Limited Population Antibacterial Drug (LPAD) Approval Mechanism

Background: The Need for a New FDA Approval Pathway for High-Priority Antibiotics

As the number of patients succumbing to antibiotic-resistant infections rises, the number of new antibiotics in development has plummeted. These findings underscore the need for antibiotic incentives and a feasible approval pathway to advance research and development (R&D) of desperately needed new antibiotics. FDA has an essential role to play in ensuring that Americans have access to safe and effective drugs. But, in so doing, the agency must ensure that the risks associated with approving new products are appropriately balanced against the products' benefits to patients and to society. To date, when it comes to antibiotics, and particularly antibiotics needed to treat patients with the most serious bacterial infections, FDA's risk-benefit equation has been out of balance. The U.S. regulatory environment is the primary reason that the few pharmaceutical companies still investing in antibiotic R&D report they plan to focus future efforts on markets outside of the United States.

The LPAD Approval Mechanism

The LPAD approval mechanism would provide an important new approval pathway for antibacterial drugs that treat patients with the most serious infections where there exists an unmet medical need (i.e., where insufficient satisfactory therapeutic options exist). It is not feasible for antibacterial drugs that treat serious infections due to highly resistant bacterial pathogens to be developed using traditional, large scale clinical trials due to the limited numbers of patients in which such serious infections occur. Instead, under the LPAD mechanism, a drug's safety and effectiveness would be studied in substantially smaller, more rapid, and less expensive clinical trials—much like the Orphan Drug (OD) Program permits for other rare diseases. LPAD products then would be narrowly indicated for use in small, well-defined populations of patients for whom the drugs' benefits have been shown to outweigh their risks. For patients with serious infections and insufficient therapeutic options, a greater degree of uncertainty about overall risk associated with a drug can be tolerated. The LPAD mechanism will not be used to approve antibacterial products that treat more common infections or where sufficient alternative therapeutic options exist.

The LPAD designation, a description of the indicated population, the rationale for limiting use, and an LPAD logo (similar to the logo pictured above) would appear in LPAD products' labeling. Through this information, FDA would be providing notice to the health care community and payors that these products carry less precise estimates of risk and, as a result, the drugs' marketing and use should be limited to the indicated population. LPAD products' limited use also would help slow the rate at which resistance to these drugs develops—an important goal of the medical, public health, and patient communities. Of critical importance, the LPAD mechanism ensures that clinical decision-making remains in physicians' hands. FDA will have no role in regulating use of approved products within the practice of medicine. However, FDA will be able to monitor LPAD products' safe use through its existing Sentinel System.

Dr. Janet Woodcock, director, FDA's Center for Drug Evaluation and Research, has stated that two companies have expressed interest in pursuing the LPAD mechanism, if the pathway is established. Woodcock also said the LPAD mechanism provides a potential way forward for companies to pursue urgently needed antibacterial drugs. IDSA knows at least seven companies with products that would fit under the LPAD mechanism and help the patients who desperately need access to these drugs**.**

Antibiotics are typically priced far below their true value to society. As with OD designations, an LPAD designation is expected to increase the price of these drugs, compared with traditionally approved antibiotics, making investment in LPAD antibiotics more attractive to pharmaceutical companies. The drugs' higher price, in turn, will encourage payors, the health care community and providers to play a more active role ensuring LPADs are used as indicated, which will help preserve the drugs' effectiveness.
Finally, the LPAD designation could be temporary or permanent. If the drug sponsor later went through a traditional study route for an additional broad indication, the LPAD designation would be removed.