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WAC-A-MOL

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While investors, media and even some payers have been touting the pricing of three recently launched drugs as sensible, it is not clear whether the lower-than-expected list prices will actually reduce costs to payers. But they are likely to result in lower co-pays for patients, which could increase access.

On March 28, **FDA** approved two drugs that were firsts for their indications: **Dupixent** dupilumab from **Regeneron Pharmaceuticals Inc.** and **Sanofi** to treat moderate-to-severe atopic dermatitis in patients not adequately controlled with topical therapies; and **Ocrevus** ocrelizumab from **Roche**'s **Genentech Inc.** unit to treat primary progressive multiple sclerosis (PPMS). Ocrevus also was approved for relapsing-remitting MS (RRMS).

Less than a week later, FDA approved **Teva Pharmaceutical Industries Ltd.**'s **Austedo** deutetrabenazine to treat chorea associated with Huntington's disease.

In all three cases the companies were lauded for how they priced the drugs. Dupixent was priced at a wholesale acquisition cost (WAC) of $37,000 a year, well below the most commonly cited comparator of psoriasis biologics, **Humira** adalimumab. **AbbVie Inc.**'s **tumor necrosis factor (TNF)** inhibitor has an annual WAC just shy of $58,000 a year.

Ocrevus' $65,000 annual price tag came in near parity with the cheapest MS drug, **Glatopa** glatiramer acetate from the **Sandoz Ltd.** unit of **Novartis AG**, which has an annual price of $63,200, and below other commonly used MS therapies, which have WACs of $70,000-$85,400 per year.

Meanwhile, the WAC for Austedo, a deuterium-substituted analog of **Xenazine** tetrabenazine, was $60,000 a year - a 61% discount to the $152,000 price tag for a daily 50 mg dose of Xenazine, a branded generic marketed by **Valeant Pharmaceuticals International Inc.** The cheapest tetrabenazine generic, launched in February, costs $39,700 annually for a daily 50 mg dose.

Pricing and reimbursement consultants who spoke with BioCentury noted that the lower list prices convey two clear benefits: lower co-pays for patients, which should translate into greater volume and access; and positive PR for the companies.

But payers could receive little to no rebate, which could mean the drugs' net cost to the healthcare system may be no different than that of their higher priced, but more heavily discounted, comparators.

DUPIXENT

Regeneron President and CEO Leonard Schleifer has publicly criticized the high prices of some drugs. For Dupixent, the company sought to determine a WAC that represented a "fair price" for the level of innovation the drug provides, according to EVP of Commercial Robert Terifay.

At the same time the company wanted to avoid having to give the larger rebates seen for marketed TNF inhibitors. Following Dupixent's approval, Schleifer said on a conference call that Regeneron expects the net price for Dupixent to be in the low $30,000s, which would imply an average rebate or discount of 19% or less.

"The thought was to put a fair price in the marketplace, but also make the product more affordable to patients."

Robert Terifay, Regeneron

To arrive at a fair price for Dupixent, Regeneron and Sanofi needed to identify the best comparator. Terifay said in the absence of approved therapies for moderate-to-severe atopic dermatitis, Regeneron decided the most appropriate comparators were biologics used to treat moderate-to-severe plaque psoriasis, such as Humira.

Express Scripts Holding Co. agreed with Regeneron's choice of comparator.

The PBM's spokesperson, Jennifer Luddy, told BioCentury, "There are older, less effective psoriasis treatments that cost more than Dupixent. And there are treatments that cost much less, but may not help patients with the most severe, debilitating form of the disease."

The intravenous formulation of branded generic Sandimmune cyclosporine from Novartis, which is used off label for inadequately controlled patients with moderate-to-severe atopic dermatitis, has an annual WAC of about $19,000, based on an average daily dose of 250 mg.

Terifay noted that Dupixent has demonstrated "much better efficacy" in its placebo-controlled Phase III trials compared to the small studies of cyclosporine in atopic dermatitis, and has a much better safety profile.

A second factor that went into setting a price was a desire to have low patient co-pays for the new drug.

"The thought was to put a fair price in the marketplace, but also make the product more affordable to patients," he said.

Most plans that cover specialty drugs require a co-pay or co-insurance that is calculated as a percentage of the list price, typically 20%. Terifay and Luddy both said a lower list price should reduce co-pays. Neither would say what Dupixent's co-pay would be.

Finally, Terifay said a March 24 report from the Institute for Clinical and Economic Review (ICER) on Dupixent's cost-effectiveness also factored into the pricing decision.

Dupixent's $37,000 list price and average net price in the low $30,000s fall within the range of cost-effectiveness established in ICER's report. The group said the drug was cost effective at prices of $17,369, $30,632 or $43,895 depending on whether the cost-effectiveness threshold was set at $50,000, $100,000 or $150,000 per quality-adjusted life year (QALY).

Regeneron provided data to ICER, and in return received early access to the report's conclusions for use in discussions with payers, ICER President Steven Pearson told BioCentury.

The lower-than-expected WAC is unlikely to translate into overall cost savings for payers, in part because of lower rebates than the 30-50% that has become common for branded drugs in indications with alternatives, and in part because the lower co-pays could lead to higher volumes of patients being treated.

Roger Longman, CEO of reimbursement consultancy Real Endpoints LLC, said the latter is typically payers' concern.

"You're not merely talking about a significant group of patients, but a significant group of patients who have not been treated with an expensive drug," he said. "This drug could be used very broadly, or there could be great demand for this drug, which, priced at this level, could be a really significant hole in budgets."

Regeneron estimates Dupixent's initial market size to be about 300,000 patients in the U.S. The drug is in Phase III testing in children and adolescents with atopic dermatitis, which could expand the market. Data are expected next year.

Regeneron said it doesn't have data on the number of children with uncontrolled moderate-to-severe atopic dermatitis; ICER's report cites epidemiology studies that state about 11% of U.S. children have atopic dermatitis, of whom 4-7% have severe disease.

In this case, Express Scripts doesn't appear to share the concern. The PBM praised the companies' approach to the launch as "responsible" and has already included Dupixent on the National Preferred Formulary.

Terifay declined to comment on the longer-term pricing strategy; however, he did say Regeneron has yet to increase the price of any of its three marketed drugs. Two have been on the market for several years: ophthalmic drug Eylea aflibercept was launched in 2011, Orphan therapy Arcalyst rilonacept launched in 2008. PCSK9 inhibitor Praluent alirocumab launched in 2015.

OCREVUS

Like Dupixent, Ocrevus' list price should make the therapy more affordable for patients compared to other options for MS.

Spokesperson Susan Wilson told BioCentury that Genentech priced Ocrevus below other MS therapies "because we believe the industry needs to reverse the trend of steadily rising medicine costs in MS."

She added that Genentech "does not intend to follow the pattern of aggressive price increases that are typical of MS medicines."

Neither Genentech nor Express Scripts would disclose likely co-pays, nor answer questions from BioCentury on whether the lower list price would directly reduce patient costs.

Longman noted that PBMs will have to include Ocrevus on their formularies for PPMS as well as for the much larger RRMS indication - except for the rare instances of indication-specific formularies, which might list a drug for one indication only.

He also speculated that Genentech could leverage the PPMS indication to offer little or no rebate, meaning the

drug's lower WAC would be similar to or the same as its net price and the net prices of other heavily discounted MS drugs with higher list prices.

"The other advantage people are beginning to think about is rather than starting the WAC price at $90,000 and then giving a rebate to the PBMs, which ends you at the same place as a net price of $60,000, you might as well start with the $60,000," he said.

"Ocrevus has this extraordinary lever into the marketplace, which is the fact it is the only drug for primary progressive MS, and will not be boxed out for the far broader market of relapsing-remitting MS, and ends up at the same place as if they'd priced it high," Longman said.

Express Scripts' Luddy confirmed that small or no rebates are common for novel, first-in-class drugs. "For drugs that are novel or provide a clinical benefit not available from any other therapy on the market, there is no incentive for the drug maker to provide a rebate," she said.

"I think that everybody has now recognized that the days of pricing willy-nilly are gone."

Roger Longman, Real Endpoints

Longman added that he still expects companies with drugs like Ocrevus to make annual price increases. But he noted that by starting with a WAC that is the same or very close to the net price, companies can retain a larger share of subsequent price increases - provided competitive new therapies haven't entered the market.

AUSTEDO

Three reimbursement consultants speculated that by settling on a low list price for Austedo in chorea associated with Huntington's disease Teva was positioning the drug for better uptake in tardive dyskinesia, a much larger indication for which it is under FDA review with an Aug. 30 PDUFA date.

"It could be that they are pricing at this level in order to penetrate the existing smaller market, knowing that if we get uptake there and there's all this off-label use that we will actually be on-label for, that is going to turn into a lot more use later on fairly easily," said Jack Mycka, global president and CEO of reimbursement consultancy Medical Marketing Economics LLC.

Longman and Darius Lakdawalla made similar comments. Lakdawalla is the Quintiles chair in pharmaceutical development and regulatory innovation at the **University of Southern California**

Teva was unable to provide an interview in time for publication.

The U.S. chorea population is about 32,000 patients. About 500,000 patients have tardive dyskinesia. Generic tetrabenazine is commonly used off label in tardive dyskinesia.

"I think Teva is extremely cognizant of the need to make sure that patients can afford this drug even when it is covered," Longman said.

"I think that everybody has now recognized that the days of pricing willy-nilly are gone," he added.

On April 11, FDA approved **Neurocrine Biosciences Inc.**'s **Ingrezza** valbenazine, making it the first drug approved for tardive dyskinesia.

While Neurocrine said it doesn't expect to announce Ingrezza's price until its May 1 launch, management has guided investors, most recently on a 4Q16 earnings call in February, to expect a list price of $20,000-$60,000 a year.

FDA approved Ingrezza without any major warnings for adverse events. Austedo and Xenazine have black boxes warning of an increased risk of depression and suicidality.

COMPANIES AND INSTITUTIONS MENTIONED

AbbVie Inc. (NYSE:ABBV), Chicago, Ill.
Express Scripts Holding Co. (NASDAQ:ESRX), St. Louis, Mo.
Genentech Inc., South San Francisco, Calif.
Gilead Sciences Inc. (NASDAQ:GILD), Foster City, Calif.
Institute for Clinical and Economic Review, Boston, Mass.
Medical Marketing Economics LLC, Montclair, N.J.
Neurocrine Biosciences Inc. (NASDAQ:NBIX), San Diego, Calif.
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland
Real Endpoints LLC, Westport, Conn.

Regeneron Pharmaceuticals Inc. (NASDAQ:REGN), Tarrytown, N.Y.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Sanofi (Euronext:SAN; NYSE:SNY), Paris, France
Teva Pharmaceutical Industries Ltd. (NYSE:TEVA; Tel Aviv:TEVA), Petah Tikva, Israel
University of Southern California, Los Angeles, Calif.
U.S. Food and Drug Administration, Silver Spring, Md.
Valeant Pharmaceuticals International Inc. (TSX:VRX; NYSE:VRX), Laval, Quebec

REFERENCES

Institute for Clinical and Economic Review. **"Dupilumab and crisaborole for atopic dermatitis: effectiveness and value."** (2017)