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What Biopharma Should Know When Implementing a Compassionate Use Program

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Risk. In the age of social media, biopharma companies have to be more careful than ever about approving or denying compassionate use of investigational drugs. There is no safe "in or out" option. Denying compassionate use can result in a social media crisis, and providing it runs the risk of damage to research and valuation. Either choice opens the company to a crisis of reputation. Thus, effectively managing the risk associated with compassionate use is not only essential, but tricky.

Patients who have exhausted all current therapies to treat a serious or life-threatening disease seek hope through compassionate use of investigational drugs or what the FDA officially defines as expanded use. Patient organizations, state governments, and the FDA are all currently taking actions to expedite access to these drugs. And that easier access could conceivably mean hundreds or thousands of requests.

Ultimately, the final decision falls on the company to provide the drug. The FDA approves 99 percent of applications for expanded use. No law or agency can force a company to allow the use of a drug. To those outside the industry, the choice may seem an easy ethical and humanitarian one. But you know it's not that simple.

"The decision for approval or denial puts companies in a difficult bind," says Jason Byron, manager, medical ethics at UPMC Presbyterian Shadyside Medical Center.

"Obviously everyone wants to help desperate patients, but the company has no ethical duty or obligation to provide compassionate use. The ethical duty is to provide safe and effective care. We're not sure these products are safe and effective until they go through the entire approval process."

If a company decides to provide compassionate use drugs, Byron says there is an ethical obligation to be fair in allocating the drugs. J&J's Janssen is trying to achieve that level of fairness by partnering with a third party. The company is piloting a collaboration with a committee formed by Dr. Art Caplan at NYU that includes physicians, bioethicists, and patients to review requests for compassionate use of Janssen Pharmaceuticals.

QUESTIONS TO ASK BEFORE EMBARKING ON A COMPASSIONATE USE PROGRAM

With no ethical or legal imperative to provide expanded use, the choice may come down to what's best for the "many." Does helping the "one" now delay research that will help the "many" later?

Leadership has to carefully analyze each request. Asking questions such as the following can help when making decisions related to compassionate use:

- Is there a reasonable scientific theory for use in this patient?
- Is there enough of the drug to supply patients outside clinical trials?
- Can the company afford distributing an expensive preapproved drug?
- How close is the company to submission?
- What are the liability risks?
- How will the company end the program?

- If a request is denied, will a social media campaign damage a company's reputation and result in a public or investor relations disaster?
- If approved, will clinical trials be delayed by adverse events, causing the FDA to require additional research?

WILL OUR FINAL APPROVAL BE DELAYED?

Richard Mosciki, M.D., FDA deputy director for science reporting, recognizes that research companies have a real concern about the possibility that adverse events occurring with expanded use may delay final approval. He says, "It's [a delay in the FDA's approval] a rare event, but not zero." Mosciki said that searching the memories of his colleagues spanning nearly four decades of drug approvals and reviews, very few situations came to mind. In fact he said in a recent review of 5,000 expanded-access INDs (investigational new drugs), only two instances of a drug being delayed were identified.

"Our reviewers are very aware that these populations are at a higher risk for adverse events," says Mosciki. "They recognize that the disease itself often causes what appear to be adverse events. The circumstances surrounding an adverse event in expanded use are different from those in the carefully selected population of a clinical trial. Reviewers understand this, and they make that distinction."

LIABILITY IS ANOTHER CONCERN

We all know that patient outcomes affect stock prices and, ultimately, a company's valuation. Furthermore, considering there are unbudgeted costs (e.g., monitoring personnel time) involved with funding a compassionate use program, investors may question leadership's decision to offer it. That's why Dan Brettler, life science practice leader at Conner Strong & Buckelew (an insurance, risk management and employee benefits brokerage and consulting firm), says liability is another concern companies should have regarding compassionate use programs. "If a company develops a strategy against offering compassionate use, it will have to be prepared to defend that position against negative social media publicity," says Brettler. "An investor may sue not only for what they think is a bad decision, but for actions management took that harm the reputation of the company. It only takes a reasonable dip in the value of stock to draw plaintiff firms out of the woodwork on just about any low-hanging litigation issue."

Insuring against these risks can be very difficult, since many are new and not well-defined. "You deal with investor loss by protecting directors and officers with liability insurance," says Brettler. "But there are only certain risks you can transfer to insurance."

Leadership has to review policies for each known or potential risk to determine if it is covered. Not all policies cover compassionate use.

DEVELOP A PROACTIVE COMMUNICATION PLAN

"Reputation has a financial value," says Hugh Braithwaite, CEO of Braithwaite Communications, a marketing and PR firm that has worked with various pharma and life sciences companies. "As much as 50 percent of a company's value can be tied to its reputation." Braithwaite suggests establishing an SOP in advance to prepare for unexpected situations. The first step is to lower the threshold for what a company defines as a crisis.

Braithwaite says any challenge to a company's reputation should be considered a potential crisis. Then define the foundation, the guiding principle, by which leadership will make decisions so emotions won't cloud considerations in the heat of the moment

Take a cross-functional approach to assess risk. Have each company function predict risks associated with potential threats to the company, e.g. a social media campaign arising out of a drug denial.

Using the established guiding principle, test responses to each of those risks, and ask,

Daniel S. Brettler - Managing Director, SVP, Life Science and Technology Practice Leader for Conner Strong & Buckelew

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"Would we do this if we cared about our reputation?"

There are three steps to crisis management:

- Validate the concern.
- Show action.
- Control the narrative.

Instinctively, validating the concern seems difficult because leadership wants to support its position. Even if a company is clinically, legally, and scientifically correct, the public may still disagree. "If 1,000 people online think it's a problem, then it's a problem," says Braithwaite.

Restraint in responding is critical. He warns it's very easy for a company to make a public statement showing sincere compassion and understanding and, in the same sentence, invalidate its concern with the word "but." Do not follow a statement of compassion with a defense of the company position. Just outline the actions the company will take.

"You have to do something, so do anything that says you care," says Braithwaite. If the company decides not to provide expanded use, it may be able to set up additional research or find alternative studies for which the patient may qualify. Leadership also can make public appearances with patients and patient groups.

Controlling the narrative is the most difficult of the tactics. "Consumers can deploy faster than a company by a factor of 10 times," says Braithwaite. Consumers have the same communication resources as industry and can use them to affect their community actions within hours or a day. Companies are slowed by board actions, approvals, and their sheer size."

This emphasizes the need for preplanning. "You can control the narrative by preemptive action," says Braithwaite. "For instance, many of the statements and comments you'll need in a crisis can be written in advance." It's good practice to become involved with

patient organizations that may benefit from your products. The company can provide information and assistance to the group, stay abreast of issues, and possibly control conversation contemporaneously.

Braithwaite says, "If you're involved with the community, you'll see trends as they develop and be able to head off problems before they occur."

A COMPANY PLAN FOR HUMANITARIAN AND BUSINESS CONSIDERATIONS

When developing a compassionate use plan for its investigational drug SAGE-S47, Sage Therapeutics reviewed its resources and analyzed future needs. The plan is a response to the humanitarian requests of patients and a way to develop future clinical research sites.

SAGE-S47 treats the orphan disease status epilepticus, which affects about 150,000 patients each year. Patients suffer unremitting seizures and are placed in ICU in a medically induced coma. Mortality and morbidity are 66 percent. Sage received individual expanded-use requests early in the research phase.

Leadership assessed it had sufficient resources and began training ICU staffs to run the 547 trial protocol. As more patient requests were received, Sage united existing protocols into one expanded-use protocol, which allowed new patients faster entry. This presented an opportunity for the company. Because Sage trained personnel in those ICUs to use the clinical trial protocol, it expects some of those ICUs to join the Phase 3 trial as clinical test sites.

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