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WHITEPAPER

Patient-centric oral solid dose formulation: Improving access and value across the product lifecycle

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Executive summary

Safety, efficacy, and quality have been the mainstay objectives of drug development and manufacturing for decades. In recent years, a fourth pillar has emerged that may hold the key to commercial success in today's increasingly competitive marketplace: patient centricity.

A common theme in healthcare, patient centricity in pharmaceutical manufacturing refers to the integration of patients' needs and preferences into drug design, development, and lifecycle decisions from early planning to production and delivery. This approach enables pharmaceutical companies to define a development path that will lead to enhanced patient acceptability of the product and, as a result, improve treatment adherence, clinical outcomes, and market access.

The demand for patient-centric drug development is being fueled by multiple considerations: the fact that patients are playing a more central and proactive role in managing their own healthcare, the growth of specialty drugs and personalized therapies, the need to compete for clinical trial participants, and increased regulatory pressure to demonstrate that new drugs can deliver meaningful improvements to patient health outcomes.[1,2]

Oral solid dose (OSD) formulations are particularly well suited to patient-centric design considerations. In addition to leading the market as a preferred drug form because of their efficiency, cost-effectiveness, shelf stability, and ease of administration, OSDs are uniquely customizable to the needs of specific patient populations. Through strategic selection of excipients, coatings, and delivery technologies, developers can alter and adjust such features as palatability and swallowability while optimizing dosing, bioavailability, release mechanism, and other performance attributes. By identifying specific characteristics of target patient populations that might inhibit safe and proper use of the drug product, developers can also make packaging and delivery decisions that will eliminate obstacles and enhance usability and compliance.

This whitepaper provides insight into the systematic application of patient centricity to the design of OSD products, focusing specifically on the following considerations:

- Patient-related characteristics that should inform drug product design decisions, such as age, swallowing impairment, motor impairment, dentition, cognitive impairment, and patient preference, among others
- Product-related characteristics that can be modified to address the needs of target patient populations, such as swallowability, palatability, dosage form, dosing regimen, release mechanism, and packaging
- The innovative technologies, materials, and processes that can be leveraged to map patient-related characteristics to product performance considerations to deliver a drug product that meets the needs and preferences of a target population

By beginning the drug design process with the patient in mind and leveraging the expertise and technical solutions needed to customize formulations to address the needs of specific patient populations, innovative developers can optimize manufacturing and bring user-friendly drug products to market more quickly.

Introduction

In pharmaceutical manufacturing, patient centricity refers to the integration of patients' needs and preferences into drug design, development, and lifecycle decisions from early planning to production and delivery.

One of the key drivers of the patient-centricity movement in drug development is today's growing concern with medication adherence. Nonadherence to drug treatment is associated with poor health outcomes and increasing costs.[3] In clinical trials, nonadherence to investigational medical product (IMP) can increase trial timelines, elevate operational costs, introduce data variability, undermine data quality, and, potentially, contribute to study failure.[4] One systematic review estimated that medication nonadherence resulted in an annual loss of 125,000 lives and was responsible for at least 10% of hospitalizations, substantial increases in morbidity and mortality, and $100 billion to $289 billion in annual healthcare costs.[5]

The growth of specialty drugs and personalized therapies, the need to compete for clinical trial participants, and increased regulatory pressure to demonstrate that new drugs can deliver meaningful improvements to patient health outcomes are also important pressures leading companies to consider the patient in all aspects of development.

Integrating patient centricity into the design and development of OSDs

A majority of drug products available on the market today are offered in OSD form, which is preferred by many patients over other forms (e.g., injectables, inhaled drugs, topical applications).[6] In one study, more than two-thirds of interviewed patients stated they would prefer daily intake of a tablet versus daily subcutaneous injections, citing ease and simplicity of administration and lack of pain as reasons for their preference.[7] Even within the OSD space, there are patient preferences and needs for specific forms (e.g., tablets versus capsules versus granules) and dosing (e.g., once daily versus twice daily), and these preferences are important contributors to a patient's satisfaction and subsequent risk of nonadherence.

As the population ages, the use of multiple medications taken simultaneously is on the rise, which increases the risk of intentional and unintentional nonadherence, drug–drug interactions, and adverse drug reactions.[8] This consideration further demonstrates the need for patient-centric drug design to identify and address any patient needs with respect to maintaining their complex treatment regimens and improving acceptability of a given OSD.

Considering the target patient population

Many pharmaceutical companies consider the patient as their "end user," but true patient centricity keeps the end user in mind from the very beginning. Patient-centric pharmaceutical drug product design (PCDPD) has been defined as the "process of identifying the comprehensive needs of individuals or the target patient population and utilizing the identified needs to design pharmaceutical drug products that provide the best overall benefit to risk profile for that target patient population over the intended duration of treatment."[9]

Many pharmaceutical companies consider the patient as their "end user," but true patient centricity keeps the end user in mind from the very beginning.

This may include specific needs associated with the population likely to need the drug (e.g., age, gender, geographic location), the disease the drug is being used to treat (e.g., symptoms of the condition, common morbidities), or a host of other factors that developers may not know about unless they engage with and solicit input from their target population.

Special populations

Some populations, including those in the following categories, have been well studied, contributing to our knowledge of specific patient-centric considerations related to OSDs.

- **Pediatric and geriatric patients**—Some of the special considerations for pediatric patients are the same as those for geriatric patients. These may include flexibility in dosing, mouth feel, palatability or taste/aftertaste, accuracy of dosing, and ease of use for caregivers. Safety of excipients, product appearance, and swallowability are also critical for patient acceptance and subsequent adherence.
- **Patients with motor impairment**—Some patients may have difficulty picking up and taking OSDs due to finger or hand impairment, limitations in arm mobility, or other motor impairments.
- **Patients with swallowing impairment**—Dysphagia is associated with many conditions and can limit the patient's ability to swallow OSDs and/or water or other liquids needed for the swallow. Similarly, dry mouth or other salivary conditions could affect the patient's ability to take certain OSDs (e.g., dissolving tablets).
- **Patients who suffer from mental illness or experience psychological distress**—Patients with depression, anxiety, psychosis, or other psychological conditions may lack motivation to adhere to treatment or have negative perceptions of OSDs that could affect adherence.

Additional populations with specific needs that are relevant to OSD design may include those with renal/hepatic clearance issues, psychosocial issues (e.g., access to caregivers, living status, employment status), health literacy limitations, or other impairments (e.g., cognitive, memory, sleep, or visual impairments).

Mapping product characteristics to patient needs

OSDs are particularly amenable to patient-centric design because there are several technical and design applications available that can be employed to meet patient wants and needs (e.g., shape, size, taste masking, and many more). Once the unique needs and preferences of the target population are identified, PCDPD can begin (see sidebar, "Finding and engaging the patient voice," for advice on identifying the needs of target populations). Working backward from the type of end product needed for the end user, the relevant product characteristics and options can be mapped out. The output of this exercise is shown in Table 1, which illustrates how certain product-related characteristics can address unique needs of special populations.

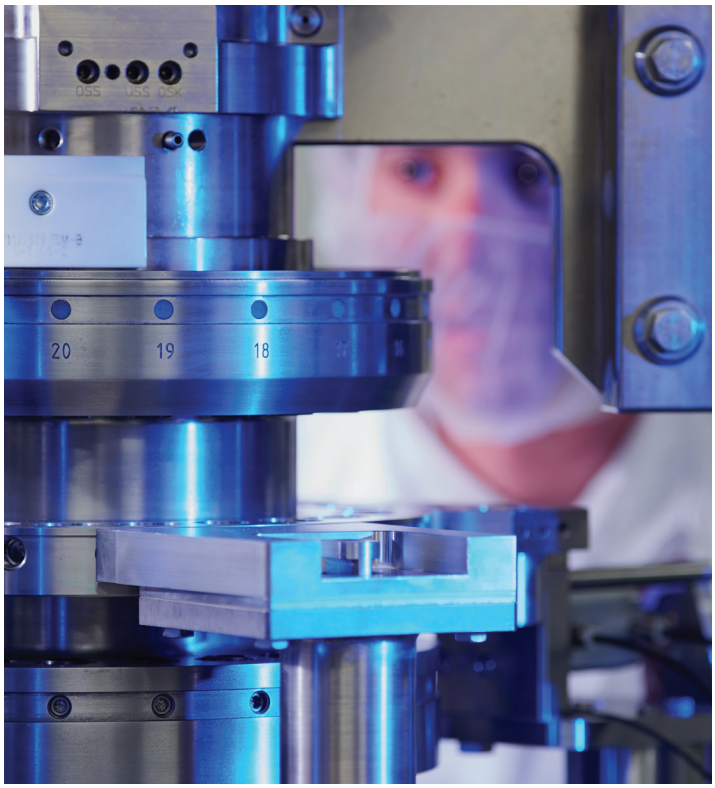

Table 1. Product-related characteristics relevant for patient-centric pharmaceutical drug product design.

Product characteristic	OSD consideration	Example population for whom considerations should be made
Dose	Once daily, twice daily, three times daily, etc.	Pediatric, geriatric, caregivers, cognitive impairments
Dosage form	Tablet, capsule, multi-particulate, solution, suspension, softgel, etc.	Swallowing impairments
Appearance	Product size, shape, color, embossing, etc.	Pediatric, motor impairments, visual impairments, cognitive impairments
Swallowability	Related to coating, solution viscosity, taste, aftertaste, mouth feel	Pediatric, geriatric, dry mouth
Dosing regimen	Frequency and duration of treatment	All groups
Packaging	Bottle, blister, sachet, stick pack, inner and outer labeling	Pediatric, motor impairments, health literacy
Container, closure system	Bottle, desiccant, cap	Motor impairments
Dosing and dosing device	Cup, applicator	Caregivers, motor impairments
Handling prior to use	Reconstitution, dispersion, dilution, divisibility of tablet	Caregivers, motor impairments, health literacy, cognitive impairments
Instructions for use	Directions on label with text and pictures	Health literacy, cognitive impairments, visual impairments

Innovative processes, strategies, and technologies

Today's manufacturing processes include several strategies and technologies that allow for patient-centric approaches to drug design across the lifecycle of the product. These processes not only can improve delivery but also can reduce the overall administration burden for patients and caregivers, thus decreasing risk of nonadherence. Following are some of the possible considerations.

- **Dose reductions**—Early development studies can identify possible formulations (e.g., amorphous form) that improve bioavailability of the drug, thus reducing the overall drug volume requirement and size of the OSD.
- **Fixed-dose combinations (FDCs)**—Two or more drugs contained in a single dosage form, such as a capsule or tablet, can reduce medication burden for patients and play an important role in lifecycle management of the product as it becomes a part of a patient's polypharmacy regimen. Several options are available for FDCs (monolayer, bi-layer, multi-particulate, tablet-in-tablet), and patient preference among those options should be assessed.
- **Modified release (MR) drug products**—By controlling the release of the therapeutic agent, MR products control drug absorption from the gastrointestinal tract. These products reduce dose frequency and the risk of blood-level fluctuations and potential toxicity. They can offer targeted delivery, reduce costs, and extend the product lifecycle. Types of MR drug products include delayed-release (enteric-coated), extended-release, and orally disintegrating tablets.

Finding and engaging the patient voice

No one is better positioned to inform a patient-centric approach to drug design than the patients themselves. But how can drug developers know what patients want? The following are some ways to incorporate the patient voice in drug development across the drug development lifecycle.

- **Desk research**—From published academic literature (e.g., *Journal of Patient Experience*) to social media (e.g., Facebook, Twitter), the internet is a treasure trove of documentation of patient experience and sentiment.
- **Partner with Patient Advocacy Groups (PAGs)**—These groups often play a major role in policymaking and payer decision-making. Early development of partnerships with PAGs can ensure their members' voices are heard at every phase of the development process.[10]
- **Formal patient interviews, ethnographies, focus groups, or surveys**—These can help companies understand the entire patient journey. Some organizations connect patients who are willing to share their experience with companies that want to learn more about a specific condition.[11]
- **Involvement in clinical trials**—Seek input from members of the target population in clinical trial design, including endpoint selection, visit schedule, etc. Incorporate patients in the development and selection of PROs for use in clinical trials.[12]
- **Discreet Choice Experiments (DCEs)**—DCEs can be applied in the pharmaceutical setting to measure a patient's preferences around various aspects of treatment (e.g., formulation and dosing).[13]

The FDA has demonstrated its acceptance of the patient voice as an important part of the development and approval process. From 2012 to 2017, the FDA held more than 20 disease-specific patient-focused drug development (PFDD) meetings with the goal of hearing directly from patients about their symptoms and the impact of their condition on their daily lives and their current treatments.[14] Additionally, the FDA is developing a series of four methodological PFDD guidance documents to discuss how stakeholders can collect and submit patient experience data and other relevant information from patients and caregivers for medical product development and regulatory decision-making.[15]

Packaging and beyond

Besides the drug itself, innovations in packaging can help improve acceptability of drugs and the overall patient experience.[17] Bottles, blister packs, tear-offs, push-throughs, sachets, and stick packs all have unique attributes that make accessing the contained product easier or harder depending on the characteristics of the patient using them. As with the design of the drug product itself, a patient-centric approach to package design should identify the target population and ascertain their specific needs and preferences, and then map packaging characteristics to those needs. Some considerations for package design include the need to keep products safe; prevent leaks, spills, and breakage; and maintain shelf life. These needs must be balanced with the patient's need to open, reclose, or reseal the package, if necessary, and extract the entire product (particularly for stick packs and sachets), while still keeping the product away from children, if applicable.

Beyond packaging, patient-centric drug design should also incorporate thoughtful labeling and directions for use. Instructions should be written at the lowest possible reading level, and graphic design techniques should be used to maximize readability and understanding. Even patient-amenable storage conditions should be taken into consideration. For example, a patient with limited mobility would likely prefer a drug that can be kept at the bedside rather than in the refrigerator in another room.

Conclusion

The concept of patient centricity as it is applied to the development of drugs involves careful thinking about the individual needs and preferences of the target population and how they can map to the specific attributes of the drug's design. Though limited in part by the requirements of each specific molecule and disease, the wide range of innovative approaches and technologies available in OSD manufacturing give developers an impressive patient-centricity toolbox.

Some companies worry that incorporating patient centricity into development may require more time and make the overall process less efficient, leading to delays in getting patients much-needed medications. Yet, time and resources devoted to the development of a drug that a patient will not take are time and resources wasted, and the opportunity to improve outcomes for those patients will not be fully realized. In reality, early engagement of the patient voice and incorporation of considerations for patient centricity can actually improve efficiency, while decreasing the risk of nonadherence and increasing the chance for better outcomes associated with the drug's efficacy.

The early integration of patient-centered development considerations is particularly important for special populations such as the very young, the very old, and those with motor or other impairments, but the approach can improve the treatment experience for all patients.

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Anil Kane has more than 25 years of experience in the science and business of taking molecules through the entire drug development process. His extensive knowledge spans early-stage development to scale-up and commercial manufacturing, and includes technical transfers between global sites and drug lifecycle management. He received his bachelor's, master's and PhD. degrees from the Bombay College of Pharmacy, University of Bombay, India, and served as a post-doctoral fellow at the School of Pharmacy, University of Cincinnati, Ohio. He also earned an executive MBA from the Richard Ivey School of Business, University of Western Ontario, Canada. He is a member of various international pharmaceutical professional organizations, and is often asked to speak about scientific topics on formulation, technology, and other technical aspects at major industry events. He has published many articles in international journals and delivered many talks at meetings and conferences around the world.

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