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Can Glaxo’s COPD triple play a solo act?

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In the race to launch a triple combination in chronic obstructive pulmonary disorder – if there is a race at all – Glaxosmithkline has the upper hand. The group today announced that it had submitted its combination of Breo and Incruse Ellipta to the US FDA, following through on an earlier disclosed plan to accelerate its timetable by more than a year.

The only other big pharma player pursuing a triple combination in COPD is Glaxo's UK rival Astrazeneca, and then only as a reformulation play on Symbicort. The value of leading this chase can be questioned given increasing generic competition and disappointing recent launches of novel projects, although the decision to push up its filing schedule has analysts increasingly optimistic about the promise of the Glaxo project known as FF/UMEC/VI.

Triple dip

Following talks with the FDA, Glaxo in June said it was planning to submit the combination of a LAMA, a LABA and an inhaled corticosteroid by the end of 2016 on the strength of data already then in hand.

That announcement was followed shortly by readout of the Fulfil phase III trial, an 1,800-patient test in which Glaxo's combo showed superiority over the LABA/steroid combination Symbicort in lung function and health-related quality of life measures. Full data were disclosed at the European Respiratory Society (ERS) meeting in September.

A second, larger phase III trial called Impact asks whether treatment with FF/UMEC/VI is better at preventing exacerbations of COPD than Breo or Anoro Ellipta, a LABA/steroid and LABA/LAMA respectively, both novel entries in their categories. This trial will not read out until sometime next year, but the FDA apparently has seen enough at least to entertain a regulatory decision.

Neither of these trials will prove conclusively whether the “closed” combination of FF/UMEC/VI is better than an open combination of a LABA/steroid plus a LAMA monotherapy – such as Glaxo’s Advair plus Boehringer Ingelheim’s Spiriva.

The private Italian group Chiesi had attempted to meet this higher bar by testing its closed triple CHF 5993 against an open combination that included Spiriva. At ERS, Chiesi released the Trinity study showing that the Chiesi combination was non-inferior to the open combination; Chiesi has submitted CHF 5993 to European regulators.

One inhaler or two?

Advair has already lost patent protection and Spiriva will follow in 2018. Sales have dropped because of a tough payer line in respiratory disease, not because Advair has faced serious generic competition, although copycats are approaching.

As launch of FF/UMEC/VI has rolled forward, analysts have pushed up their forecasts – *EvaluatePharma’*s consensus stands at $672m in 2022, up from just $75m in June. It is still a far cry from the $8bn Advair was pulling down at its peak in 2013, and replacement products like Breo, Anoro and Incruse look like, combined, they will come about $1bn short of making up the Advair losses. It should be noted that the forecasts for these three new products have shrunk since launch.

In a US payer environment in which value is becoming a greater factor in coverage and reimbursement decisions, Glaxo needs to hope that its closed triple does better than Chiesi’s in head-to-head study against open combinations. Indeed, Boehringer has been circumspect about whether adding a third agent to COPD combinations can help patients.

Without a superiority claim it could be very difficult to persuade pharmacy benefit managers that once-daily doses of a closed triple are worth a premium price versus one puff of Spiriva and two of Advair. And, as generics enter, PBMs may grow less generous.

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