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Supplementing Clinical Development with a Managed Access Program

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Good news travels fast, especially when positive clinical trial data sparks demand for access to an investigational drug from physicians and their patients. However, patients might be unable to participate in a clinical trial for a variety of reasons, such as the following:

- The patient does not have access to a clinical study site.
- The patient does not qualify for a clinical trial.
- Enrollment in a study has closed.

While the primary pathway for patient access to new drugs is through the standard course of development, approval and commercialization, a Managed Access Program (MAP) can enable early access to patients when the following criteria have been met:

- The drug is intended to treat a serious medical condition
- No satisfactory approved treatment alternative is available
- The MAP will not disrupt ongoing or planned clinical trials.
- The primary objective of the MAP is to provide treatment, not collection of data for regulatory submissions.
- The likely benefits to the patient outweigh the potential risks.
- The MAP is affordable to the company.

The term "Managed Access Program" encompasses a variety of regulatory mechanisms globally, with the primary objective of providing treatment to patients prior to marketing approval. The mechanisms include Expanded Access Program (EAP), Named Patient Program (NPP), Autorisations Temporaires d'Utilisation (ATU) nominative (individual) or cohort (group) programs, and Compassionate Use Program (CUP).

MAPs can be implemented on a patient-by-patient basis, or, in some countries, for a group of patients. MAPs address the "access gap" that exists at any time during a drug's lifecycle when patient demand exceeds patient access for a drug. The greater the unmet medical need, the larger the access gap.

When a company establishes a MAP, it is usually for one of the following objectives:

- To make a drug in clinical development available to patients who are unable to participate in a clinical trial
- To make a treatment available to study participants after the completion of a study, but before it becomes commercially available
- To make an approved drug available to patients with a different therapeutic indication or in a different population
- To make a treatment that has been approved in one country available in a country where it has not yet been approved or where approval is not expected.
- To make a treatment available when commercialization is unlikely even though the drug benefits a small population with, for example, a rare disease
- To make a drug available after development or commercialization in a specific market has been terminated but current patients still need treatment

MAP Benefits to the Company

MAPs can offer a number of additional advantages to a pharmaceutical company, including the following:

- Provides a treatment option to fill the gap between clinical research and commercial supply.
- Generates valuable information from pre-approval use in clinical practice.
- Might uncover patient sub-types not represented in clinical trials.[1,2]
- Might help identify patients who can, instead, be referred to a clinical trial.
- Enhances the company's reputation and avoids negative publicity.

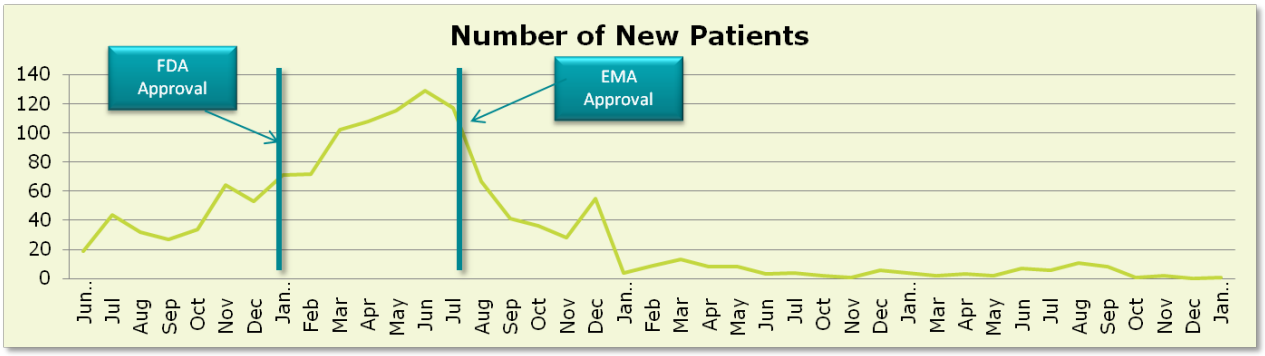
Patient Participation in a MAP

As a drug progresses through clinical development and subsequent commercialization, various events can trigger patient demand for the drug. For instance, an investigator might present positive clinical data at a scientific conference. Or, the media might be especially interested in the drug because it is first-in-class with a novel mechanism of action, it has an improved safety profile, or it offers a new option for an underserved population, such as patients with a rare disease. As positive news propagates through the traditional and social media, it can generate an empowered, vocal patient population seeking — if not demanding — early access.

Figure 1 shows a representative pattern of MAP participation. In this case, a large biotechnology company with a diverse pipeline of specialty and orphan drugs had a product in development for an oncology indication. While awaiting U.S. and EU approvals, the company experienced a high level of demand from physicians and patients who were aware of the published clinical trial data. The drug represented a major advance over existing therapies that were currently being used off-label, with limited efficacy and significant side effects. The company put a MAP in place to address the large number of requests for access to the drug.

As shown in Figure 1, the number of patients gaining access to the drug via the MAP grew steadily prior to FDA approval, and continued to climb during the period leading up to EMA approval. Once approved by both agencies, new participation in the program tapered off as commercial supply became available. The MAP ultimately delivered product to more than 950 physicians and their 1,300 patients in 43 countries.

Figure 1. New Patients Entering MAP



Source: Idis MA, November 2012

Planning and Preparation

MAP planning and preparation should begin six to 12 months in advance of anticipated demand. Developing and implementing a MAP requires coordination of many stakeholders across the company, including, but not limited to, clinical operations, medical affairs, regulatory affairs, pharmacovigilance and supply chain/logistics. A cross-functional team can ensure that:

- Criteria for participation are established
- Drug supply is adequate to support the program
- Physician educational materials are available
- Data on adverse events will be captured
- Enrollment in clinical trials is not compromised
- Regulatory approvals are obtained where needed

Determining whether or not to charge for the drug in a MAP can be a complicated decision that should be addressed on a country-by-country basis. The decision whether to provide free access or to charge for the drug depends on a number of factors, including the following:

- The program's objectives
- The company's ability to fund the program
- The feasibility of charging, as permitted by economic factors and regulations in specific countries
- The cost and projected price of the drug
- The availability of treatment alternatives
- The company's attitudes on compassionate use

Historically, MAPs begin at the end of the Phase III clinical program or when a drug has been approved in at least one market. However, with the increasing number of products being fast-tracked, companies have recently begun MAPs earlier, in some cases as early as Phase II. Earlier initiation is especially common with rare and orphan diseases, where treatments are not available and development pipelines are limited.

If a MAP will be running while registration trials are ongoing, it is important to define the scope of the populations(s) and indication(s) for the MAP. Clear and logical inclusion criteria support responsible review and approval of early patient access requests and identification of those who should be channeled to a clinical trial. A MAP running in parallel with a Phase II trial requires more stringency, usually limiting the program to those patients who fall outside the enrollment criteria for the clinical trial, or for patients who cannot gain access to a trial site. Later in the development process, broadening the criteria for inclusion into the MAP can be considered.

Transitioning Study Participants

Withdrawing a drug from study participants who are benefiting from an investigational treatment, or not making the treatment available to study subjects who received the placebo, can raise ethical issues. Regulatory authorities can require a study sponsor to make the study drug available to participants after the study is over and until it can be obtained commercially.

One option is to offer study patients participation in an open-label extension study (OLE). OLEs typically continue to monitor patients and collect data similar in nature and frequency to that collected for registration studies, even though that data might have very limited

value to the study sponsor. MAPs offer a more economical solution. Generally, MAPs collect only safety data, require little, if any, site monitoring, and pay physicians little or nothing for their participation, depending on the amount of data collected.

Transitioning study participants from a registration study to a MAP is appropriate when the rationale includes:

- Treatment, rather than collection of data, is the primary focus.
- The company wants to provide continuing access to treatment for patients who benefited from the treatment during a clinical trial or were in the placebo arm.
- The company wants a cost-effective alternative to an OLE study.
- The company no longer wishes to develop and commercialize the product, even though physicians and patients have identified a treatment benefit.

Conclusion

MAPs can address the needs of patients who lack the ability to obtain medicines within a clinical trial or through commercial channels. In a world of global communications and social media, physicians, patients and advocacy groups can apply great pressure on a company to provide access to their treatments in development. Pharmaceutical companies can anticipate the timing and quantity of possible patient demand during the development process. MAPs should be considered as an integral part of every product strategy. Advance preparation for this demand will ensure successful MAP implementation.

References

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