Evaluate Vantage

September 22, 2021

Incyte and Seagen face tricky launches

Elizabeth Cairns

Black box warnings could limit the sales of their newly approved therapeutics.

Approvals that come with a sting in the tail are a risk run by all drug developers, but arguably hit harder when the recipient is a smaller group. Both Incyte and Seagen suffered this fate this week, their respective drugs Opzelura and Tivdak gaining US approval but with black box warnings on their labels.

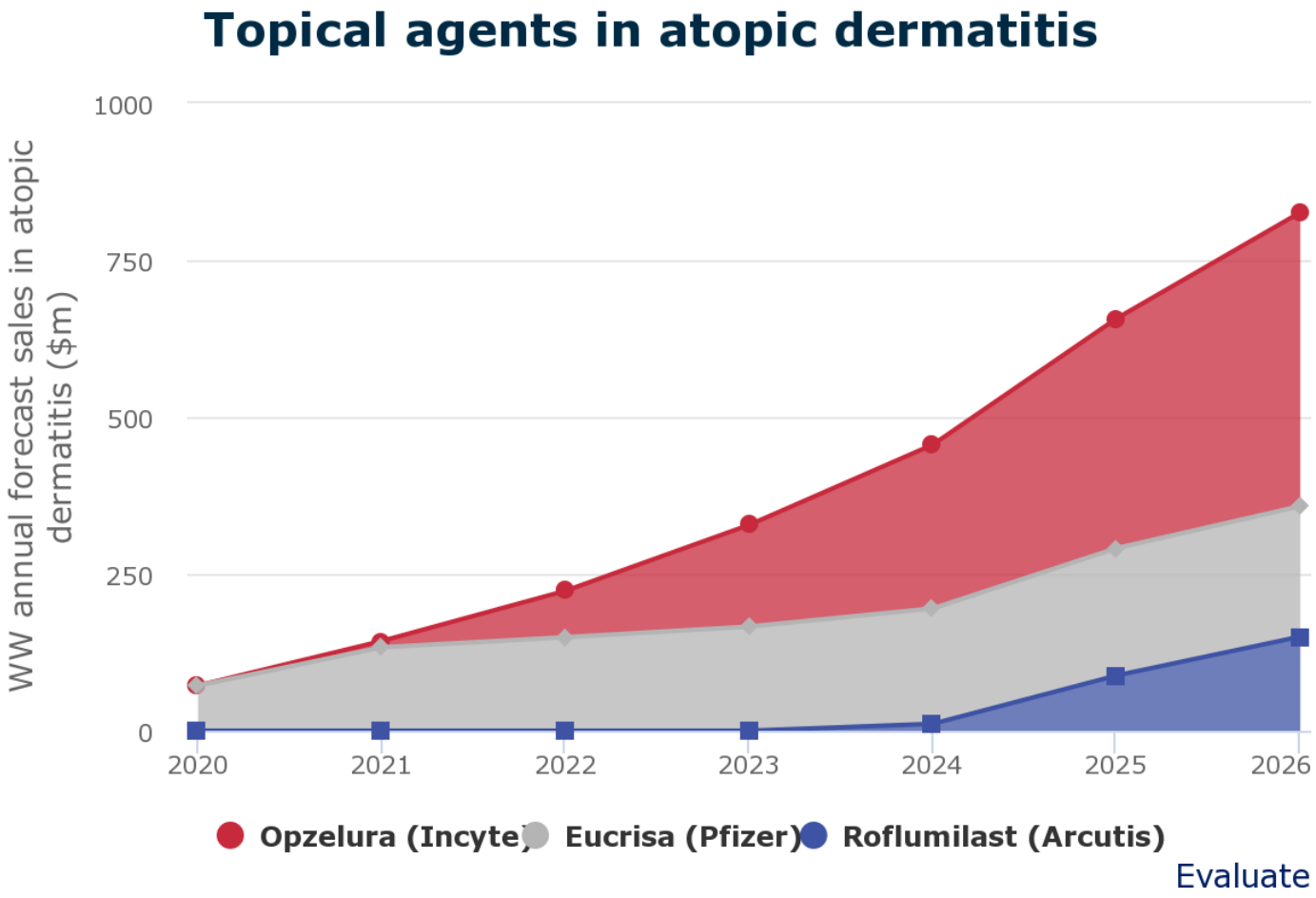
In both cases the anticipated sales for these products could take a knock. Tivdak's black box seems to have come largely out of the blue, and even that for Opzelura was worse than had been hoped.

As a Jak inhibitor Incyte's ruxolitinib, now branded Opzelura, was always a likely candidate for a black box warning, reflecting known risks of this class of medicine. But the atopic dermatitis medicine is a cream formulation, so there had been some optimism that any warning would be limited to the side-effects specifically linked to Opzelura. These are concerning enough: serious lung infections, skin cancers, blood clots and low blood cell counts.

But the FDA has included language covering risks seen with oral Jaks, too, like sudden cardiac death, lymphoma and other cancers, other serious infections and cholesterol increases.

Also disappointing was the FDA's apparent insistence that the drug be used for "short-term and non-continuous" treatment. The calcineurin inhibitors used in atopic dermatitis have similar language on their labels, but Pfizer's Eucrisa, a PDE4 inhibitor, does not.

Opzelura was one of Incyte's best hopes for diversifying its dependence on Jakafi before that product's patent expires in 2027. Opzelura is currently forecast to sell $779m in 2026, *Evaluate Pharma* data show, with analysts seeing 60% of this number coming from dermatitis. The remainder come from vitiligo, in which a filing is due before the end of the year. If the label crimps these opportunities, Incyte might be forced to look for other revenue streams.



Shrinking sales figures are also on the cards for Seagen and its partner Genmab, whose antibody-drug conjugate tisotumab vedotin, now called Tivdak, gained accelerated approval ahead of its mid-October Pdufa date for recurrent or metastatic cervical cancer, in the second-line and later setting.

Tivdak's label warns of a number of possible side effects, but the black box concerns ocular toxicity. Leerink analysts write that ocular adverse reactions were seen in 60% of cervical cancer patients given Tivdak in clinical trials. They included conjunctival effects (40%), dry eye (29%), corneal reactions (21%) and blepharitis (8%). Grade 3 ocular adverse reactions were seen in 3.8% of patients and included severe ulcerative keratitis, seen in 3.2% of patients.

Eyes on the prize

According to the label, an ophthalmic examination is mandated for patients before every dose, and as clinically necessary. These could prove cumbersome for some patients, especially since ophthalmologists tend to be non-hospital based, and could limit uptake of Tivdak.

Another aspect that could cause sales forecasts to fall is pricing.

Seagen management said that the product would be sold for $70-$90,000, after discounts, for a full course of treatment. This was lower than many analysts had modelled; Leerink reduced its forecast for peak revenues for Tivdak from nearly $1.8bn to just over $1.3bn. Sellside consensus compiled by *Evaluate Pharma* has the product selling $372m in 2026.

This could be an attempt to compete on price with Keytruda; it also notable that talk of price competition in this checkpoint class is getting louder by the week. Merck's big gun is already approved in second-line cervical cancer, for patients who express PD-L1, and data presented last week at Esmo could soon see it move into front line use.

Drug launches by smaller companies are often a source of worry, and Seagen and Incyte have been hobbled from the start. Investors might wish to remind themselves that even an approval with a regulatory admonition is better than nothing.

44-(0)20-7377-0800

Evaluate Americas
+1-617-573-9450

Evaluate APAC
+81-(0)80-1164-4754