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UK's breakthrough therapy plan goes one better

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The UK drug regulator has seen the US FDA's bet and raised it, today announcing a scheme that looks like its American counterpart's "breakthrough therapy" designation but going a step further by offering the opportunity for early access to experimental innovative medications.

The two-step programme could allow patients to use unapproved drugs outside the clinical trial setting based on positive phase II data alone, before UK or European agencies have authorised commercial sale. Though risky, this approach attempts to ease the concerns of the pharma and biotech sector as well as patient groups that regulation cannot keep up with the pace of innovation.

Unclear benefit

The US version of breakthrough therapy has led to some unexpected developments and some approvals in about 18 months of existence. Imbruvica, Gazyva and Sovaldi are three designated drugs that are now on the market, although the effect of breakthrough therapy on the speed of approval can be debated.

Probably more surprising is the big pharma and biotech tilt of the designations so far – of 32 products disclosed to have been given the prized label, only about six are candidates without big pharma or biotech sponsorship (*Vantage Point – One year on, breakthrough designation remains an enigmatic accolade, August 22, 2013*). Given the muscle big companies can put behind their filings as it is, this questions whether the FDA's resources are being devoted to bringing forward overlooked, innovative drugs in the hands of cash-constrained biotechs.

The UK's approach, under discussion as part of a life sciences strategy since 2011, raises the stakes in that patients not part of a clinical trial could benefit directly from the regulatory push of the designation. Drugmakers can petition for a "promising innovative medicine" designation for molecules showing a positive risk-benefit profile to treat conditions for which there is no treatment or conditions for which the available treatments are unsatisfactory.

The document published by the MHRA acknowledged that sufficient data would not be available for many projects before phase III, but said candidates with "exceptional" data would be eligible at the conclusion of phase II trials.

With the designation, drugmakers could proceed to the second step, asking for a scientific opinion authorising unlicensed or off-label use, even before they have filed for a marketing authorisation. "Sufficiently compelling" data would result in the early access approval.

The catch: companies would need to provide the medication for free.

Drugs that reach patients using the pathway would still be subject to standard licensing requirements and, significantly, still be subject to the tough cost-benefit technology appraisal of NICE that has derailed some advanced drugs and forced others to undergo price cuts.

For how long?

In theory, this could see an agent being used by patients for months, or even a year or more, before regulators like the European Medicines Agency or national licensing authorities give their blessings.

The advantage for industry is that, in return for giving away expensive advanced medicines to Britons, there would in theory be a bigger patient population from which to draw scientific conclusions, in particular on safety, since the early access patients would not have the representative control population of a clinical trial.

Acheiving promising innovative medicine designation means early involvement from the MHRA and NICE to help with clinical trial design. This could also help drugmakers design a study to establish the scientific and, equally importantly, pharmacoeconomic case to back a drug. The promise of a speedy approval process giving access to a population of more than 60 milion people is difficult to ignore.

The UK authorities also have an ulterior motive – attempting to spur researchers to open clinical trial sites and,

following from that, investment from drugmakers. The closure of Pfizer's big laboratory in England three years ago was a wake-up call about the need to kick-start the whole sector (*Pfizer's R&D cull yet to take shape, February 7, 2011*).

It is important to point out the element of risk to this programme. Quickly waving through advanced medicines in areas of unmet need is one thing, but letting them be used outside the clinical trial setting is another, and it would not take much to discredit this programme. However, most of the patients willing to use unlicensed and off-label drugs are likely very sick and with few or no medical options, thus shifting the risk-benefit profile in favour of access.

Still, the value of these enhanced approval programmes remains unproven, meaning UK regulators are taking a pretty big chance. It will be interesting to see if authorities in other major economies follow this lead, or if this programme remains one of a kind.

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