The Benefits of a Breakthrough: The Advantages of FDA Breakthrough Designation for Patients and Medical Device Manufacturers

April 2021 - **Mark Gosnell, Principal Consultant, Avania**

The goal of the FDA Breakthrough Devices Program is to provide patients and healthcare providers with timely access to innovative medical devices that may provide more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. The intended purpose is to speed up the development, assessment, and review of those products, while preserving the statutory standards for pre-market approval, 510(k) clearance, and De Novo marketing authorization, consistent with the agency's mission to protect and promote public health. The benefits to a medical device company for participating in the program may include increased speed to market and potential interest from the investment community. This paper is written to present the benefits of seeking FDA Breakthrough Designation status.

Not many devices receive breakthrough designation. The U.S. Food and Drug Administration (FDA) has awarded breakthrough designations to over 400 devices as of February 2021, accelerating in recent years. If your device fits the criteria, the designation confers multiple advantages to patients, manufacturers, and healthcare providers.

If you are considering applying for a breakthrough devices designation, prepare for a data-intensive process in close interaction with the FDA. The benefits of your hard work could result in a reduced time to market and the ability to improve the health and quality of life for many more patients.

Breakthrough Devices Program: Overview

The FDA has offered some type of expedited process for breakthrough devices since 2011. First, the FDA developed the Innovation Pathway pilot program to facilitate development and speed up review of breakthrough technologies.

In 2015, the agency launched the Expedited Access Pathway (EAP) program; this was then modified to the current Breakthrough Devices Program, which arose as part of the 21st Century Cures Act. The FDA issued final guidance on the Breakthrough Devices Program in 2018.

The voluntary program applies to medical devices and device-led combination products that allow "more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions."[1] The program applies to products subject to review under a PMA, 510(k), or De Novo classification.

Eligibility Requirements

For the FDA to consider a device or diagnostic for the Breakthrough Devices Program, it must meet two important criteria:

- The device provides for more effective treatment or diagnosis of life-threatening or irreversibly debilitating human disease or conditions.
- The device meets **at least** one of the following:
  - Represents breakthrough technology
  - No FDA approved/cleared alternatives exist
  - Offers significant advantages over existing FDA approved/cleared alternatives
  - Device availability is in the best interest of patients

How Patients Benefit: Better Treatments Sooner

An expedited regulatory approval/clearance process means patients and healthcare providers get more immediate access to beneficial devices and diagnostics. If a new device can help diagnose an acute stroke faster and more accurately, for example, getting it into the hands of providers six months sooner translates into many lives saved.

When applying for a breakthrough device designation, the manufacturer may submit "relative patient perspective information" as evidence of eligibility.[2] Reviewers also consider this information during pre-market approval (PMA) and De Novo classification requests.

Patient information gives manufacturers useful real-world information on current treatments and the impact of a disease or condition on one's quality of life. Relative input from caregivers and/or healthcare providers may also be considered.

While presumably the FDA would want as many people to benefit from novel devices and diagnostics as possible, it will not compromise statutory standards to do so. Its final guidance says a breakthrough devices designation preserves those standards consistent with its mission to protect and promote public health.

How Device Manufacturers Benefit

Medical device manufacturers benefit from breakthrough designation throughout a product's life cycle. The FDA recognizes breakthrough devices as products that stand to immediately help people. That's why they give these devices priority review.

1. Increased interaction with the FDA

The Breakthrough Devices Program centers on "interactive and timely communication" during the pre-market review phase, data development plan, and request for clinical protocol agreement.[1] Once it grants breakthrough designation, the FDA makes staff available to address questions concerning conditions and clinical testing expectations. The FDA also involves senior management in the review process.

The "sprint" discussions offered through the program allow the agency and sponsor to resolve specific issues quickly. Sprint discussions typically involve one topic (e.g., animal study protocol design) and defined goals. These interactive discussions happen within a specified time period, which varies based on need.

This level of communication with the FDA requires manufacturers to produce detailed information quickly, which is a challenge for many companies. However, in the process, manufacturers get ongoing access to high-level FDA managers—the insights gained can help make future submissions more efficient.

2. Efficient and flexible clinical study design

The FDA promotes the use of efficient, flexible study designs. When appropriate, it will consider:

- Prespecified endpoints regarding the minimum clinically meaningful effect
- Intermediate and surrogate endpoints
- Composite endpoints
- Adaptive study designs

3. Commercialization support

As companies innovate, the lingering question remains: Will payers reimburse providers for use of the device or diagnostic? New and emerging rules provide breakthrough device developers some needed relief around reimbursement challenges.

Breakthrough devices that meet certain cost criteria may receive an add-on payment from the Centers for Medicare and Medicaid Services (CMS) rather than demonstrate the substantial clinical improvement standard required under the existing new technology add-on payment (NTAP) system. The change was proposed to take effect in fiscal year 2021. The add-on payment is intended to provide Medicare reimbursement while sponsors gather real-world evidence.

The Office of Management and Budget (OMB), which is part of the Executive Office of the President, has approved a policy that would require Medicare and other insurers to cover breakthrough devices for up to four years.

"This final rule establishes a Medicare coverage pathway to provide Medicare beneficiaries nationwide with faster access to new, innovative medical devices designated as breakthrough by the Food and Drug Administration (FDA). The Medicare Coverage of Innovative Technology (MCIT) pathway will result in 4 years of national Medicare coverage starting on the date of FDA market authorization or a manufacturer chosen date within 2 years thereafter. This rule also implements regulatory standards to be used in making reasonable and necessary determinations under section 1862(a)(1)(A) of the Social Security Act (the Act) for items and services that are furnished under Part A and Part B."[3] This final rule was to take effect March 15, 2021.

However, on March 12, 2021, CMS postponed the implementation of the final rule for at least 60 days, thus delaying the immediate Medicare reimbursement for devices authorized through FDA's Breakthrough Device Program.[4]

Claims submitted with unassigned codes often get denied; therefore, physicians and providers are hesitant to purchase breakthrough devices, no matter how great the benefit. The new policy was assumed to cause a likely increase adoption of breakthrough devices. This ruling is intended to provide national Medicare coverage as early as the same day of FDA market authorization for breakthrough devices.[5] Whether or not the claims process will improve for breakthrough technologies remains to be determined as a result of this delay.

4. Interest from investors

Investors want to know a company's products have value to patients and physicians. They also want to see a return on their investment. A breakthrough devices designation gives investors confidence in your company. If the FDA has already recognized your product as one that will advance public health and/or offer superior treatment, investors are more likely to take a chance on your company.

Safety, Effectiveness, and Uncertainty

Breakthrough devices subject to a PMA are not absolved from proving reasonable assurance of safety and effectiveness through the rigorous examination of pre-market and post-market data. However, as part of its benefits-risks determination, the FDA will accept timely post-market data for breakthrough devices to fast-track development and review.

The FDA will accept a greater level of uncertainty with breakthrough devices, provided the uncertainty is balanced by other factors, such as the benefit to patients and adequate post-market controls to support pre-market approval. Review FDA guidance documents to learn more about its process.

Achieving a Breakthrough: How to Apply

Do you have a product in development that fits the criteria for breakthrough designation? Keep the following points in mind:

- You can apply for breakthrough designation any time before submitting for marketing authorization.
- The request is handled as a pre-submission application.
- As part of the breakthrough designation criterion of more effective treatment or diagnosis, the sponsor needs to show a reasonable expectation that the device can function as intended, and the functioning device can more effectively treat or diagnose the identified disease or condition. While it may be possible to accomplish this with bench or animal data, clinical data collected outside the United States or as part of an IDE clinical study is recommended. Therefore, when to apply for breakthrough designation needs to be carefully considered. For example, applying before an early feasibility study (EFS) investigator device exemption (IDE), the submission may increase investor interest, but if no clinical data is available, it may reduce your chance of receiving breakthrough designation.
- Request a breakthrough designation before starting the pivotal clinical trial to take full advantage of flexible study design opportunities.

Content for a breakthrough designation request includes the following:

- Cover letter indicating "Designation Request for Breakthrough Device"
- Background on disease/clinical need
- Device description
- Indications for use (clearly outline patient population meeting breakthrough criteria)
- Regulatory history (prior FDA interactions)
- How your product meets breakthrough criteria
- Planned marketing application type (i.e., PMA, 510(k), De Novo) and rationale

Following receipt of the breakthrough device designation request at the FDA, the agency will issue a decision to grant or deny the request within 60 days. In general, the FDA will interact with the sponsor by Day 30 and advise if any additional information is needed for review.

Conclusion

The FDA reserves a breakthrough device designation for select medical devices and diagnostics that serve an unmet need and/or provide substantially more effective treatment or diagnosis for debilitating and life-threatening conditions. The path to approval under the Breakthrough Devices Program requires intense focus on data and interaction with the FDA. The benefits to your company and to patients, however, are worth the effort.

Do you have a potential breakthrough medical device in development?

Talk to Avania to find out how we can help

Resources

[1] "Breakthrough Devices Program." FDA final guidance document, December 18, 2018. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/breakthrough-devices-program

[2] "Patient Preference Information—Voluntary Submission, Review in Premarket Approval Applications, Humanitarian Device Exemptions Applications, and De Novo Requests, and Inclusion in Decision Summaries and Device Labeling." FDA guidance document, August 24, 2016. https://www.fda.gov/media/92593/download

[3] Medicare Program; Medicare Coverage of Innovative Technology (MCIT) and Definition of "Reasonable and Necessary," https://www.federalregister.gov/documents/2021/01/14/2021-00707/medicare-program-medicare-coverage-of-innovative-technology-mcit-and-definition-of-reasonable

[4] https://public-inspection.federalregister.gov/2021-05490.pdf

[5] Medicare to cover breakthrough devices, https://www.medicaldesignandoutsourcing.com/medicare-to-cover-breakthrough-devices/