

The 3DP Revolution:

Planning Effective Brand Extension for In-Market Drugs



Introduction

Numerous drug companies are set to reach loss of exclusivity (LOE) on several high-performing small molecules between 2018 and 2022, putting \$74.2 billion in pharmaceutical sales at risk. When LOE kicks in, generic alternatives are then able to enter the market at an oftentimes dramatically reduced price point. As generic equivalents to high-value therapies hit the market, the consequences to drug developer revenues are substantial – exacerbated by the fact that, once LOE passes, payers begin using methods to cut brand access in favor of newly-launched generics and biosimilars.

Generic pharmaceuticals have been rapidly growing their share of the overall market in recent years. Between 2011 and 2017, the US generics market grew at a CAGR of 13%.¹ In 2017, 86% of prescriptions were dispensed as unbranded generics, which is a record high. Generic drug manufacturers are projected to continue boosting their position in the pharmaceutical market in the next few years, with generic sales projected to grow their share of market by 3% per year through 2020.²

There are a number of competitive threats that pharmaceutical companies confront as their patent-protected therapies careen toward eventual LOE. By planning as early as possible and leveraging the right technology, firms can strategically get ahead of looming challenges in the market that include both generic products and new branded drugs.

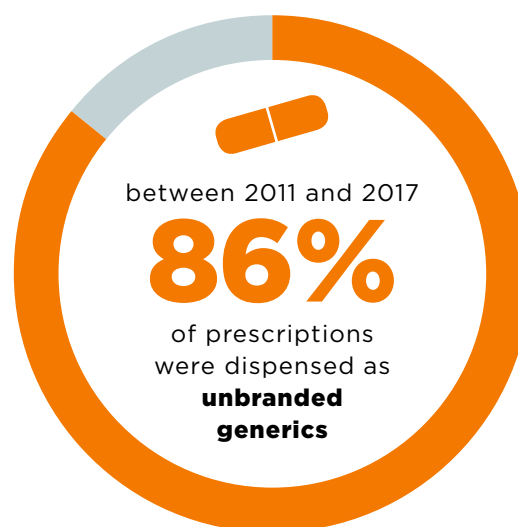
With the right partner, drug companies can take advantage of a variety of Lifecycle Management (LCM) strategies that prolong intellectual ownership

of their innovative therapies while simultaneously allowing them to expand the ways their drug can address currently unmet patient needs – therefore making their drug less substitutable by new, competing branded products.

Threats to In-Market Drugs

There are a number of top-performing pharmaceutical products on track to hit their LOE date in the next 12 months, including a number of therapies that generate \$1.0 billion to \$4.0 billion annually. For high-selling drugs like this, just a single day of sales lost to generic manufacturers can easily translate to tens of millions in lost revenue.

However, it's not just generic and drug category competition that presents a challenge to the market share controlled by branded drug manufacturers. Before generic developers manage to get a therapeutically equivalent product approved, branded drugs frequently face threats from new chemical entities (NCEs) entering the market. Novel compounds can enter the market and achieve the same therapeutic benefit, but may offer some new, defining characteristic that sets it apart, like greater efficacy, improved safety, higher functionality, or some other patient-centered trait.



1 US Generic Drug Market: Industry Trends, Share, Size, Growth, Opportunity and Forecast 2018-2023 https://www.researchandmarkets.com/research/4xchq8/us_generic_drug?w=5

2 IQVIA, Global Generic and Biosimilars Trends and Insights <https://accessiblemeds.org/sites/default/files/2018-02/Doug%20Long.pdf>

It's hard to predict when competition from sooner-than-expected generic products or fresh NCEs will arrive, but well-planned lifecycle management (LCM) strategies can enable pharmaceutical companies to kickstart many time-consuming steps as soon as possible in order to better protect themselves against imminent competitive threat.

What LCM strategies can be employed to immunize branded drugs from these threats? There are already some methods that pharmaceutical companies use to alleviate upcoming competition. Usual practices include co-pay cards, brand for generic contracting and authorized generic entry.

However, organizations can best defend against eventual loss of market share by revisiting the small molecule in question, reevaluating its dosage form with the latest technologies in mind, and rethinking the drug's position in the market. This is where the

most successful brand extension strategies are born.

Some examples of these strategies include reimagining existing formulations to reach a new patient population, coming up with an entirely new dosage form, or even combining one with another API to craft a brand-new tandem therapy. Strategies like this can boost growth of brand loyalty and be non-substitutable thanks to the drug's novel characteristics, further preserving brand share.

Introducing ZipDose

In order to be successful in these brand enhancement and extension strategies, companies must leverage the newest technology. Thankfully, an innovative solution is already here, and it's providing drug companies with a next-generation platform to help them preserve brand share and expand into new markets. It's called ZipDose – the world's first and only FDA-validated, commercial scale 3D-Printing



(3DP) system used for pharmaceuticals. The 3DP technology of ZipDose enables the development of novel dosage forms that extend beyond the capabilities of existing orally disintegrating tablets (ODTs).

ZipDose refers to the formulations that result from the additive manufacturing process of a 3D-printing system building dosage forms layer by layer, which generates a drug with a highly porous structure that dissolves quickly and is amenable to a full-range of formulation and taste masking options. The result is a more advanced solution to ODTs commonly produced today, and comes with a number of advantages.

This patent-protected technology allows drug companies to rework their in-market APIs in ways previously not considered, opening up a plethora of possibilities that enable a number of avenues toward brand enhancement and extension. And, while ZipDose is a powerful tool that can be applied to already-launched therapies, it's also the most efficient ways of formulating NCEs from the ground up.

Why 3DP?

Designing dosage forms with ZipDose holds a number of advantages when compared to conventional ODT technology. It's all about the process: 3DP uses a powder-liquid ink jet to intricately print a tablet layer by layer, resulting in a porous structure that enables the quick ingress of liquid. Unlike freeze-drying (lyophilization) or soft compression, which are the industry standards for typical ODT formulation, ZipDose's 3DP process doesn't use any sort of molding technique or compression forces, and 3DP formulations are dried using a moderate temperature combined with low humidity for just a short period of time.

This manufacturing process allows for additional protection and stability, and is why ZipDose can achieve a number of complex functionalities

simultaneously that standard tablets and capsules simply cannot, such as:

- **Rapid dispersion at high loads:** With a dispersion time ranging from 1 to 15 seconds, this technology can pack up to 1,000 mg of API into a single tablet. Conventional ODT technology only allows for a dose size of up to 250 mg (in the United States), with dispersion speeds ranging from 3 to 60 seconds.
- **Versatile Formulation and Taste Masking:** The 3DP manufacturing process allows formulators to utilize a full range of formulation and taste-concealing technologies because it accommodates more material (such as sweeteners and flavors, cyclodextrins and ion exchange resins for complexation, or coatings) into the interwoven tablet, achieving a full range of taste masking options more consistently than with traditional fast melt manufacturing.
- **Combining Multiple APIs:** A tandem therapy can be designed and layered alongside each other.

ZipDose is not limited to water insoluble APIs, and it is also capable of designing both extended-release and pre-gastric absorption drugs. The adjustable powder layering offers simplicity in dosage load variation, and can be used to rapidly change dose loads – which could come in handy during adaptive clinical trials.

3DP Technology and Brand Extension for In-Market Drugs

How does 3DP technology serve as the jumping off point for a number of brand extension strategies for in-market drugs? Successful therapies that are already commercially available (in conventional capsule and tablet form) can be reworked using ZipDose as a pathway to unlocking new patient populations. Limitations on taste masking or dose load that previously held formulators back can be revisited with 3DP technology.



Taste, Swallowing & Pill Burden

Two of the biggest opportunities for brand extension revolve around two major factors for patient adherence: taste and ease of administration (how hard a medication is to swallow).

When it comes to whether or not any given patient will stick to their medication regimen, the taste of a drug plays a critical role. This is why successful taste masking in products with higher levels of API are crucial.

“Taste is such an important part of the patient experience that it must be factored in at the highest level of consideration in planning the product profile,” says Don Wetherhold, Aprecia’s SVP of Business Development. “If the taste of a drug is unpleasant, the risk of medication avoidance is very high.”

Swallowing is another big factor. Many medications on the market, including numerous that must be taken at least once daily, are quite large – and more patients experience difficulty getting them down than many would think. In fact, 40-50% of US patients admit to having difficulty when swallowing medications, even if swallowing isn’t something they usually have a problem with in their day-to-day eating and drinking.

It’s a common experience that frequently goes unchecked. For patients who suffer from Dysphagia, the clinical term for difficulty swallowing, 60.3% don’t tell their doctors about it and 79% don’t tell their pharmacist.

Market studies indicate that desire for ODTs are actually quite high in the general patient population, with 70% of consumers reporting that they would ask their doctor for ODTs. Additionally, 70% of the patient population indicated that they would purchase ODTs and 80% admitted to preferring them over regular tablets or liquids.

Existing fast melt technologies have been able to address this issue to a point, but have been limited by low dose load ceilings. Therefore, traditional ODT technologies have not been applied commercially to drugs that necessitate high doses of API, which are usually the largest medications and frequently the hardest to swallow.

Difficulty swallowing presents a negative impact to patients’ adherence to their prescribed treatment regimens. This is true across all therapeutic areas, and both payers and providers want patient adherence to improve.

“Patients who hide their medication avoidance issues may experience refractory or reemerging symptoms that can sometimes result in the patient having a new medication added to their existing treatment regimen, a medication switch, or an increased dose,” says Wetherhold. “All of these adjustments can result in side effects, added costs, or even safety issues for the patient.”

Aprecia’s ZipDose effectively addresses this issue, efficiently formulating meds that are easier to take and administer. With 3DP dosage forms that rapidly disintegrate into any liquid with a palatable taste,

treatment regimens are easier to stick to – which benefits all stakeholders across the spectrum.

Taking the First Step

Brand extension strategies must be planned as soon as possible in order to fit in formulation and filing, while also considering patient data, patient preferences, and insights on ideal points of market entry. This will not only help protect revenue down the road, but it will also enhance the product's overall value proposition for payers.

“LCM strategies require due diligence, buy-in from executive teams and preparation across the entire pharmaceutical value chain from development to commercialization,” says Wetherhold. “Starting this process early can give organizations a crucial head start to being ready with an answer when competitive threats emerge.”

LCM options can include other products in a company's portfolio as well, and there may even be branded products in the same therapeutic area for which brand extension would make sense. Moreover, organizations can promote a newly reformulated product with their existing sales force, maximizing the productivity of their sales efforts and giving sales representatives more incentive to get ahead of targets and leverage brand equity across products.

Conclusion

With inevitable competition eventually threatening popular in-market drugs, Apreece's ZipDose technology offers drug companies the unique ability to preserve their brand share and extend their current patient population for successful therapies. By taking advantage of the next-generation of NCE formulation, existing branded drugs can be reworked to address unmet needs in the market and better adhere to patient preferences – going far beyond what conventional fast melt technologies can do. All it takes to unlock these innovative opportunities is finding the right partner to map out the best LCM strategies and maximize the potential of any therapy, either NCEs or currently-available products. ●



Apreece is a unique drug delivery technology platform company that's committed to transforming the patient and caregiver experience by reducing pill burden or simply making medicines easier to take. We imagine a world where medications are no longer challenging for patients to take or for caregivers to give. And we inspire each other every day to seek innovative solutions that address administration and adherence needs.
