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# Navigating the Pharmaceutical Odyssey

## Strategies for Late-Lifecycle Success amidst looming patent loss and declining ROI for new launches

2024

# Introduction

The dynamic landscape of the pharmaceutical industry is expecting a transformative shift, which is set to redefine how we perceive and approach drug development and commercialization. While the focus has predominantly been on new launches, a profound change is redirecting focus to drugs in their later stages of life.

Though we are entering an era marked by cutting-edge innovations – think of applying AI in drug discovery, mRNA [1] vaccines or CRISPR technologies [2] - pharmaceutical companies are increasingly urged to turn the spotlight towards late-lifecycle brands.

With an impressive patent cliff looming over the industry, putting a significant portion of revenues at stake, and the returns of drug discovery on the decline, late-lifecycle brand management will have an important role to play in generating continued revenues. Embracing the value they bring to organizations with significant sales originating from late-lifecycle brands is not just a strategic imperative for future-proof revenue flows, but also a commitment to a future where every patient receives optimal care.

Evidently, these brands typically need to navigate challenges that are significantly different from launches or patent-protected drugs, such as loss of exclusivity (LoE), generic competition and market saturation. In this context, pharmaceutical companies may struggle to define the right strategies to protect their late-lifecycle portfolios.

In this point of view, we'll shed more light on the changing context that pharmaceutical companies need to prepare for, balancing building launch versus late-lifecycle capabilities, showcasing Successful and less fortunate late-lifecycle examples and sharing recommended top- and bottom-line strategies for continued profitability for late-lifecycle products.

1. mRNA or messenger ribonucleic acid
2. Clustered Regularly Interspaced Short Palindromic Repeats

# Seizing the Future

## A call to action in the face of an upcoming patent cliff

Patent expiry or loss of exclusivity marks a pivotal moment in the lifecycle of a pharmaceutical drug. It's not just a legal milestone, but it also usually comes with significant financial implications. Upon loss of exclusivity, an important percentage (up to 80% on average within the first year after LoE)[3] of the product's revenue is at stake, leading to ramifications affecting not just the company's balance sheets, but potentially the very core of its financial health too.

In the pharmaceutical industry, a colossal patent cliff is looming, set to be one of the most challenging in history resulting in 190 drugs, including 69 blockbusters, that will lose patent exclusivity by 2030. For the U.S. market, representing approximately 50% of the global pharmaceutical market, a 46% revenue decline is projected for the world's top 10 pharma giants over the next decade. The storm peaks in 2029, putting at risk $59 billion in industry sales. From now until 2030, a staggering $236 billion is projected to be at risk in the US.[4]

Amid this daunting scenario, there's a seemingly hopeful aspect: drugs currently in phase 3 of their clinical trials could generate $73.2 billion in new launches[5] by 2030.[6] However, it's crucial to recognize that this figure falls significantly short, covering only around 31% of the anticipated revenue loss.

For those looking to focus on new drug development and ramp up launches, it's crucial to note the 2023 Deloitte research findings[4]. The average return on investment (ROI) from research and development reached a concerning low of 1.2% in 2022, the lowest since tracking began in 2010. Additionally, the average time for a new drug to move from clinical trials to approval increased from 6.9 years in 2021 to 7.1 years, leading to a rise in the average cost of developing a new drug by $298 million to $2.3 billion in 2022. Forecasted peak sales per asset averaged $389 million in 2022, down from $500 million in 2021. In light of these trends, safeguarding sales from mature products has become increasingly vital.

### Why should this matter?

The pharmaceutical landscape is shifting, and decisive action today determines whether you'll thrive in this changing environment. This isn't a prophecy; it's a call to action. Success belongs to those willing and prepared to navigate the stormy waters. The question isn't whether change will be needed; it's about how swiftly and effectively you will adapt.

Beyond the immediate financial impact, it's about safeguarding your company's future profitability, since the loss of revenue due to LoE is not often not directly filled in by revenues from new launches, and ensuring a longer product availability to sustain patient access and the best patient experience to as many lives as possible for a longer time.

Acknowledge the revenue at stake, embrace change and secure your place in the future of pharmaceutical Success. The storm is coming, but so is the opportunity for those ready to navigate it. Will you be among the victors?

3. Source: IQVIA, Price declines after branded medicines lose exclusivity
4. Source: Pharmavoice: How steep is pharma's patent cliff?
5. *Donanemab, Evobrutinib, Tolebrutinib, Fitusiran, Marstacimab, Concizumab, Roatinlimab, PRA023/MK7240, Bimekizumab, Zolbetuximab, Datopotamab deruxrecan, Imetelstat, Ensifentrine, mRNA-1345, Depemokimab, Tirzepatide, Iptacopan & KarXT projected sales*
6. *projections made by Crédit Suisse*

# The Pharmaceutical Odyssey

## Navigating Patent Loss with Strategies of Success and Setbacks

Late-Lifecycle Management in the pharmaceutical industry is a dynamic strategy to counter the hurdles posed by expiring patents for pharmaceutical drugs. To grasp its importance, let's first dive into the drug lifecycle. From research to LoE, patented drugs enjoy exclusive rights. But once these patents expire, the game changes. Late-Lifecycle Management aims to provide an answer to this challenge by proactively managing this much-dreaded loss of exclusivity for continued commercial Success, far before patent loss occurs.

When implemented well, Late-Lifecycle Management brings capabilities to support pharmaceutical companies in not just adapting to a changed reality, but help them thrive as well. Companies deploying smart strategies—new formulations, expanded indications, and exploring untapped markets—create the chance to keep the momentum going after patent protection is lost. It's a proactive, vibrant approach to stay ahead in an ever-changing and fiercely competitive pharmaceutical landscape.

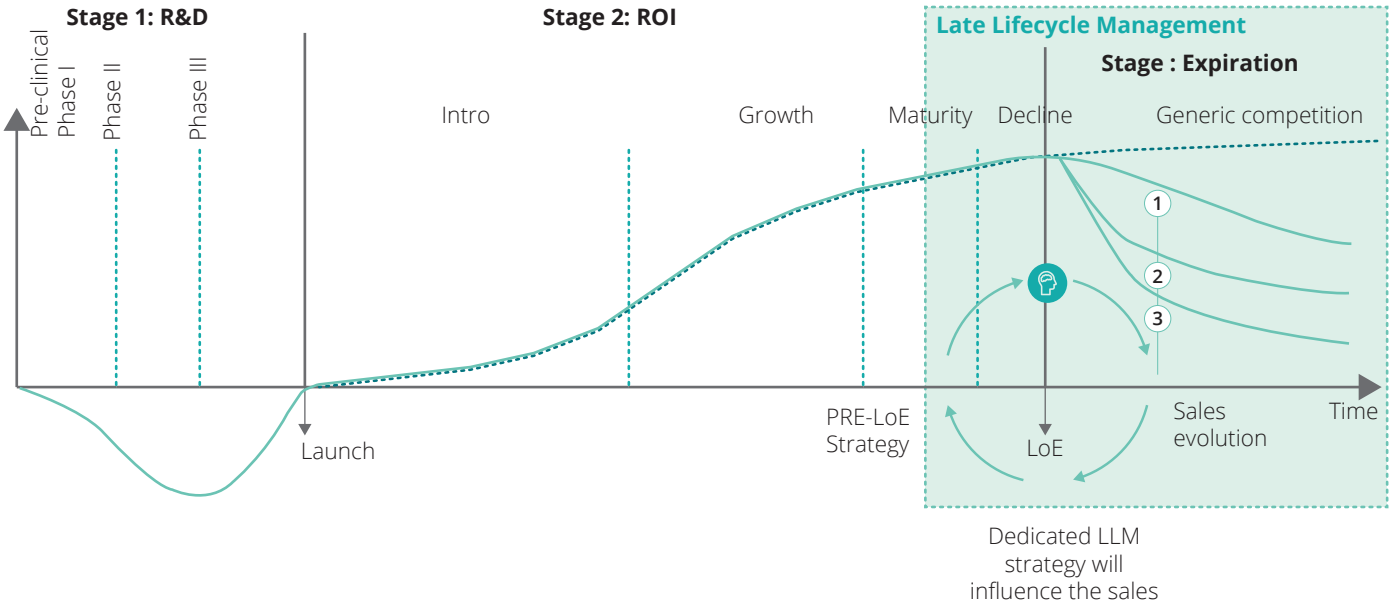



Figure 1: The product lifecycle can be divided into 3 stages:
(i) The R&D stage focuses on the discovery & development of new drugs. Products that were labeled efficient and safe after Phase 3 clinical trials are prepared for launch.
(ii) The ROI (return-on-investment) phase represents the time in which the drug is marketed and sold post-regulatory approval, with the aim to maximize sales and profitability, thereby recovering the substantial investment made during the R&D phase.
(iii) The expiration stage starts when the drug's patent protection expires, allowing generic manufacturers to produce cheaper versions of the drug, typically resulting in a significant drop in the original drug's market share and revenue.
Implementing a dedicated LLM for each brand specifically enables a pharmaceutical company to increase its revenue of late-lifecycle brands from 3 to 1, boosting the overall net sales. In order to maximize the potential of LLM, it is advised to start defining & implementing the most optimal strategy at least 5 years prior to the expiration phase.

**Industry examples:**
In this ever-changing market, the battle against patent expiration has become a defining chapter for industry giants. Companies deploy various strategies to weather the storm, with outcomes that vary significantly in terms of Success.

### Expansion of Target Patient Population

Expanding the population size of the potential beneficiaries for the drug through obtaining new approvals is one of the strategies for offsetting the impact of the expiring patent.

Roche's Avastin has achieved continuous growth by employing this strategy: continuing to grow, through a strategy of obtaining new approvals tailored to specific patient populations.

### Strategic Partnerships

Roche joined forces with Emcure to launch a more affordable brand (Bicletis) of its established product Herceptin, echoing the strategy Bristol Myers Squibb employed with Opvido in emerging markets. Gilead opted for authorized generics for its Hepatitis C drugs, Epclusa and Harvoni, while AbbVie adopted country-specific strategies for Humira to minimize the impact of new biosimilars on the market.

### Reformulations and New Formulations

Reformulations have also proved to be effective in the Late - Lifecycle Management of drugs. Otsuka's Abilify, a drug reformulated and repurposed throughout its lifecycle, represents a Successful implementation of this reformulation strategy.

In a similar vein, AstraZeneca adopted a late-lifecycle strategy in the face of generic competition, introducing an over-the-counter (OTC) version and pursuing new formulations of Nexium. This strategy helped Nexium maintain substantial revenue, showcasing the Success of adaptive strategies.

### Portfolio Diversification

Jazz Pharmaceuticals struggled with its mature product Xyrem before diversifying its portfolio and introducing Xywav. Following Xyrem's prolonged exclusivity, patent battles and criticism for patenting an FDA-required safety program, Jazz ultimately faced patent loss for Xyrem.

Eventually, the addition of Xywav, a product very similar to Xyrem, but containing less sodium, proved to be Successful, with Xywav gaining momentum and generating significant global sales.

**Not every company emerges unscathed due to the impact of generic drugs and price competition**

Pfizer faced a serious challenge when the generic version of Lipitor, Atorvastatin Hexal®, entered the market with an 85% price cut. This case highlights the risks of entering in a price war and not anticipating the price impact of new entrants.

AstraZeneca's leading respiratory drug Symbicort is a similar example of suboptimal Late - Lifecycle Management; after losing the drug's exclusivity in the U.S., the company experienced a decline in sales and struggled with price pressures, patent lawsuits and the introduction of generic versions. As such, these manufacturers found themselves facing in an important reduction in the revenues that their drugs had been generating for years.

## Conclusion

In the pharmaceutical landscape, industry players are learning that the Success or failure of Late — Lifecycle Management **relies strongly on the strategic choices made** when facing the inevitable loss of exclusivity. Various victorious examples include stories of **resilience, innovation and adaptability,** ultimately setting up pharmaceutical companies for continuous commercial Success.

# Proposed strategies for Late-Lifecycle Management

Having worked with many industry actors in the past, we have developed a deep understanding about the strategies that did work and about those that did not generate the intended results. As such, there are several business strategies that can prepare you to weather the storm, whether you are faced with patent expiries or wish to proactively ensure your portfolios will be protected from any future, adverse events.

We would like to distinguish between **2 major categories** top- and bottom-line strategies, as described below and supported by Deloitte use cases


## Top-line strategies

Improving the top-line is all about protecting and maybe even growing the revenues generated from your maturing portfolio. This can be done in multiple ways, as is illustrated below.

### Growing your sales volume

Either by switching from prescription to over-the-counter (OTC) products, making them more accessible for your patients, or through making them available via other – for example online – channels, in case they aren't yet.

**Use case 1**

With a growing trend of OTC switches in the pharmaceutical market and a growing interest of patients to take their health into their own hands (hence, preferring to take responsibility and ownership in the kind of drugs they are using for their ailments), it is worthwhile investigating whether switching your prescription drugs to OTC would be desirable, allowed and feasible. As a result, and supported by market insights on the changing preferences across geographies and/or areas of growth, companies can regain focus on for their maturing portfolio, and ultimately return back to growth after diminishing revenues over the years.

**Use case 2**

In order to grow sales volumes, pharma companies are exploring to expand their business for late-lifecycle products in the e-commerce market. In doing so, it is important to identify markets that offer the best opportunities to start up an e-commerce channel for these products based on different angles (e.g.; commercial, regulatory, supply chain, local preferences, etc. ) and how this translates into a clear roadmap for implementation to ensure the launch is Successful.

### Pricing

With looming loss of exclusivity and the entry of generics on the market, price reductions can be expected for established brands. While it is difficult to predict the future and pharma companies don't know what to expect and how to adjust their prices in the face of change, several elements can be considered to make price predictions and project the expected impact in your markets.

With a more concrete view on what the market and your competitors may do, you can more accurately and securely design and develop an appropriate response, minimizing the risk of a price war or extreme price cuts.

**Use case**
To both project the expected pricing impact of LoE for its portfolio, and define a plan of action to formulate an appropriate response, a LoE tool/model can be utilized, which simulates the expected responses in the market helping the pharma company with the upcoming patent cliff. After establishing the model, it is continuously fed with analog — and market data to refine its results and become more and more accurate and adapt to changing market conditions. By implementing of both own and market data, a pharma company is able to tailor the model to each specific product.

**Product mix**
(generics, biosimilars, introduction of a cheaper brand, adding a reformulation or indication of an existing drug): Another way to pre-empt competition and grow your sales base, would be to introduce product line extensions and adjust the product mix, in the form of your own generic, a biosimilar or launch a cheaper branded product, a reformulation or an additional indication. These strategies usually offer, without too much additional research and development, a way to enhance the lifecycle management of a product and fend off the Successful entry of competitor generics.

**Brand marketing**
Of course, increasing your brand awareness through enhanced marketing for your branded products remains a great alternative to ensure your products stay top-of-mind among patients, health care practitioners and pharmacists. Customers may be willing to continue to pay a price premium for the originator brand if they consider the perceived value and benefits justify this.

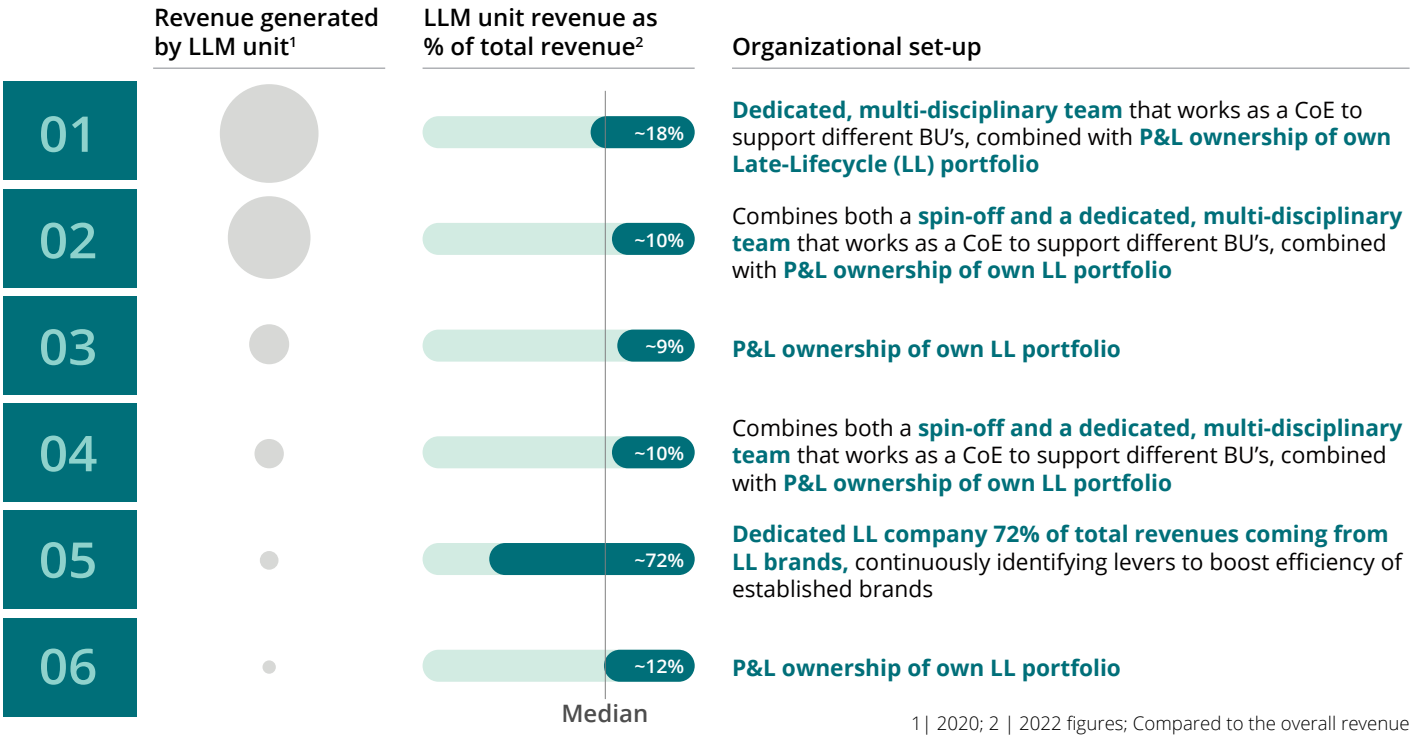
## Bottom-line strategies

Growing your bottom-line is about improving your profitability, either through cost containment, improving efficiency or making strategic choices that positively impact your profits.

**Divestments**
One potential solution to increase the efficiency of your resources, may sound surprising, but would be looking into divestment of some of the products in your portfolio. A critical evaluation of the profitability of your portfolio will allow you to free up resources which allows could potentially be re-allocated to newly launched or in-market brands and enhancing their overall performance (e.g.; through enhanced sales efforts, marketing & branding, stakeholder engagement, ...)

**Use case**
Pharmaceutical companies often have an extensive product portfolio of which not all products are actively promoted anymore, or in line with the core focus of the company. As a result, not all brands are delivering the desired results, resulting in the fact that profits are mainly driven by just a few core franchises. One of the core strategies can be to refocus on only these core franchises that are delivering the strongest results, and prepare a plan for divestment of the other brands. The reduction in number of brands enables a company not just in regaining profitability, but also decreased complexity while increasing overall portfolio focus.

**Positioning of late-lifecycle brands and corresponding capabilities within different pharmaceutical companies**




1| 2020; 2 | 2022 figures; Compared to the overall revenue

Figure 2: Given their evolving portfolios, many pharmaceutical companies are re-positioning their late-lifecycle brands and corresponding capabilities to enhance the understanding and implementation of LLM which is crucial to maximize the value of the corresponding assets

### Organizational structure

In the face of LOE it is worthwhile to re-evaluate the company's organizational model: as late-lifecycle drugs and new launches require a vastly different approach in terms of strategy, resources & time allocation, it makes sense to create a distinct organizational split to Successfully manage mature brands, while giving more innovative products the attention they require.

**Use case**

The organizational structure, usually set up during earlier stages of a brand's product lifecycle, is not always the right structure to drive sales for products as they mature, all the while causing a significant cost base for supporting functions. Different commercial models can be defined to more optimally manage late-lifecycle assets — three of which are described below.

1. Continue to manage them under the business unit managing their respective therapeutic area, even after loss of exclusivity. This means that the asset would continue to follow the strategy of the entire portfolio, likely absorbing too much resources (overhead & other costs) in its balance sheet, hence underestimating the value that the asset brings to the organization;

2. Transfer ownership of the mature asset, away from the current business unit (likely organized under the applicable therapeutic area) and to a dedicated Late-Lifecycle business unit. Following this organizational model, growth of mature brands would be driven by putting strategic focus on the capabilities required to maximize their value, both to the organization and more importantly, to their patients;

3

Set up a Center of Excellence (CoE) or a dedicated organizational structure to centralize the Late-Lifecycle management capabilities in support of the existing business units currently managing them. Concretely, the CoE or new unit would support primarily in advising on an optimal commercial strategy, which is embedded in the overall portfolio strategy;

### Commercial operating model

In case the overall organizational structure is solid, or when it is not in scope to revise the entire company structure to improve the bottom-line for your mature product portfolio, rethinking the commercial organizational set-up might prove to be quite impactful.

There is a myriad of ways to bring your products to the market, and applying some changes here could significantly reduce your cost base while delivering superior sales. Investigating your options might lead you to either (i) sell via your own salesforce, (ii) transfer these activities to a team of dedicated partners in various markets, (iii) out-license your brands or (iv) choose to set up an e-commerce channel (either yourself or via a partner or using a platform).

**Use case**

To boost profitability, pharma companies are (re)designing improved and more fit-for-purpose commercial Go-to-Market models. In order to decide on the most optimal model, it is important to analyze the performance of the existing sales teams and partners to identify which set-up could drive the strongest results (direct vs. indirect via partners). Advantages of a streamlined indirect partner model across markets could be a reduction of complexity, the variabilization of costs and improved sales. In order to ensure a smooth and Successful implementation of this strategy, pharma companies should carefully design their communication and transition plan for the affected sales people. Therefore, the entire organization needs to be taken onboard of the change, receive training and guidance on how to operate in this new way of working. Once established, the commercial model allows for easy extension to other late-lifecycle brands, broadening its Success with limited resources.

### Manufacturing

Another way to contain costs, increase efficiency and reduce risks, would be to transfer the development and manufacturing of late-lifecycle products to a CMO or CDMO (Contract Development & Manufacturing Organization). In doing so, companies can flexibly scale the production based on market needs, make cost variable and get access to significant expertise in drug manufacturing.

**Use case**

To reduce complexity and avoid wasting precious time and resources on maintaining and improving the production lines for its mature products, pharma companies are shifting the production of mature products from own manufacturing plant towards a CMO, resulting in +/- 50% of savings compared to the cost level with its own production plant. Next to this, it is also important to note that by moving the production towards a CMO, production capacity is freed up within the own plant that can be used for the production of new products.

Considering the strategies outlined above, we encourage pharmaceutical companies to take a comprehensive approach to their Late-Lifecycle assets and tailor their strategic responses effectively as they face an impending patent cliff. While it's common to view mature assets as mere cash generators to be exploited without significant investment, there's an opportunity to elevate them beyond this perspective. With proper focus and dedication, mature brand can transform into strategic business partners or levers, driving substantial value to fund new drug development, and provide ongoing support to patients in improving the quality of their lives for years to come.

## Conclusion

Significant challenges are looming over the pharmaceutical industry with many established brands facing patent loss and new drug development showcasing reduced returns. In the face of these challenges, established brands could emerge as transformative pillars for the industry's future. The upcoming patent cliff threatens major revenues, while investments in new launches are proving to become more time-consuming and costly, while also becoming increasingly less Successful – all of which are emphasizing the importance of Late-lifecycle Management (LLM).

Successful industry examples highlight resilience and adaptability, while cautionary tales underscore the importance of appropriate strategies for mature brands.

We are proposing solutions involving top-line strategies focusing on revenue protection and growth, and bottom-line strategies enhancing profitability. Success belongs to those who innovate in adversity since proper LLM has the ability to offset 5-15% of the anticipated revenue gap the industry is facing. Acknowledge the revenue at stake, embrace change and secure your place in the future of pharmaceutical Success.

**The storm is coming, but so is the opportunity for those ready to navigate it. Will you be among the victors?**

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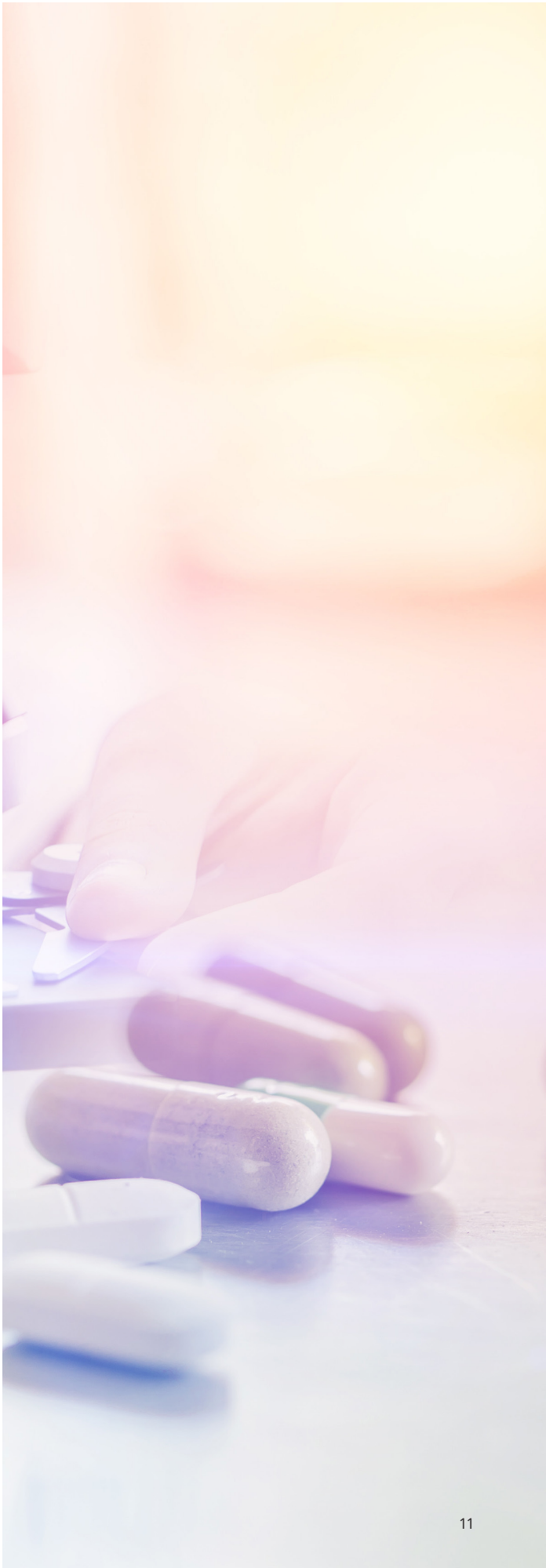

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