POSITION PAPER
FROM SÜDPACK ON THE TOPIC

Developing polypropylene-based primary packaging materials for solid pharmaceutical products – from the perspective of a packaging-material manufacturer

January 2023

SÜDPACK MEDICA

TABLE OF CONTENTS

SÜDPACK MEDICA

FOREWORD

The topic of sustainability has long been high on the agenda in the pharmaceutical industry. Increasingly, pharmaceutical manufacturers are committing themselves to mission statements based on sustainability and striving to achieve the related goals, such as climate neutrality and a reduction of their ecological footprint over the coming years. Nevertheless, the chemical-pharmaceutical industry is currently facing enormous challenges. In addition to high energy and water consumption, both the global supply chains and, above all, the associated large quantities of harmful residual materials – chief among them, packaging waste – are therefore in the spotlight.

On the other hand, there is a growing interest in finding sustainable solutions among all stakeholders and in wider society. The same applies to the level of interest shown by political and governmental institutions, which have either already enacted country-specific and cross-border regulations to reduce the consumption of packaging materials and make them recyclable, or are continuing to vigorously promote projects of this kind. The most prominent initiatives include the German Packaging Act, the European Green Deal, the Corporate Sustainability Reporting Directive (CSRD), the European Union's plastics strategy and, last but not least, the much-discussed CO_2 tax and the plastic tax. Despite the fact that pharmaceutical primary packaging is not currently subject to any statutory requirements with regard to mandatory recyclability, many packaging manufacturers are addressing this issue now in order to ensure their future legal safety.

Against this background, a rethink on an industrial scale is now imperative – especially in an industry whose products form the basis for human health and protection and are thus crucial to the overall prosperity of our society.

But how can the transition to more sustainable packaging solutions succeed in light of the pharmaceutical industry's stringent requirements with regard to performance, conformity, quality assurance and economic profitability? After all, this sector is strongly characterized by traditional procedures, lengthy development and approval processes and, above all, a high level of safety awareness.

SÜDPACK is confident that significant potential in terms of sustainability lies untapped here – particularly when it comes to the respective packaging concepts. Accordingly, the company has implemented a project with the goal of proving that primary packaging materials for solid pharmaceutical products based on polypropylene (abbreviation: PP) can serve as a viable, recyclable and therefore sustainable alternative to packaging made from PVC/PVdC materials – and can be processed just as efficiently on standard packaging lines.

This white paper highlights the initial situation as well as the various options, challenges and milestones within this groundbreaking project, whose goals were ultimately achieved in full. And thanks to the lessons learned, our company is now in a position to offer the pharmaceutical industry significant advantages when it comes to developing sustainable packaging concepts.

SÜDPACK MEDICA

THE PROJECT

... was based on a new product developed by the globally active film manufacturer SÜDPACK. In 2021, SÜDPACK Medica, one of the company's four high-performing business units, presented its first polypropylene-based, halogen-free film for the production of blister packaging for pharmaceutical and other solid applications. It thus presented the pharmaceutical industry with a sustainable alternative – with an excellent barrier profile – to the widely used PVC/PVdC blister materials, which to date have proven difficult to integrate into common recycling streams.

Although there have been repeated efforts in recent decades to use polymers other than the ubiquitous polymer PVC as the base plastic, none of these alternative materials have yet managed to gain a significant market share in the pharmaceutical industry – with the exception of polypropylene. Despite this promising potential, however, the first choice for many packaging applications remains the highly developed, high-performance PVC films that have proven their worth over some 60 years, and for a number of reasons. New systems must therefore always benchmark themselves against these existing solutions and, above all, make a compelling case for themselves as viable alternatives.

Some PP-based blister solutions for parenteral and solid applications are already available on the market in isolated cases. Via the aforementioned project, however, SÜDPACK aimed to develop a new kind of "turnkey solution" for the pharmaceutical industry. The goal was to create a standard solution for a wider range of applications that, thanks to its advanced level of development, enables companies to launch their own packaging projects with significantly shorter development times on their own machines. It should also allow new projects to benefit from the lessons learned via the previous projects and trials.

Furthermore, due to the favorable material yield and positive results in terms of productivity, the resulting solution makes comprehensive total-cost-of-ownership calculations possible, which can in turn serve as the basis for decisions regarding investments and material utilization. Thus, each kilogram of polypropylene that is introduced can be formed into a larger quantity of blister packaging due to its lower density compared to PVC-based systems, for example. This is a key factor with regard to sustainability and cost efficiency.

The process of adapting the material's properties to the respective machine concepts and requirements was key to the project's success. For this purpose, certain prerequisites had to be created and important aspects taken into account:

- Establishment of standards and platform products in order to cover the needs of the market in the best possible way
- Avoidance of small-scale solutions that may be associated with disadvantages in terms of security of supply, costs or even consistent quality
- Reduction of the development time
- Bundling and outsourcing of development work for existing and future solutions

The coordinated and targeted project work resulted in significant advantages for customers in terms of process reliability, compliance with regulatory and legal requirements, time-to-market, and thus overall profitability.

Of particular importance in this context is the fact that the material structures developed by SÜDPACK can be processed reliably on packaging lines. The PP films from SÜDPACK were extensively tested on numerous standard commercially available machines to ensure good machinability and smooth processing.

SÜDPACK MEDICA

SPECIAL FEATURES OF THE RAW MATERIAL SELECTION PROCESS

To date, the commonly used blisters for solid pharmaceuticals have consisted of a plastic thermoforming film based on PVC and an aluminum lidding film. Both materials are securely and inseparably sealed together – their separation and thus recycling in the current recovery stream is therefore not readily possible.

The blister contours themselves are formed during the thermoforming process on the packaging machine. The pharmaceutical products, such as tablets or capsules, are hygienically inserted into the individual recesses (cavities) of the blisters, which are then sealed with a lidding film. The patient can remove the tablets from the blister by pushing them through and out of the lidding film.

The PVC-based materials currently in use have been continuously developed over the decades and consistently optimized for use in packaging machines. The machines themselves have also been adapted to process this type of film. Both the manufacturers and users have therefore accumulated a wealth of experience in this area.

New solutions, however, present a challenge for all stakeholders – especially for the machine manufacturers and the packaging-material producers, who in the current climate want to – or rather, must – offer customers and users attractive service packages while always ensuring compliance with the respective statutory requirements and regulations. Last but not least, ambitious requirements must be met in terms of ensuring the recyclability of packaging materials and shrinking their ecological footprint along the supply chain. In particular, the choice of material plays a key role here – and it is a decision that will set the course for many years to come.

In principle, various material concepts are conceivable in the thermoplastic (and thus thermoformable) polymers segment – including solutions based on polypropylene, polyester, and polyethylene. In these single-material blisters (or "mono-blisters"), the forming and lidding films consist of the same base material. Separation of the films is not necessary, so in principle there are no obstacles to recycling. All three polymers are recyclable, but in all cases the risk of contamination from non-emptied cavities must be considered. Similar to polyethylene, polyester has a selective application profile. Besides its mechanical properties, it is primarily the barrier properties that include or rule out a particular polymer for the respective applications. Polypropylene, on the other hand, is one of the preferred polymers in this segment due to its specific properties, broad application profile and established recycling stream.

Whether a raw material such as polypropylene is actually suitable for the described applications will depend on many factors. Here are the most important ones at a glance:

- Functional aspects
- Regulatory aspects
- Strategic and economic aspects
- Sustainability criteria

It should be noted, however, that during both raw material selection and product development it is always essential to take into account the material-specific special features in terms of the individual options in the forming, filling, and sealing process. In the following, the main challenges on both the material and machine side are presented and explained in general and in specific cases using the example of polypropylene.

Functional aspects: product protection

Pharmaceuticals are sensitive products with special properties. A suitable packaging concept must therefore reliably protect the packaged product against external influences and at the same time ensure that the active ingredients in the drugs cannot volatilize. Stability tests must also be carried out to demonstrate that the packaged drug remains stable within a certain tolerance area and that the packaging is also capable of safely protecting the product until its expiration date.[1]

Specifically, the packaging material's water vapor barrier plays a particularly important role for dry, moisture-sensitive pharmaceuticals, especially if the medicinal drugs concerned require approval for use in all four WHO climate zones. In other cases, however, a reliable oxygen barrier must be integrated into the packaging. Since pharmaceutical companies generally operate globally and distribute their products worldwide, product protection is therefore also of paramount importance during transport and storage in different temperature ranges and climate zones.

Functional aspects: processability of sustainable material structures

There is also much to consider with regard to the processability of the films. An important quality criterion here is the film's thermoforming capability and forming behavior – the material must allow a larger processing window as well as uniform forming. In other words, the

[1] for example, see Stability testing in accordance with ICH and WHO requirements | SGS Deutschland (sgsgroup.de)

SPECIAL FEATURES OF THE RAW MATERIAL SELECTION PROCESS

more evenly the material thickness is distributed in the cavity, the better the plastic's barrier effect will be maintained. Since the barrier effect in polypropylene is created by the material itself and not by means of a comparatively thin coating, the measurement of the residual wall thickness provides more reliable information about the expected barrier effect.

In this context, the "dimensional stability" factor represents one of the biggest challenges for film manufacturers and machine builders. In other words, the material must only warp, shrink or swell to the minimum possible extent after heating, melting, recrystallization and cooling. High dimensional stability is critically important to allow subsequent repackaging into folding boxes. This also applies to other applications, such as trays for pre-filled syringes, ampoules, and high-calorie specialist foodstuffs. Films with a significantly higher thickness in the range of 500 – 1,000 µm are used in these cases. These films are also optimized to ensure maximum dimensional stability after thermoforming, including during demanding downstream processes such as autoclaving.

Comparison: PVC and PP

The PVC/PVdC blister materials that have predominantly been used to date have set high standards in terms of their thermoformability and tolerance areas. Thanks to its barrier properties and large processing window, aluminum is also ideal for the production of lidding films for blister packaging. In fact, a combination of both materials has thus far proven the best choice in terms of meeting the demanding requirements of the pharmaceutical industry, including machinability aspects.

However, polypropylene is also a smart option for certain applications. This material is a semi-crystalline non-polar thermoplastic that belongs to the polyolefin group. It is obtained by polymerizing the monomer propene with the aid of catalysts. It is odorless, skin-friendly and physiologically harmless – and therefore ideal for drinking-water-supply applications and for use in the food and pharmaceuticals sectors. PP is suitable for both powdery and dry products – and especially for the areas of application discussed in this white paper. However, due to their chemical structure and the resulting properties, polypropylene films demand much more precise and thus challenging processing operations.

For example, the heat capacity of polypropylene is already very high at room temperature. It also takes more time and energy to heat the film to its processing temperature and then to cool it down again. This effect increases with higher crystallinity and temperature. The problem occurs equally in the heating station before forming and again during sealing. In various areas of a thermoforming machine, this behavior is decisive – and in some cases physically limits the maximum achievable processing speed and cycle performance (for machines adapted to PVC films). However, PP also offers the advantage of superior thermal resistance due to its higher melting temperature. Thanks to a targeted alteration to the product's structure, the new SÜDPACK film also demonstrates the potential for very high cycle rates.

In terms of the barrier profile, PP can be considered at least equivalent, if not superior, to PVC. Polypropylene naturally possesses an excellent water vapor barrier. In addition, PP is highly resistant to acids, alkalis, solvents, alcohol, and water. Exposure to fats and oils results in only slight swelling.

Processability of PP in concrete terms

Thanks to its broad expertise in the field of coextrusion, SÜDPACK is already in a position to optimally adapt the material-specific special features of PP films to the requirements of blister packaging lines. This will ensure that they can be easily processed on existing packaging lines with only minor modifications. Further development work is being carried out apace at SÜDPACK's headquarters in Ochsenhausen with the goal of leveraging the company's unique coextrusion technology to achieve even higher barrier levels for PP in the future.

In addition, the recrystallization process of these PP films has been successfully optimized via targeted engineering steps in the extrusion process. As the crystalline content increases, polypropylene exhibits higher forming strength, so more force is required for optimum forming. For example, this means special measures must be taken when a machine stops/starts to ensure a reliable process and avoid wasted film.

Overall, PP films are generally more demanding than amorphous PVC films in terms of their thermoforming characteristics. However, in the course of the project it was shown that this can also be easily controlled when processing PP films and that high cycle rates are also achievable.

Furthermore, when processing PP films, it is important to be aware that their properties can vary greatly on account of different manufacturing processes. One example is the film's shrink-back behavior. It is therefore expedient to evaluate PP films from different manufacturers separately in order to determine their processability on a given machine.

For the sake of completeness, it should be pointed out that PP also offers important advantages in terms of its

sterilization potential. Unlike HDPE, PVC and APET, PP is one of the few polymers that is suitable for steam sterilization. With suitable adjustments to its formulation, the film can also be designed for sterilization using gamma radiation. However, the films' sterilization potential is not relevant with regard to packaging for powdery or dry products.

Regulatory aspects

Conformity issues always need to be addressed as part of the approval study. It is therefore a major advantage if the base polymers from which the films are made already meet the requirements for pharmaceutical grades in accordance with the European Pharmacopoeia (Pharmacopoeia Standard). But it is not only the raw materials in the medicines themselves that are strictly controlled – the packaging must also be pharmacopoeia-compliant.

A "Drug Master File" that specifies the relevant pharmacopeia-compliant raw materials is used to register medicinal products and their packaging with international regulatory authorities such as the U.S. Food & Drug Administration (FDA) and the European Medicines Agency (EMA).

Strategic and economic aspects

It is encouraging that there are already several active suppliers of thermoformable PP films on the market, all competing to offer the best solution. This is desirable from the customer's perspective and significantly stabilizes the supply situation. In terms of both the raw materials and the packaging materials, the market is therefore secure and favorable for customers with several suppliers per use case.

The film producers know which special features are required in the area of primary packaging for challenging liquid applications in the pharmaceuticals industry, and have adapted their products accordingly. This knowledge also makes it easier to implement or enforce important secondary obligations for their raw-material suppliers. This includes, in addition to basing the product's structure on an explicit pharmaceutical grade, ensuring that

- the recipe consistency is guaranteed and documented,
- assurances are obtained regarding the suppliers' obligations to provide information in the event of process and recipe changes, and
- a safety-oriented inventory policy is comprehensively clarified.

Security of supply can be ensured by means of appropriate business continuity concepts. To ensure the overall success of the PP-based solution, it is essential that all stakeholders throughout the value chain act intelligently – and above all cooperate with each other expediently – when executing the respective tasks relating to change controls, incoming goods and sample inspection protocols, and delivery assurance. By comparison, the requirements for primary packaging for solid pharmaceuticals are significantly less stringent.

In terms of the economic aspects, PP offers a comparatively good spreading rate due to its favorable density and therefore makes it easier to maintain a high degree of efficiency in terms of the filling process and the material yield. Specifically, the density of PP is between 0.895 g/cm³ and 0.92 g/cm³.

This model calculation shows how much input material is actually required (compared to PVC) to package a defined quantity of tablets or capsules in PP-based packaging: one square meter of a 250 µm-thick PVC film weighs approximately 337 g, while its PP counterpart of the same thickness only weighs approximately 225 g. In the case of PP, one kilogram of material therefore provides almost 50% more surface area and thus more blisters. Even if the material thickness is increased to 300 µm in the case of PP, this advantage is still just under 25%.

Sustainability criteria

Compared to other plastics, PP convinces as a polymer thanks to its extremely favorable eco-balance. Various life cycle assessments have shown that PP results in fewer greenhouse gas emissions compared to other fossil raw materials.

A screening life cycle assessment conducted by Sphera has proven that is associated with a reduced climate impact (in CO_2-eq) as well as lower energy and water consumption compared to other popular blister solutions.

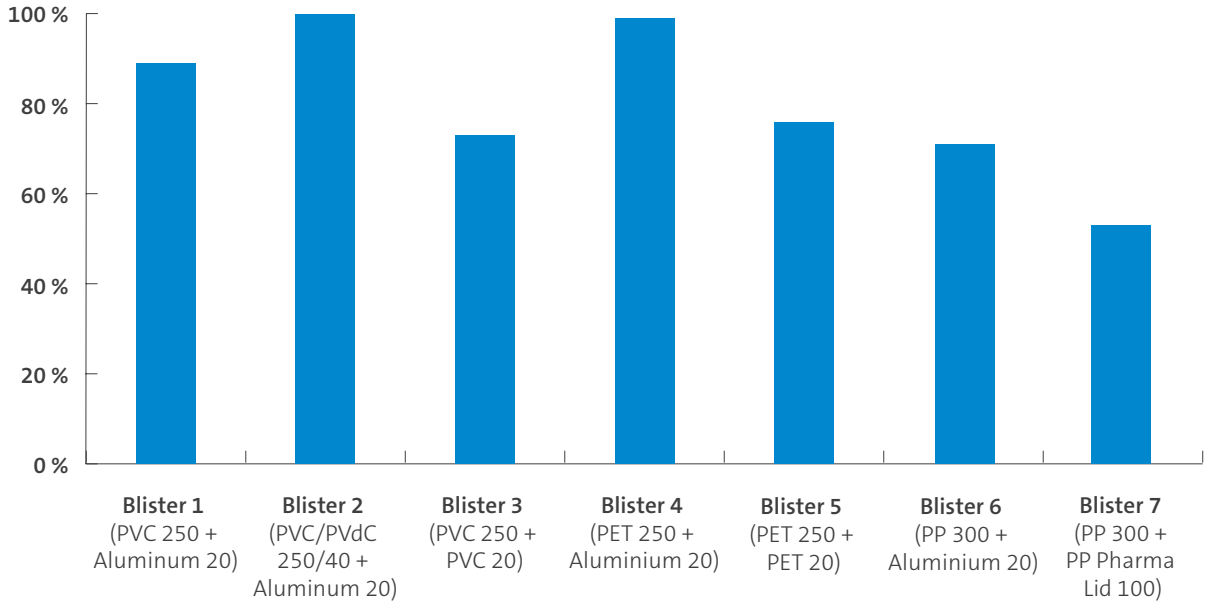
In addition, PP is now part of the globally established polyolefin recycling stream, although the contamination risks in these recyclate streams must always be considered.

For example, according to the "resources saved by recycling" study, conducted for the eleventh time in 2018 by the Fraunhofer Institute for Environmental, Safety and Energy Technology (Fraunhofer Umsicht) on behalf of the Alba Group (a Berlin-based waste disposal and recyc-

ling company) the results with regard to plastics recycling show that ...

"... for example, the primary production of 1 t of polypropylene – the world's second most widely used plastic – consumes around 5.2 t of raw materials and releases 1.7 t of greenhouse gases. In contrast, the production of 1 t of polypropylene from secondary raw materials consumes on average only 224 kg of resources and releases 966 kg of greenhouse gases."

However, even if the recycling option is ruled out, thermal recovery of PP as a so-called "end-of-life option" is comparatively unproblematic even in the worst case. This is because PP is one of the flammable plastics; its primary combustion products are carbon dioxide, carbon monoxide and water. Accordingly, the recovery process for PP is not restricted to specialist waste incineration plants. Furthermore, its low-residue incineration process – during which neither halogens nor heavy metals are released – is a major advantage.



[2] Tabone M et al. 2010, Sustainability Metrics: Life Cycle Assessment and Green Design in Polymers

SPECIAL FEATURES WITH REGARD TO PROCESS AND PLANT DEVELOPMENT

If PP is to establish itself as a recyclable, sustainable material in the field of packaging concepts for both parenterals and solid applications, various technological requirements must also be met. These relate to the drug manufacturers' existing packaging lines, which must now be configured to process PP films with as little additional cost and effort as possible. They also concern the development of new, innovative solutions to help optimize the filling process.

For both options, the goal of the packaging-machine manufacturers is to ensure maximum flexibility so that the respective machines can process different materials without any problems – and thus efficiently. In other words, without unplanned downtimes or significant start-up losses, and with the lowest possible use of resources.

Additional requirements include:

- Short changeover times
- High process stability, even for small orders
- Compact plant size
- Suitability for both rotary and plate sealing

A VISION BECOMES REALITY: THE PROJECT'S IMPLEMENTATION PHASE

SÜDPACK has seen significantly stronger demand for resource-saving, material-efficient and, above all, recyclable material structures in recent years. Accordingly, the company has continuously expanded its product portfolio, especially in the area of PP- and PE-based film solutions.

The film concept

SÜDPACK Medica has developed a 300-µm-thick, PP-based thermoforming film designed for use on standard filling lines – Ecoterm Pharma. The specific raw materials for this product were based on the search profile described above – where available, these are usually pharmacopoeia-compliant polymers. The final product was examined by a renowned service laboratory to check the main important conformity issues and begin the process of preparing the Drug Master File and the necessary declarations of conformity. The polymers in question are classified as recyclable and meet all current requirements with regard to product protection, stability, machinability and, above all, sustainability. The recyclability of PP films has already been officially confirmed by leading German institutes.

The resulting product is characterized by highly reproducible shrinkage behavior, which in turn results in optimal dimensional stability after the cooling phase. High reproducibility is extremely important in terms of creating comparable thermoforming and sealing conditions both within each delivery batch and from batch to batch.

SÜDPACK MEDICA

Important project milestones

Da SÜDPACK in den vergangenen Jahren eine deutlich stärkere Nachfrage nach ressourcenschonenden, materialeffizienten und vor allem recyclingfähigen Materialstrukturen verzeichnete, wurde das Produkt-Portfolio insbesondere im Bereich der PP- und PE-basierten Folienlösungen kontinuierlich ausgebaut.

As the first step, comprehensive market screening of the available raw materials and additives was carried out – with the primary goal of ensuring both delivery capability and product quality for the long term. This was followed by the actual product development phase on the basis of the film structures previously developed by SÜDPACK. Particular focus was placed on the shrink-back behavior of the PP film – an essential property of blister films.

After this development phase, the materials were extensively tested on commercially available packaging lines to determine their processability and properties throughout the thermoforming process. This was followed by a final evaluation and the definition of quality criteria and control mechanisms, which are essential for standardization and reproducibility.

Lastly, the integration of these solutions into SÜDPACK's product portfolio marked another important step towards a concrete offering for customers. In accordance with the guiding principle "standing still means going backwards", the findings from this project are now being successively incorporated into future projects. New, solution-oriented approaches are also being consistently created that will benefit future product generations.

Overall, the growing demand for recyclable packaging concepts is creating noteworthy advantages for the pharmaceutical industry. Customers thus benefit from significant project synergies, especially in terms of significantly shorter lead times and time-to-market.

Summary

The intensified search for sustainable alternatives to PVC-PVdC high-barrier films for the production of blister packaging has triggered sustained pressure to find substitutes within the packaging industry. In order to establish stable, functional solutions very quickly, project-based collaboration between the machine manufacturers and packaging-material producers delivers enormous advantages.

By pooling both parties' expertise and knowledge of specific market requirements and making regular comparative assessments of the product's development status, the development cycles can be significantly shortened and the service for end customers improved. At the same time, both parties can continuously learn from each other and gain insights into each other's challenges and opportunities. This results in long-term benefits that can in any event feed into future projects.

SÜDPACK MEDICA

ABOUT SÜDPACK

SÜDPACK Medica AG is headquartered in Baar (CH) and is one of the leading suppliers of sterile packaging solutions in Europe as well as a pioneering partner for the global medical, pharmaceutical and diagnostics industries. The company is part of the SÜDPACK company group and was founded in 1989.

The core competency of SÜDPACK Medica is the development of plastic-based packaging solutions for sterile goods. The product and performance range of SÜDPACK Medica extends from standard solutions to tailor-made, customer-specific packaging concepts. It includes the production of coextruded flexible and rigid films, which are used as base and lidding films – as well as pre-made pouch solutions for a wide variety of products.

SÜDPACK Medica also benefits from the SÜDPACK Group's long-standing leadership in technology and innovation in the coextrusion of polymer-based film solutions.

The production of SÜDPACK Medica products is performed at four sites in France, Germany, Switzerland and the Netherlands. These sites are equipped with the latest plant technology and manufacture to the highest standards of quality and hygiene, including the capacity to operate under clean room conditions.

For optimal support and collaboration with their customers around the world, SÜDPACK Medica relies on a specialist team working in quality, sales, development and application technology, one that has long-standing expertise in polymers and process engineering and in the market for sterile packaging. This makes SÜDPACK Medica a competent solutions partner for their customers when it comes to the implementation of packaging solutions, including those with the most demanding requirements.

SÜDPACK is committed to sustainable development and fulfills its responsibility as an employer and towards society, the environment and its customers. With its own site for processing biopolymers and its own compounding facilities, the SÜDPACK Group is also among the trailblazers in the production of forward-looking, sustainable and recyclable packaging concepts.

Impressum

SÜDPACK Holding GmbH
Ecoformstr. 1
88416 Erlenmoos
Tel. +49 (0) 7352 / 925 – 01
Fax +49 (0) 7352 / 925 – 1100
info@suedpack.de
www.suedpack.de

January 2023

SÜDPACK MEDICA