almost sure to receive the novel anti-PCSK9 biologicals. Those with familial hypercholesterolaemia with elevated LDL-C, for example, would be an obvious choice as they are a relatively small group that often cannot achieve control on cheaper statins, and are at elevated risk of cardiovascular events. Thus the cost exposure is relatively low and can be offset somewhat by preventing hospitalisation and cardiac procedures.

More expensive

The choice to allow less severely ill patients to use the PCSK9s is where it could get expensive. Obviously, if these are prescribed to every American with elevated LDL-C – a grouping that in five years will number around 70 million – the CVS prediction begins to look plausible.

But nobody expects this scenario to transpire, so a more realistic evaluation is necessary. A clearer picture emerges when one looks into the forecast models from a couple of sellside analysts for alirocumab, to be marketed as Praluent.

Wait a minute - how much?			
Shape of the potential US PCSK9 market in 2020, thousands of patients			
	CVS/Caremark**	Leerink	JP Morgan
Total hypercholesteraemia	n/a	66,876	75,867
Treated	n/a	33,107	36,416
Candidates for PCSK9 treatment			
Familial hypercholesterolaemia	620	n/a	655
Homozygous	n/a	n/a	under 1,000
Heterozygous	n/a	n/a	655
Statin intolerants	1,000-3,000	3,396	2,367
Treated with PCSK9s	n/a	472	213
Statin resistants/not achieving LDL-C goals	1,000	6,537	16,988
Treatable with PCSK9s	n/a	550	4,247
Total initial market	~3,500	1,022	5,115
Assumed annual cost per patient	$7,000-$12,000	$4,967	$9,716
Maximal* annual cost, 2020	$36bn***	$5.1bn	$49.7bn
Alirocumab US sales forecast, 2020	n/a	$1bn	$1.6bn
**Assumes every eligible patient will take PCSK9 agents*			
***Annual forecast, not 2020*			
****Does not include CVS's coronary heart disease forecast*			

The familial hypercholesterolaemia population is small, with those diagnosed as inheriting the condition from both parents numbering around 300, a small enough population that one treatment for it, Kynamro, is designated an orphan drug. The heterozygous population is a bigger at about 600,000, but together these conditions represent a small share of the US population.

These are slam-dunk patients that are almost assured to be eligible for coverage on the PCSK9 labels – and at $10,000 a patient a year the cost would be $6-7bn a year if every single one were taking them. But it is in populations like patients intolerant to statins or those unable to lower LDL-C satisfactorily where their widespread use is in dispute.

For example, the CVS executives, led by chief medical officer Troyen Brennan, wrote that covering the initial population of familial disease and statin resistance would represent a $16bn cost exposure. Analysts are nowhere close. The *EvaluatePharma* consensus for the PCSK9 class, which also includes the Pfizer project bococizumab, is $4.9bn in 2020.

Why is this so much lower? Dr Brennan is clearly offering a worst-case scenario. Leerink's analysis, on the other hand, was based on a physician survey that suggested, for example, that while as many as 45% of their patients did not achieve LDL-C levels below 100mg/dl, only 21% warranted a new therapy when available.

In addition, the physicians surveyed said that only 58% of patients not achieving adequate LDL-C reductions were on high-intensity statin treatment, suggesting plenty of scope to improve dosing protocols for millions of patients before moving them onto PCSK9s.

CVS's rainy-day forecast hinges on widespread use of PCSK9s in coronary heart disease, a scenario so implausible that its inclusion can only be characterised as scaremongering. Payers obviously have a vested interest in painting such a picture of price-gouging, just as pharma and biotech companies have in talking about their life-saving medicines. A more reasoned view of the PCSK9 outlook suggests that CVS is well off the mark.

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