Understanding the FDA's Priority Review Voucher System

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In 1984 the FDA passed the *Orphan Drug Act*[1] *in an effort to push the industry to pursue the treatment of rare diseases that afflict less than 200,000 patients a year in the U.S.* Under the original *Orphan Drug Act*, companies were eligible for several extra years of marketing exclusivity, without generic competition, if they were able to get their drug approved for qualifying rare diseases. Industry responded by increasing the number of rare disease therapies pursued and approved more than tenfold.

In 2007 the FDA passed the *Food and Drug Administration Amendments Act (FDAAA) and* issued a limited number of special "priority review" vouchers that allowed drug manufacturers to expedite the review of any one of its new drug products, thereby reducing the standard drug submission review time from a target of 10 months to an expedited six-month review cycle.

Priority review should not, however, be confused with accelerated approval or fast track designation. Priority review does not omit safety and efficacy studies or require approval within a given time frame. It only sets a target of six, rather than 10 months, for FDA review.

Priority Voucher Program Attributes

Eligible candidates are granted two vouchers and receive priority review for each voucher: the drug winning a voucher for a neglected or rare disease, and the drug using a voucher for another indication. By moving a drug to faster review, there is the potential to slow other drugs. To provide the FDA with more resources and mitigate this cost, the voucher holder must pay the FDA an additional user fee ($2,457,140 in fiscal year 2019). Priority review vouchers (PRVs) do not expire. Likewise, the priority review voucher program for neglected diseases does not sunset. The current program for rare pediatric diseases will expire in October 2020 unless Congress renews the program, although a drug designated as a rare pediatric treatment can still receive a voucher if the drug is submitted and approved by the October 2022 deadline.

Qualifying Submissions

FDA incentive programs include orphan-drug designation and the associated benefits under the Orphan Drug Act for rare disease drugs; programs to encourage study of drugs used in pediatric populations; various programs to facilitate and expedite development and review of new drugs to address unmet medical needs in the treatment of serious or life-threatening conditions; and programs for certain tropical disease products and antibacterial products. In 2016 the 21st Century Cures Act (Cures Act) added a section (Section 565A) to the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360bbb-4a) requiring the FDA to award a priority review

voucher (PRV) to sponsors of certain medical countermeasure (MCM) applications that meet the criteria specified in that section. While there are existing incentive programs to encourage the development and study of drugs and biologics that may also be applicable to MCMs, section 565A of the FD&C Act provides an incentive specifically for development of certain MCMs, that may be used alone or in some cases in combination with other incentive programs. The full list of qualifying diseases can be found on the FDA's website.

Market Value

A voucher's market value derives from three factors: shifting sales earlier; longer effective patent life due to earlier entry; and competitive benefits from earlier entry relative to competitors. In 2015, Sanofi paid $245 million for a priority review voucher. Although the EMA had approved Amgen's cholesterol drug Repatha months ahead of Sanofi/Regeneron's product, Sanofi/Regeneron was able to be first to market in the U.S. because they used a priority review voucher. The market for vouchers has vacillated since the inception of the program with record values over $300 million realized in 2015 and 2016. Since then they have levelled off considerably, to the $80 million to $150 million level.

Priority Voucher Limitations

Initially both the Tropical Disease and rare pediatric priority voucher programs contained limitations regarding FDA notification and the number of times a voucher can be transferred or sold. However, these restrictions were lifted in 2014 with the passage of the *Adding Ebola to the FDA Priority Review Voucher Program Act.*[2]

Program Risks and Considerations

It is important to remember that a priority voucher does not assure approval by the FDA. Both *FDASIA*[3] and *FDAAA*[4] stipulate that the FDA only strives to come to a *decision* within six months. In fact, both the acts contain language that allows the agency to take longer than six months to complete its review if required: it is not a guarantee of six months. The tropic disease guidance reiterates that the FDA has a goal of 90 percent or greater reviews for submission in this program, while the rare pediatric voucher guidance clarifies that the *FDA aims to complete its review of the filed application and issue an approval or complete response letter within this timeframe. It does not mean that the application will be approved within this timeframe.* The rigor and criteria for submission review is the same as a standard review, and priority review will not save a bad drug from being rejected.

Conclusions

Few programs have attracted as much commentary as the PRV programs initiated by the FDA. Their effectiveness as an incentive for industry to pursue rare disease, MCM, and tropical disease drug therapies is yet to be determined. Structural inconsistencies still detract from the program. For example, the program does not recognize the value of pursuing innovative new drug therapies for rare diseases unless they are the first to address a qualifying rare disease. So, a less

effective drug submission could be granted a voucher while a potentially superior follow-on drug therapy would not qualify.

References

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