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Qualified infectious disease product designation: What's to GAIN?

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According to the Centers for Disease Control and Prevention (CDC), more than 2.8 million antimicrobial-resistant infections occur each year in the U.S. and are associated with more than 35,000 deaths annually.[1] The Generating Antibiotic Incentives Now (GAIN) Act was signed into U.S. law in 2012 to enrich the drug development pipeline targeted at resistant pathogens.

Background

Antimicrobial resistance has been hailed a 'silent pandemic' and continues to receive attention as a serious public health concern, especially in vulnerable populations including older adults and individuals who are immunocompromised and/or hospitalized. Amid a steady decline in new antibiotic development and related regulatory approvals from 1980 through 2010,[2] the GAIN Act was passed into U.S. law on July 9, 2012 as Title VIII of the Food and Drug Administration (FDA) Safety and Innovation Act (FDASIA)—a means to stimulate the development of new drugs targeted at infections from bacteria or fungi resistant to existing treatments.[3] GAIN positions incentives and provides additional guidance to sponsors developing antibacterial and antifungal drugs intended to address serious or life-threatening infections through a regulatory designation known as Qualified Infectious Disease Product (QIDP).[4] Incentives available to sponsors for drugs that achieve QIDP status include eligibility for Fast Track and Priority Review designation (even in the absence of demonstrating significant improvements over existing therapies—required criteria when these programs are applied to non-QIDP drugs) along with five years of additional market exclusivity.

Benefits of a QIDP designation

Fast Track designation. One of four expedited programs from the FDA to address serious or life-threatening conditions, Fast Track confers more frequent interactions with the Agency, eligibility for Accelerated Approval (assuming certain criteria are met), and Rolling Review of a marketing application whereby sections of the New Drug Application (NDA) can be reviewed by the FDA once completed instead of waiting for the entire application to be submitted. The FDA will grant Fast Track designation to a QIDP if requested by the sponsor.

Priority Review designation. QIDPs are automatically eligible for Priority Review, which provides a 6-month review target by the FDA for NDAs rather than the standard 10-month target. The FDA provides Priority Review to the first application or efficacy supplement submitted for a specific drug product and indication for which QIDP designation was granted. A Priority Review designation does not affect the length of the clinical trial period nor alter the scientific and medical standard for approval or the quality of required evidence.

Exclusivity extension. GAIN provides financial incentives for sponsors with QIDPs in the form of 5-year exclusivity extensions which are added to the end of nonpatent exclusives provided by the Food, Drug, and Cosmetics Act (FD&C Act), starting from the date of the NDA. In brief, nonpatent exclusivities stall entry of competing generics for at least three years in the case of new clinical investigations, five years for new chemical entities, or seven years for drugs targeted to rare diseases—yielding total exclusivity periods for QIDPs of 8, 10, or 12 years, respectively.

QIDP and qualifying pathogens

A QIDP is defined in section 505E(g) of the FD&C Act[5] as "an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections, including those caused by 1) an antibacterial or antifungal resistant pathogen, including novel or emerging infectious pathogens or 2) qualifying pathogens" as listed in 21 CFR 317.2.[6] The FDA interprets the provision intended to treat a serious or life-threatening infection as defined by QIDP as if it is intended to "diagnose, prevent, or treat such an infection", similar to other programs under the FD&C Act.[4]

The FDA, in consultation with relevant scientific and medical experts, published the first list of qualifying pathogens in 2014 and is also required by law to reassess the list at least every five years. Currently, 21 pathogens have been identified with the potential to pose a serious threat to public health for which QIDP designation requests can be based.[6] The FDA determines the list of qualifying pathogens with consideration for the following factors:

- Impact on the public health due to drug-resistant organisms in humans
- Rate of growth of drug-resistant organisms in humans
- Increase in resistance rates in humans
- Morbidity and mortality in humans

While a drug intended to treat a serious or life-threatening bacterial or fungal infection caused by a pathogen not included on the qualifying list may be eligible for QIDP designation, a drug that is intended to treat an infection caused by a pathogen on the qualifying list may not always be eligible for QIDP designation.

QIDP designation

The QIDP designation is available to new chemical entities or those which contain an approved active moiety (eg, novel, fixed-dose combinations or reprofiled drugs for novel indications or using novel proprietary delivery systems). More than one QIDP designation may be granted for the same active ingredient as the designation applies to a specific drug product from a specific sponsor for a specific indication. This means a single sponsor may receive a designation for multiple dosage forms of the same active ingredient, or for multiple indications. Antivirals, antiparasitics, biologics and devices are not eligible for QIDP designation nor are drugs which are infeasible to study in humans due to anticipated toxicity.

A sponsor may request a QIDP designation any time prior to submission of a marketing application, either as a pre-Investigational Drug Application (IND) correspondence or a submission directly to an open IND. A request for QIDP designation should contain the following:

- A summary of data which supports the activity of the drug as antibacterial or antifungal (e.g., *in-vitro* data, data from relevant animal models of infections and/or available data from Phase 1, Phase 2, or Phase 3 trials in humans)
- The specific serious or life-threatening indication(s) for which the sponsor is developing the drug and related rationale for developing the drug in the proposed infection(s)
- If available, information to demonstrate the product is a drug with the capacity to treat a serious or life-threatening infection caused by resistant pathogens or qualifying pathogens

When requests for multiple indications are combined in a single submission, the FDA recommends a separate rationale for each indication for which QIDP designation is requested. The FDA will respond to a QIDP designation request within 60 calendar days of submission.

History of QIDPs under GAIN

In the five years following enactment of GAIN, the FDA reported the review of 161 QIDP designation requests.[7] Through September 30, 2017, the FDA granted 147 QIDP designations; of which, approximately one-half were for novel drugs. The majority of novel antibacterial products were granted QIDP designation for more than one indication. Common indications for which a QIDP designation was granted by the FDA included acute bacterial skin and skin structure infection, complicated urinary tract infection, community-acquired bacterial pneumonia, hospital and/or ventilator-associated bacterial pneumonia and complicated intra-abdominal infections.

A total of 14 requests were denied, either on the basis that the product was not intended to treat or prevent an infection that is serious or life-threatening or the product fell outside the scope of GAIN.

In the same time period, the FDA approved 12 drug products with QIDP designation among nine drug substances—although none work via a new mechanism of action. All 12 products received new chemical entity exclusivity; thus, the GAIN extension provided each with 10 years of total exclusivity. Two of the drug products, CRESEMBA® (isavuconazonium sulfate) capsule and injection for treatment of invasive aspergillosis and invasive mucormycosis, also received orphan drug exclusivity and, factoring in the GAIN extensions, these products were provided 12 years of orphan drug exclusivity in addition to the 10 years of new chemical entity exclusivity.

A recent, published analysis determined an additional 11 drug substances with QIDP designation were approved between 2018 and 2022.[8] Indications among the 20 total QIDP-designated and approved drugs included genitourinary infections (n=9), gastrointestinal infections (n=6), skin infections (n=5), pulmonary infections (n=3) and systemic infections (n=1). The majority of the approved drugs targeted bacterial pathogens (75%).

The FDA issued a final guidance in May 2021 detailing the Agency's policies and procedures related to the designation of a QIDP under GAIN.[4]

Fortrea is an industry leader in clinical development programs for infectious disease. Our team of experts is well positioned to provide the relevant regulatory knowledge and key therapeutic insights to obtain a QIDP designation and other regulatory designations meant to encourage and streamline drug development in infectious disease.

Learn more about regulatory incentive opportunities for your program at fortrea.com

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