# UNRIVALLED MOISTURE PROTECTION WITH A BREAKTHROUGH BLISTER SYSTEM

amcor

# INTRODUCTION

Due to an increasing prevalence of chronic illnesses and growing geriatric populations, demand is expanding for drugs that prevent or treat diseases such as cancer, blood disorders, auto-immune diseases and other medical conditions. Indeed, the global biological drugs market will continue to expand at a CAGR of 10% between 2014 and 2020[1].

However, these drugs and their active pharmaceutical ingredients (APIs) are highly sensitive, complex structures meaning they may exhibit undesirable chemical, physical or pharmacological changes when exposed to moisture, particularly in humid environments, leading to ineffective or even unsafe products.

To date, cold form blister packaging has been widely used for drug protection and extended shelf-life as it offers a near complete barrier against light and oxygen as well as ease of use and patient dosage. However, with today's drugs more moisture-sensitive than ever, traditional cold form packaging solutions lack a critical functionality: optimum moisture protection. As a result, manufacturers need to incorporate desiccant, in some format, into their packaging.

This white paper explains why complete moisture protection is vital for many pharmaceutical products and outlines a groundbreaking approach to pharmaceutical packaging which offers increased barrier capabilities, speed to market and significant cost savings.

# AN ADVANCED DESICCANT SOLUTION

Packaging suppliers have recognized the need for increased protection of highly sensitive drug products against degradation from moisture, oxygen and light – factors which can lead to loss of stability, shortened shelf-life or ineffective drug delivery.

For this reason, desiccant particles now play an active role in controlling humidity and are considered essential to the quality, stability and appearance of many packaged pharmaceuticals. Current options are wads in bottles, pellets located in adjacent blister cavities, pouches inserted with a blister into an overwrap, and tablets for moisture absorption via a channel system within the blister pack. However, these solutions exhibit a number of limitations for manufacturers, such as increased complexity of the manufacturing process and supply chain, opportunity for error and rejects, significant costs due to multiple materials that must be sourced and risk of desiccant consumption by the patient. In some cases, they may also not protect each tablet or capsule individually, meaning barrier function is compromised as soon as the pack is opened during normal use.


To overcome these issues, packaging suppliers have put significant R&D efforts into finding an effective, consistent and safe solution that would minimize manufacturing complexity, enhance supply chain efficiency, and streamline processing and overall costs. Research has concluded that a cold form blister solution with an integrated desiccant in the sealant layer helps solve various production and quality issues, as well as protecting each blister individually and enhancing consumer safety by removing the risk of desiccant consumption. The five key benefits for pharmaceutical manufacturers adopting this integrated solution are further explained below.

## 1 Accelerated speed to market

A pharmaceutical product's success is largely determined by how quickly it gets to market, so achieving full-scale production in less time has both its competitive advantages and financial benefits. Such benefits include extended patent protection and market exclusivity which can increase drug sales by 5% or more and consequent ROI compared to slower competitors.

For example, a 'blockbuster' pharmaceutical is defined as one that generates US $1 billion revenue a year[2], which translates to almost $20 million revenue loss for every week the product launch is delayed. Similarly, generic companies have a lot to gain from speed to market as the first generic pharmaceutical to get to market enjoys a 180-day exclusivity period, and afterwards, the largest market share (typically 30%) and sales of up to $1.2 - $2.7 million per day.

Streamlining product launches increases speed to market but manufacturers must also demonstrate their products are safe, work for the intended use, and that they can be reliably and repeatedly produced to meet the international standards of quality. Regulatory agencies therefore require stability to be validated before market approval, a process costing at least $150,000.

Using a packaging solution with an integrated desiccant not only provides complete protection against moisture ingress but can also accelerate stability tests, reducing costs and increasing speed to market by 5 – 10%. Generic pharmaceuticals may also use an integrated desiccant solution to simplify the formulation of a drug by avoiding protective coating of the product, also increasing speed to launch.

## 2 Improved barrier function

After packaging, the stability of highly sensitive drugs may be affected by water transfer through the packaging components, known as cross-diffusion, as moisture ingress can reduce the efficacy of the API. However, drug effectiveness and safety can also be compromised by oxygen and light exposure or due to harmful leachable impurities and extractables. As a result, the barrier capabilities of pharmaceutical packaging are critical for the protection of niche, highly sensitive drugs and for drugs manufactured and / or sold in hot and humid climates, i.e. products in developing markets where medicinal aid can fail due to insufficient protection against climatic conditions.

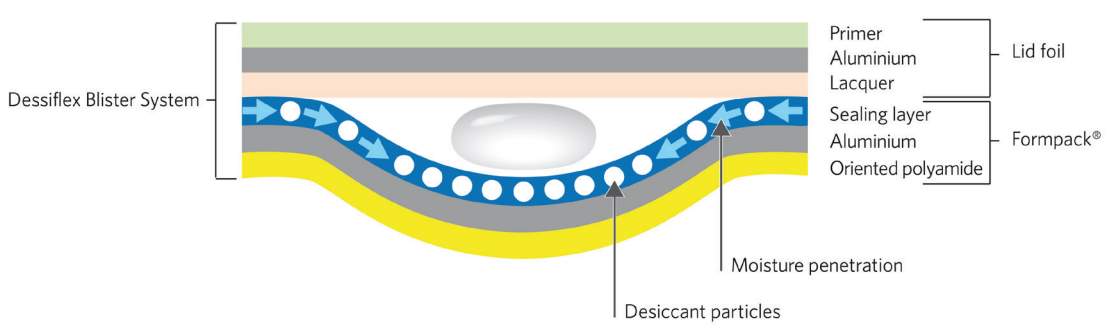
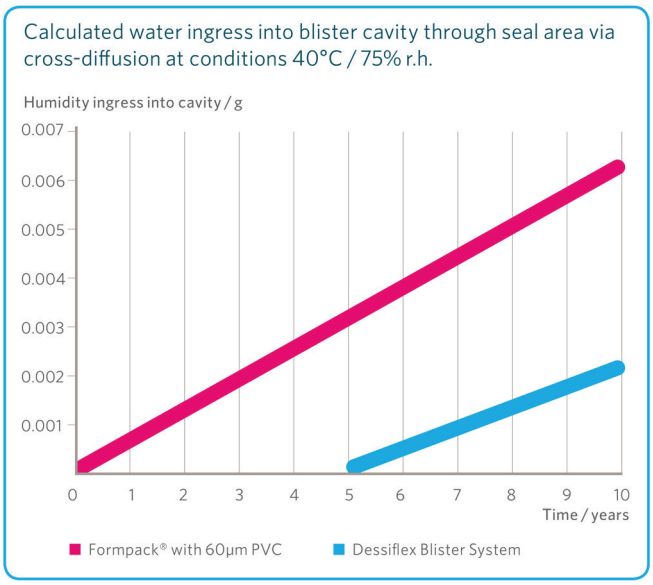



*Figure 1. Desiccant particles integrated within the blister's sealing layer prevent cross-diffusion.*

Although 25% of drug products on the market are sensitive and require optimal moisture protection, current solutions exhibit limitations. For instance, barrier effectiveness may be compromised due to opening of the packaging during normal use. For this reason, manufacturers are always looking to use more advanced pharmaceutical packaging that will increase product protection, stability and shelf-life by reducing the impact of cross-diffusion through the sealant layer and offering delamination resistance.

As well as this, increased shelf-life due to more effective pharmaceutical packaging decreases the number of drugs expiring so avoiding patient consumption of out-of-date drugs and reducing waste of drugs by up to 5%. In return, pharmaceuticals will observe an increase in ROI as a consequence of the drug being available on the market for longer.

Research has proven the advantages of using pharmaceutical packaging with desiccant integrated into the multilayer. In one study, results from a data logger, which recorded humidity (r.h. and temperature) demonstrated that it took approx. 12 hours (at 40°C / -1°C) to 24 hours (at 23°C / -3°C) to lower the humidity in the blister to 0% r.h. and kept the cavity at this humidity value for half a year.




*Graph 1. The integrated desiccant solution keeps the cavity dry (<10% r.h.) for 5 years in 40°C / 75% r.h. conditions.*

As shelf-life is typically half a year for sensitive drugs in humid climates, this increase in shelf-life stability is hugely valuable for pharmaceutical companies. As well as this, data shows this form of packaging can delay all moisture ingress into the blister cavity (<10% r.h.) for over five years even in hot and humid climates (40°C / 75% r.h.) compared to standard cold form blister solutions, which allow moisture ingress immediately (graph 1); and it also provided excess desiccant capacity to dry tablets that require it. Having the ability to delay moisture ingress simplifies the logistics for product launches and increases the shelf-life stability of pharmaceutical drugs.

## 3 Maximizing production and supply chain efficiency

To stay competitive in the market, pharmaceuticals must constantly upgrade quality and manufacturing systems and control operating costs with an efficient and streamlined supply chain to make production easier, quicker and less costly. The type of packaging a manufacturer uses can have a significant impact on efficiency and should offer:

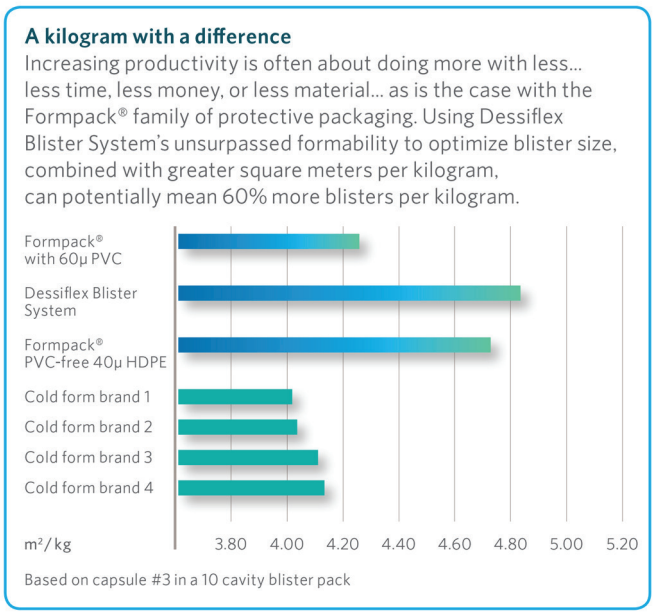
- Maximum fracture-free forming capabilities: studies show the integrated desiccant system demonstrates excellent machinability
- Optimal 'spring-back' characteristics
- Energy efficiency: enabled by improved sealing temperatures (~10N/15mm seal strength above 120°C) and in-blister drying capabilities
- Superior yield to reduce material changeovers and downtime.

Integrated desiccant packaging solutions offer this combination of desirable features. For example, studies showed excellent blister machinability and long-term resistance to delamination in this type of packaging. These properties ensure reliable production processes and higher lidding bond strength compared to standard cold form blister solutions. Overall production savings were: 10% reduction in machine usage, 1% waste reduction and 14.5% yield improvement. Supply chain complexity was also reduced because the number of packaging components was decreased.

## 4 Lower packaging costs – significant value for customers

Packaging has become an essential part of the drug delivery system. The global pharmaceutical packaging market is projected to witness a CAGR of approximately 8% between 2015 – 2020, fuelled by off-patenting of drugs and the expansion of the generics market[3]. Using a quality integrated desiccant solution helps decrease overall packaging costs as by using it, manufacturers can avoid the complexity of additional components such as pouches, overwrapping or separate desiccant and blister cavities. As well as this they can achieve lower costs per unit compared to bottles or PVdC blisters as an example.

Graph 2 demonstrates the cost effectiveness of an integrated desiccant solution, showing that pharmaceutical manufacturers can obtain >4.8$m^2$ of blisters per kg of material with Dessiflex Blister System compared to ~4.1$m^2$ of material or less in other commonly used cold form brands. This is due to the material's excellent formability, small cavity design and increased yield resulting in low material usage and increased number of blisters per kilogram.




*Graph 2. The m²/kg achieved by using different cold form blister solutions.*

## 5 Reduced carbon footprint

Cutting carbon emissions is an environmental, social, ethical and financial consideration for the entire pharmaceutical industry which is becoming increasingly important. For instance, manufacturers must take into consideration emissions for APIs, transport and distribution, formulation and packaging as well as the use phase and disposal of packaging during the production of a drug.

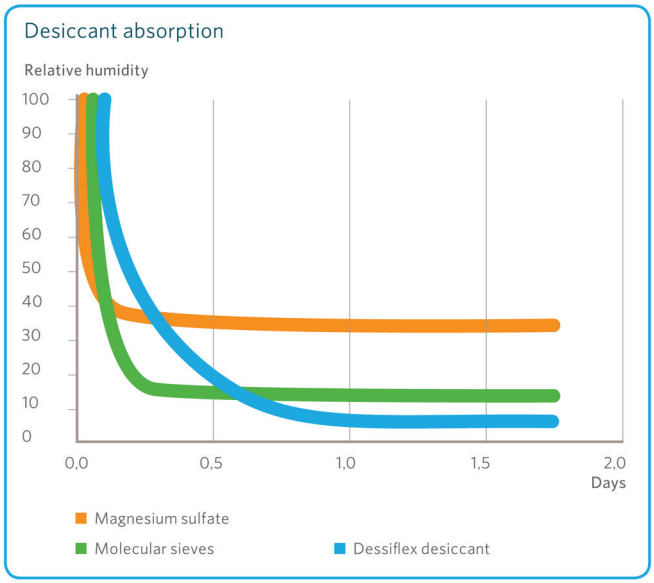
Better sustainability and reduced energy use as well as lower environmental fees can be largely achieved by choosing environmentally-friendly packaging material such as halogen-free sealants or PVC-free packaging. However, a large number of suppliers still include halogen-based, PE materials in their packaging solutions. Also, for pharmaceutical companies trying to accomplish reduced volume of packaging by choosing material that will provide improved yield and reduced waste of drugs by improving shelf-life of products through effective packaging, choosing an integrated desiccant material may be beneficial.

# DESSIFLEX BLISTER SYSTEM – A PROVEN SOLUTION FOR 10 YEARS

For pharmaceutical companies looking for a packaging solution which offers the industry's most effective barrier capabilities, speed to market and lower manufacturing costs, there is a well-established and patented option available worldwide, which has been adopted by some of the world's largest pharmaceutical brands.

Dessiflex Blister System is a PVC-free, cold form blister solution developed by Amcor Flexibles. It is registered with the FDA and European Pharmacopeia and protected by an EU patent. While it offers all the benefits of other cold form blister solutions it also allows manufacturers to speed up stability trials, enabling launch 5-10% faster, and considerably extends product shelf-life.

Unlike other desiccant solutions, Dessiflex Blister System features a highly effective desiccant integrated into the sealing layer which reacts chemically and irreversibly with moisture, significantly increasing protection against cross-diffusion and ensuring total product stability. Graph 3 demonstrates the superior drying capabilities of Dessiflex desiccant compared to other desiccants commonly used by the pharmaceutical industry. It also offers enhanced brand protection thanks to an easily recognizable blue color for easier product identification.




*Graph 3. Dessiflex's desiccant is more effective than others commonly used in the pharmaceutical industry, drying down to < 10% r.h.*

# CONCLUSION

The increasing demand for biologics is strengthening the need for innovative packaging solutions in the global pharmaceutical market. The benefits of using an integrated desiccant solution such as Dessiflex Blister System include: increased speed to market, unsurpassed moisture protection as well as significant cost savings, increased ROI and reduced waste throughout the global supply chain.

Combined with the advantages Amcor provides in waste reduction, higher productivity and support services, such as fracture-fee guarantee when tooling is designed by Forsis® simulation and PhiCheck analysis, Dessiflex Blister System creates significant value for customers. This groundbreaking and innovative material should be a significant consideration for pharmaceutical manufacturers who are looking for more effective packaging solutions, significant cost savings and long-term competitive advantage.

To learn more, please contact: **globalpharma@amcor.com**

[1] *Biological Drugs Market: Global Industry Analysis, Size, Share, Growth, Trends and Forecast 2014 – 2020. Transparency Market Research, 2014.*

[2] *Pharmaceutical Sector Inquiry Report, European Commission, DG Competition, 2009.*

[3] *Pharmaceutical Packaging Market by Packaging Type, by Raw Material, by Drug Delivery Type, by Region (North America, Europe, Asia-Pacific, RoW) – Forecasts to 2020. Markets and Markets, 2015.*