

Five Types of Exclusivities

By Lee H. Rosebush

Efforts to extend the life cycle of pharmaceutical products frequently involve innovations and improvements in product design, formulation, route of administration, and treatment indications. In addition, negotiation of agreements with competitors, including generic and biosimilar manufacturers, is frequently employed as part of a life cycle management strategy. However, recent changes in patent, regulatory, and antitrust laws have introduced greater complexity and higher risk into these strategies.

On October 23, 2015, a distinguished panel of BakerHostetler partners led an exclusive seminar in person and online at which they discussed these and related issues and provided suggestions for developing successful life cycle management strategies. Partner Lee Rosebush explains the various types of exclusivity.

Patents, and the protection they provide, are essential components of a company's strategic approach to bringing products to market and obtaining returns on investment that fund further research and development activity. There are powerful regulatory exclusivities in addition to patent rights that a drug sponsor should utilize to protect its products in the increasingly competitive pharmaceutical marketplace. Understanding the different exclusivities available and the pathways to obtain them will help shape a pharmaceutical company's research and development strategy and enhance its competitive advantage.

Regulatory Exclusivities

Rosebush discussed five types of Food and Drug Administration (FDA) regulated exclusivities available for pharmaceutical products: new chemical entity (NCE) exclusivity, new clinical investigation (NCI) exclusivity, orphan drug exclusivity, pediatric exclusivity, and biologics license application (BLA) exclusivity. These regulatory exclusivities provide significant protections that incentivize sponsors to develop and market safe, effective drugs. Each exclusivity has specific criteria an applicant must meet as well as limitations on what competitive activities are excluded.

New Chemical Entity Exclusivity

A sponsor may apply for NCE exclusivity for "a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the Act." The active moiety of a drug is the molecule or ion responsible for the physiological or pharmacological action of the drug. Rosebush differentiated enantiomers, which can be eligible for NCE exclusivity if they are new active moieties, from other chemical moieties (e.g., those that cause the drug to be an ester or a salt) that are not considered active moieties and therefore ineligible for NCE exclusivity.

NCE exclusivity can be obtained by submitting either a 505(b)(1) or 505(b)(2) application. A 505(b)(1) applicant will submit to the FDA safety and efficacy data generated in clinical trials performed by the applicant to support its request for exclusivity. A 505(b)(2) applicant relies at least partially on prior clinical data that the sponsor did not generate. While most NCE applications are granted under 505(b)(1), Rosebush emphasized that the FDA's analysis focuses solely on the active moiety, and if a 505(b)(2) applicant can provide sufficient data to substantiate such a new active moiety claim, the FDA will likely grant the NCE.

NCE exclusivity typically lasts five years and prevents the submission of any 505(b)(2) or Abbreviated New Drug Applications (ANDAs) for drugs containing the same active moiety. In certain circumstances, applications can be filed four years after the NCE is granted, which increases the likelihood of litigation on the back end of the NCE exclusivity period. Rosebush stressed that NCE exclusivity prohibits "me too" manufacturers relying on published clinical data from filing 505(b)(2) applications but does not prohibit the submission of 505(b)(1) applications. A sponsor will have to rely on its patent rights to exclude the 505(b)(1) applicant from entering the marketplace.

Sponsors should be aware, Rosebush cautioned, that there may not be a high bar set for competitors to convince the FDA of a new active moiety. The FDA recently indicated that it would not delve that deep

into the science when determining a product's active moiety. This reasoning led to a competitor receiving NCE exclusivity for a precursor product that must be metabolized into the sponsor's NCE protected product to produce the desired pharmaceutical effect. Further demonstrating the FDA's willingness to grant NCE exclusivity, the competitor used the 505(b)(2) pathway and relied on only a single Phase III clinical trial instead of the typical two trials.

New Clinical Investigation Exclusivity

NCI exclusivity can be granted to applicants submitting 505(b)(1), 505(b)(2), or supplemental applications. As the name implies, the sponsor must perform clinical studies, which the FDA defines as "an investigation in humans, the results of which (1) have not been relied upon by FDA to demonstrate substantial evidence of effectiveness of a previously approved drug product for any indication or of safety in a new patient population and (2) do not duplicate the results of another investigation relied upon by FDA to demonstrate a previously approved drug's effectiveness or safety in a new patient population." Rosebush pointed out that this definition precludes NCI exclusivity for studies that focus on bioequivalency or bioavailability, such as the studies used to support an ANDA.

NCI exclusivity prohibits the FDA from approving a 505(b)(2) or ANDA for three years, but it does not prevent applicants from submitting their applications. NCI exclusivity is available for "recycled" drugs, or those drugs deemed to have the same active moiety as previously approved drugs, provided the new drug relies on a new clinical study. "Recycled" drugs can include extended-release versions of drugs currently on the market or new salt forms of the drugs. NCI exclusivity is also granted for new indications, dosage regimens, patient populations, and formulations. Rosebush noted that if an applicant sponsors a clinical trial and has an indication at least slightly different than the reference drug, the applicant likely qualifies for NCI exclusivity.

Orphan Drug Exclusivity

Drugs intended for conditions that affect fewer than 200,000 people in the United States may be eligible for orphan drug designation. Sponsors who will be unable to recoup the costs associated with developing an orphan drug can also apply for orphan drug designation. Even treatments for unlikely events, such as bioterrorism, are eligible for the designation.

Orphan drug designation provides full market exclusivity, which means the FDA will not approve another sponsor's marketing application for the same drug with the same indication for seven years from the date of the orphan product's approval letter from the FDA. Rosebush cautioned that there are exceptions to the market exclusivity, including the sponsor not meeting demand

or withdrawal of the orphan drug from the market. Furthermore, if a competitor can demonstrate clinical superiority to the orphan drug, the competitor can bypass the orphan's exclusivity.

Rosebush explained that, in addition to the seven years of market exclusivity, a sponsor can apply for and receive orphan drug status before the drug gets full FDA approval. Applying early for orphan drug designation is advisable because sponsors receive tax advantages and reduced filing fees for drugs that receive this designation. Also, a sponsor can ask representatives from the FDA's Office of Orphan Products Development (OOPD) to attend future FDA meetings. From the perspective of the OOPD, granting orphan drug status without getting the drugs to market does not meet the objective of developing drugs for treatment of rare diseases. Thus, the OOPD representatives may provide valuable input at the meetings to assist a sponsor's efforts to get a drug formally approved.

Rosebush advised that receiving an orphan drug designation does not limit the sponsor to the orphan indication. While the drug will enjoy the market exclusivity for the orphan indication, the sponsor may still pursue a more broadly applicable indication. For example, Viagra, a well-known pharmaceutical treatment for erectile dysfunction (ED), was initially used to treat pediatric pulmonary hypertension, a condition affecting fewer than 200,000 people in the United States. Viagra received orphan drug designation for the pediatric pulmonary hypertension indication, but Pfizer was still able to get a broad label for ED at a later date.

Sponsors should be aware that orphan drug prices are regulated by the 340B Drug Pricing Program, which provides purchase price discounts to hospitals and pharmacies for orphan drugs. While these discounts are substantial (22.3 percent), they do not apply to non-orphan indications. For Viagra, a 340B eligible pharmacy would pay the discounted price for the pediatric hypertension indication, but it would pay full price for the ED indication.

Pediatric Exclusivity

Pediatric exclusivity is unique because it is only available for a drug if the FDA requests a sponsor to undertake pediatric studies for a specific indication. Rosebush emphasized that the sponsor can initiate contact and ask the FDA to request the pediatric studies. If a sponsor complies with the FDA's request to perform pediatric studies, the drug will receive the six-month pediatric exclusivity even if the drug is never approved for the pediatric indication studied by the sponsor. The six-month pediatric exclusivity period is added to any FDA exclusivity the drug enjoys, as well as the patent rights covering the drug.

BLA Exclusivity

Biologics are also entitled to FDA-regulated exclusivities. Unlike the five-year exclusive period for NCEs or the three-year term for NCI, section 7002 of the Patient Protection and Affordable Care Act (PPACA) provides 12 years of exclusivity for approved Biologics License Applications (BLAs). BLA exclusivity is unavailable for supplements or subsequent applications by the same sponsor for a change that results in a new indication, dosing schedule, dosage form, delivery system, delivery device, or strength. Only applications by the same sponsor for changes to an existing biologic that result in a modification of safety, purity, or potency can be granted an additional 12 years of exclusivity. Biologics can also receive orphan drug and pediatric exclusivities.

Conclusions

Sponsors need to be aware of the regulatory exclusivities that are available in addition to patent protection. These exclusivities are designed to encourage the development of new, safe, and effective treatments. While taking advantage of these exclusivities may help a sponsor realize a return on investment, failure to utilize the regulatory exclusivities, Rosebush warns, can result in increased competition, and sponsors using potential research and development resources to fund expensive litigation.

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