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FDA's Breakthrough Bar May Be Set Too Low, Jenkins Says

by Derrick Gingery

Office of New Drugs Director recommends that EMA be careful how its sets the bar for its similar PRIME program to ensure it remains meaningful.

PHILADELPHIA – If FDA's John Jenkins could start the breakthrough therapies program again, he probably would make it tougher for sponsors to gain the designation.

Jenkins, director of the Office of New Drugs, said June 30 during a session at the Drug Information Association annual meeting that it remains an open question whether the agency has the bar for breakthrough products in the right place.

He also indicated he was not sure many of the existing designees have met the level of therapeutic advance envisioned when the program was created in 2012.

"The word that was used a lot [during a workshop on breakthrough criteria] was transformative," he said. "And I'm not sure that a lot of our designations really have lived up to that word of being transformative. They've been incremental. They've been advances in an area where there's an unmet medical need."

The highly popular program promises increased agency involvement early in the development process. The intent of the program is to help groundbreaking products get to market faster.

The Bar 'Is What It Is'

There have been questions about FDA's criteria for selecting breakthrough designees since the program was created as part of the 2012 FDA Safety and Innovation Act.

After the session Jenkins reiterated that people could question whether the threshold FDA chose is actually at the transformative therapy level. But he also indicated the agency has been consistent in how it has applied it.

Asked whether it was too easy to gain a breakthrough designation, Jenkins responded: "It is what it is."

As the head of the office that receives the majority of breakthrough requests, Jenkins can see first-hand the effects of where the bar is set.

And it is easy to see why he might want it raised because that could cut down on the number of requests as well as reduce the number of products in the program, which the agency has found a considerable resource burden.

But FDA likely would have a difficult time adjusting the bar now that the program is several years' beyond launch.

Jenkins' assessment of the breakthrough program also is interesting given that FDA has made specific efforts to ensure that the standard set is applied consistently. While individual review divisions make decisions on whether a product deserves a designation, the Center for Drug Evaluation and Research's Medical Policy Council also evaluates the requests (Also see "*Inside FDA's Debates On 'Breakthrough'*" - Pink Sheet, 11 May, 2015.).

As the program took shape, FDA stated that it could not enumerate specific requirements for the designation and that it would know a breakthrough therapy when it saw one.

But once it had designated a number of products, several common themes emerged, such as the level of efficacy seen compared to existing therapies (Also see "*FDA Breakthrough Designation Standards Revealed (Kind Of)*" - Pink Sheet, 1 Dec, 2014.).

Make The Program Meaningful, FDA Tells EMA

Jenkins' comments came as part of a request for advice he would give the European Medicines Agency as it sets up its PRIME (priority medicines) program, which has similar aims as breakthrough.

EMA awarded its first designations through the program a few weeks ago (Also see "*First EU PRIME Designations Go To Biogen, ChemoCentryx, Kite, NovImmune*" - Pink Sheet, 6 Jun, 2016.).

Jenkins said EMA must be careful in how it sets its bar for the PRIME program because it will be resource intensive for the EMA staff.

And he reiterated after the session that if the agency has too many priorities, then it cannot fulfill any of them.

"It essentially designates something as a super priority product," he said. "If you have too many

super priority products, then you can't devote the attention that you're promising to devote, you don't have the resources to do that, unless you do that at the expense of your other portfolio of work that you have to do."

Peter Marks, who became director of the Center for Biologics Evaluation and Research at the beginning of the year, agreed, recommending that PRIME maintain a high standard.

"Unfortunately, whether we like it or not, patients understand, they hear the word breakthrough and they put a lot of hope in these products and if everything becomes a breakthrough, then it's going to all be meaningless," Marks said.

Breakthrough requests and designations have far exceeded estimates. Since the program launched, CDER and CBER have logged about 415 requests and about granted 130 designations (Also see "*'Breakthrough Therapy' Designations*" - Pink Sheet, 2 Nov, 2015.).

The heavy workload was a topic of prescription drug user fee reauthorization talks. Both sides considered whether fee revenue could be directed to the breakthrough program to help FDA handle its popularity (Also see "*PDUFA Negotiations: Early Communications, Breakthrough Still On Docket*" - Pink Sheet, 18 Feb, 2016.).

The agency has tried other methods to reduce the breakthrough workload, including quickly rejecting unworthy designation requests (Also see "*Breakthrough Requests: FDA Adds Quick Screen To Pare Workload*" - Pink Sheet, 13 Nov, 2015.).

FDA also offers preliminary advice on the possibility of a designation (Also see "*Breakthrough In Two Pages: FDA Offers Preliminary Advice*" - Pink Sheet, 23 Mar, 2016.).

Entering the program also has not guaranteed marketing approval. Some products have failed despite the agency's help, including *Clovis Oncology Inc.*'s EGFR inhibitor rociletinib (Also see "*Clovis Plans Rucaparib Commercial Launch, After Abandoning Rociletinib*" - Pink Sheet, 6 May, 2016.).