

The Named Patient Program (NPP)

Managing Access to Innovative Medicines Beyond US Borders

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Pharmaceutical and biotechnology companies have a number of options for meeting the demand for specific medications that have not yet received marketing approval. Such prelicensing demand is typically seen when a drug is completing late-stage clinical trials or during the interim between the end of trials and before market authorization. Because of increased product pipeline visibility, companies are experiencing increased demand for the wide variety of drugs in development or those approved in one country but awaiting approval in others. Innovative drugs for chronic or rare (orphan) indications are frequently sought before licensing. Oncology drugs are also subject to high preapproval demand, particularly from patients who are not responding to licensed and available therapies.

Within the United States, preapproval demand can generally be met through one of four mechanisms: participation in clinical trials, treatment protocol, treatment investigational new drug applications (INDs), or single-patient INDs. The latter two mechanisms — often grouped under the umbrella label of compassionate-use programs or expanded-access programs (EAP) — provide channels for groups of patients or individuals who do not otherwise qualify for clinical trials to access potentially life-saving medications



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if no other medical alternatives exist.

But, what if the demand originates overseas? Manufacturers can make medications available in countries outside the United States before approval in such markets through named patient programs (NPPs). These programs — well known in Europe and elsewhere outside the United States — enable physicians and patients to obtain access to medicines in their home nation before marketing approval has been granted there. Through these programs, patients in Europe with unmet medical needs can access drugs approved or in late-stage clinical trials in the United States before those drugs have been licensed in the patient's home country.

NPPs are an ethical way to manage patient access to medicines prior to approval and can bring significant value to pharmaceutical companies in terms of physician and patient goodwill, opportunities for physician and pharmacist education, data capture, and

product visibility. Here I provide an overview of the basics of an NPP, the medical and regulatory implications of these programs, and the benefits of partnering with organizations that specialize in developing, launching, and operating NPPs.

RELEVANT SCENARIOS

Consider the following:

- A global pharmaceutical company has received approval for a new oncology product in the United States and foresees significant demand from Europe, Australia, and Japan, where the product has not yet been licensed but where it will be rolled out as approvals are announced. As expected, this manufacturer has started receiving calls from foreign physicians requesting access to the drug, and the news of its impending US release is already circulating in online patient communities focused on the particular indication.

- A small biotechnology company in the United States has recently completed a phase 3 clinical trial of a new cardiovascular disease (CVD) product in France. The results are quite promising, and subjects in the drug arm of the trial have asked to be allowed to continue taking the drug. However, the company has not yet finished preparing its new drug application to the United States Food and Drug Administration (FDA), and it does not plan to file for

European Medicines Agency (EMA) approval for another year. Even after the applications are submitted, each regulatory body will take some time to hand down a decision (including a decision on reimbursement), although all indications suggest that the drug will be approved.

Can the company in the first scenario manage access to its oncology product in markets where the drug is not yet approved and remain in compliance with regional regulatory agencies? Or will it risk creating ill-will by denying access to a potentially lifesaving therapy to patients in need? How can the small biotech company manage access to its CVD drug for its former trial participants overseas, allowing them to continue the treatment on which they have come to rely?

In both of these scenarios, an NPP would allow the company to address these concerns by providing controlled access to the drug. NPPs allow companies to systematically respond to product requests directly from physicians or through national health services (depending on local regulations) on behalf of specific or “named” patients.

BENEFITS

NPPs can benefit pharmaceutical companies in a number of ways, not the least of which is management of demand originating from unlicensed markets. For example, such programs allow manufacturers to:

- Address worldwide demand for innovative medicines, providing controlled access to patients in need, particularly for chronic or rare diseases, even before a drug has received regulatory approval in any market
- Help patients who had been taking a particular drug as part of a clinical trial to continue the treatment once the trial has ended
- Facilitate prelaunch physician training regarding a product’s proper use and administration
- Improve uptake upon launch based on the existence of a pool of physicians and pharmacists who were already familiar with the product
- Capture “real-life” data to support marketing activities
- Gather additional adverse event data

- Track and maintain supply of a product to meet an anticipated demand.

Pharmacovigilance — the detection, assessment, understanding, and prevention of adverse events — is a significant factor in many companies’ decisions to become involved with NPPs. Adverse-event data are collected and reported through a regulatory-compliant pharmacovigilance plan. Such data gathered through an NPP could be used as supporting evidence for a company’s market access strategy. (Note that in most nations, collection of outcomes or efficacy data through an NPP is not permitted. Once outcomes or efficacy data are collected, the NPP has become a clinical trial and must follow the relevant regulations.)

NPPs enable complete control over prelicensing demand because of the process by which requests are addressed. Requests for drugs available through an NPP are received individually from physicians or national health services and must name the intended patient and his or her diagnosis. Thus, a manufacturer may have greater control because it can track demand more effectively, ensuring that only patients meeting set selection criteria have access to the drug. These programs also reduce the risk of counterfeiting as well as the risk that a physician in an unlicensed market will simply attempt to procure a drug from a licensed market on his own without proper training in its use.

This level of access control can be an advantage for companies considering seeking regulatory approval for additional indications. Because NPP adverse-event data can more closely reflect a drug’s “real-life” use, additional information on interactions and side effects can more easily be captured and analyzed for improved safety warnings and recommendations.

Companies have the option of charging for the drugs managed through NPPs. In most nations, payment comes through the national health system or directly from the patient, although a company can still provide medication at no charge if it chooses. For smaller companies, the ability to charge for NPP access can provide an important boost in revenue.

FINDING THE IDEAL MOMENT

If a manufacturer believes that a product will be the subject of significant patient and physician demand in the preapproval stage, it is best to start planning as early as possible for an NPP. Ideally, an NPP should be included in a company’s

WHAT’S IN A NAME?

Terminology surrounding the various mechanisms allowing for unlicensed drug access can be somewhat confusing. Here is a short list of the names commonly applied to these kinds of programs and the differences between them.

Expanded-Access Program: Any US program that allows patients who do not qualify for clinical trials to access new medications for treatment purposes before those medications have received FDA approval.

Treatment Protocol: A formal addendum to a clinical trial that allows companies to make an investigational drug available to large numbers of patients who do not qualify for study but who could benefit from the treatment regimen being investigated in the trial.

Treatment IND Application: A type of expanded access program recognized under FDA regulations. It allows an investigational new drug (IND) to be used for treatment if it is intended to treat a serious or life-threatening illness, if no suitable alternative is available, and the manufacturer is pursuing clinical trials aimed at supporting marketing approval in the United States. Regulations allow the FDA to permit access if drugs are in phase 3 trials or, under certain circumstances, phase 2 (1, 2).

Single Patient IND: Similar to a treatment IND but specific to an individual patient. Also called a Single Patient IND for Compassionate or Emergency Use (3).

Compassionate-Use Program: Colloquial name for expanded access program. This term is not officially recognized by the FDA (4).

Named Patient Program (NPP): Available for nearly 20 years in the United Kingdom and Europe, NPPs allow patients access to medications not licensed for marketing in their country if no suitable alternative is available or exists. Physicians request the drug on behalf of a specific “named” patient. Manufacturers may charge for the drug and are generally reimbursed either by the relevant national health service or directly by the patient. The terminology “expanded-access program” is often used interchangeably with NPPs.

development and approval plans for a particular drug from the beginning. With the program actually launching when the drug is in phase 3 clinical trials, about the same time the manufacturer is putting its global marketing and launch strategy into place. The time required from consideration of the NPP to program launch can be anywhere from a few weeks to six months, depending on parameters such as the nature of the drug, the number of markets expected to request it, and the organization's internal decision-making and approval process.

An NPP may initiate either centrally within a company's global marketing department or within a particular national arm; either way, it is best to include key stakeholders in the initial planning stage to ensure that everyone's needs are met and to get optimal buy-in at the outset. This means that regulatory, medical, operations, supply chain, and marketing departments must all be involved in NPP development from the beginning, as well as any affiliates in the markets you may wish to target.

THE COMPLEXITIES OF NPPs

Although some large pharmaceutical manufacturers have established their own in-house NPPs, many have found that managing the programs is very resource intensive, primarily because the regulatory environment in which NPPs operate can be quite complex and is constantly evolving.

Most countries legally allow for NPPs as a means of providing medications to patients when local alternatives are either unavailable or inappropriate. However, guidelines for unlicensed drug importation and prescription tend to vary widely nation-by-nation. Each of the 30 member states in the European Economic Area has its own set of nationalized regulations that must be understood and adhered to within an NPP. In addition, even after a drug receives EMEA approval, it may still take several months for that approval to filter through to the proper authorities in each country and for reimbursement decisions to be made. During this time, physicians and patients may be able

to access that drug through an NPP.

Companies can also find the logistics of NPP supply daunting. Generally, pharmaceutical companies are structured to meet the needs of distributors requiring bulk shipments. They may find it difficult to adjust to the needs of individual physicians and patients around the world who may require only a few doses at a time.

Given the extra time needed to meet various regulations and develop the necessary logistics, smaller biotechnology and biopharmaceutical companies may not have the resources available to consider an in-house NPP. Even larger companies, medical, regulatory, and marketing personnel are likely to be focused on managing clinical trials, preparing licensing applications, and preparing for launches in approved markets, and thus be unable to efficiently respond to NPP requests.

EFFECTIVE PARTNERSHIPS CAN CREATE EFFECTIVE NPPs

Establishing a program in conjunction with a strategic NPP partner can be expected to yield many benefits for a sponsoring company. Such a partner can have in-house resources for patient registration, physician training, regulatory affairs, quality assurance, compliance, and logistics that reduce the time and cost of running an NPP while adding value to the program. A strategic partner can also advise companies on the timing and scope of global NPPs and help them integrate such programs into their drug launch strategies.

Unlike contract research organizations, which tend to concentrate on clinical trial management or domestically focused expanded-access programs (e.g., treatment INDs), a strategic NPP partner will have extensive experience in dealing with multiple markets, languages, and regulatory environments simultaneously and will be able to leverage this expertise to facilitate the smooth and rapid NPP operation.

If you are looking for an NPP partner, you need to ensure it can

- Develop, implement, and manage the entire program from start to finish
- Advise on relevant "real-life" data capture that may be helpful for

reimbursement and health technology assessments (HTA)

- Ensure effective data capture and provide regular full reporting
- Facilitate pharmacovigilance, gather adverse-event data, and relay that data back to drug manufacturers for timely analysis and reporting
- Implement screening processes to ensure that requesting patients meet your company's criteria for drug access
- Address market-specific regulatory and importation procedures
- Offer storage and distribution facilities and services, allowing manufacturers to set aside a predetermined amount of product, warehouse it with the NPP specialist, and know that as requests come in the products will be appropriately labeled, packaged, and shipped
- Provide 24-hour telephone coverage ensuring that requests are processed promptly.

CASE STUDY: AN NPP IN THE REAL WORLD

One global pharmaceutical company received FDA approval for a new antibiotic for the treatment of life-threatening infections. Knowing there would be significant international demand for the drug, the company recognized the need to define a mechanism for managed access to the drug overseas. It wanted to control global demand after launch in the United States while capturing global market data in support of a three-year staggered release strategy. The company also had stringent and complex guidelines for patient screening criteria and a requirement that requests had to be fulfilled within 24-hours, regardless of their country of origin.

The company was able to address its requirements by engaging a strategic NPP partner. The partner established multiple warehouse locations on three continents, put the proper import processes in place, and set up a 24-hour order and shipment service, facilitating rapid request fulfillment. In addition, the partner worked with requesting physicians to ensure that patients met the screening requirements (a move that let the company identify key opinion

leaders in different markets), and provided detailed monthly reports on requesting locations and physicians, indications, and dosages.

The NPP, which is still ongoing, has allowed the company to provide managed access to its drug in 20 countries while gathering critical demand and uptake information and identifying brand advocates in multiple markets.

BE PREPARED TO MEET GLOBAL DEMAND

Physicians and patients worldwide are more well-informed than ever before because of the Internet, advocacy groups, and media coverage. As a result, pharmaceutical and biotechnology companies should continue to expect global demand for early access to their innovative medicines. The use of NPPs is essential to meet this demand. These programs provide manufacturers of all sizes with a legal and ethical means to

- Make innovative medicines available in a controlled way to meet preapproval demand from physicians and patients
- Create a prelaunch group of physicians and pharmacists instructed in

a drug's proper use

- Gather additional marketing and pharmacovigilance data
- Improve forecasting based on the volume of prelaunch requests made from various markets.


The benefits of NPPs are best realized when a company incorporates planning for such programs early in a drug's clinical development stages and includes all relevant parties in that process. Although some companies prefer to manage their NPPs in-house, others prefer to partner with NPP specialists who are equipped to manage logistical and regulatory complexities. Regardless of approach, these programs are essential for meeting global demand for preapproval access to innovative medicines.

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