



WE CREATE
NEW OPPORTUNITIES
FOR YOUR API

NEW SOLUTIONS FOR YOUR API

LTS leads the way in transdermal therapy systems (LTS TTS) and oral thin films (LTS OTF). As a B2B partner to the pharmaceutical industry, we offer solutions at all stages of drug development:



From feasibility assessments, research and development of new formulations to clinical trials (up to phase II), production and packaging. On behalf of its partners, LTS develops and manufactures transdermal patches (LTS TTS) and oral thin films (LTS OTF), known as oral wafers. LTS develops innovative transdermal systems creating new opportunities for pharmaceutical actives



As a B2B partner of the pharmaceutical industry, LTS does not sell any of its own-branded products, making it a dedicated technology partner of the pharmaceutical industry rather than competing with classical pharmaceutical companies..

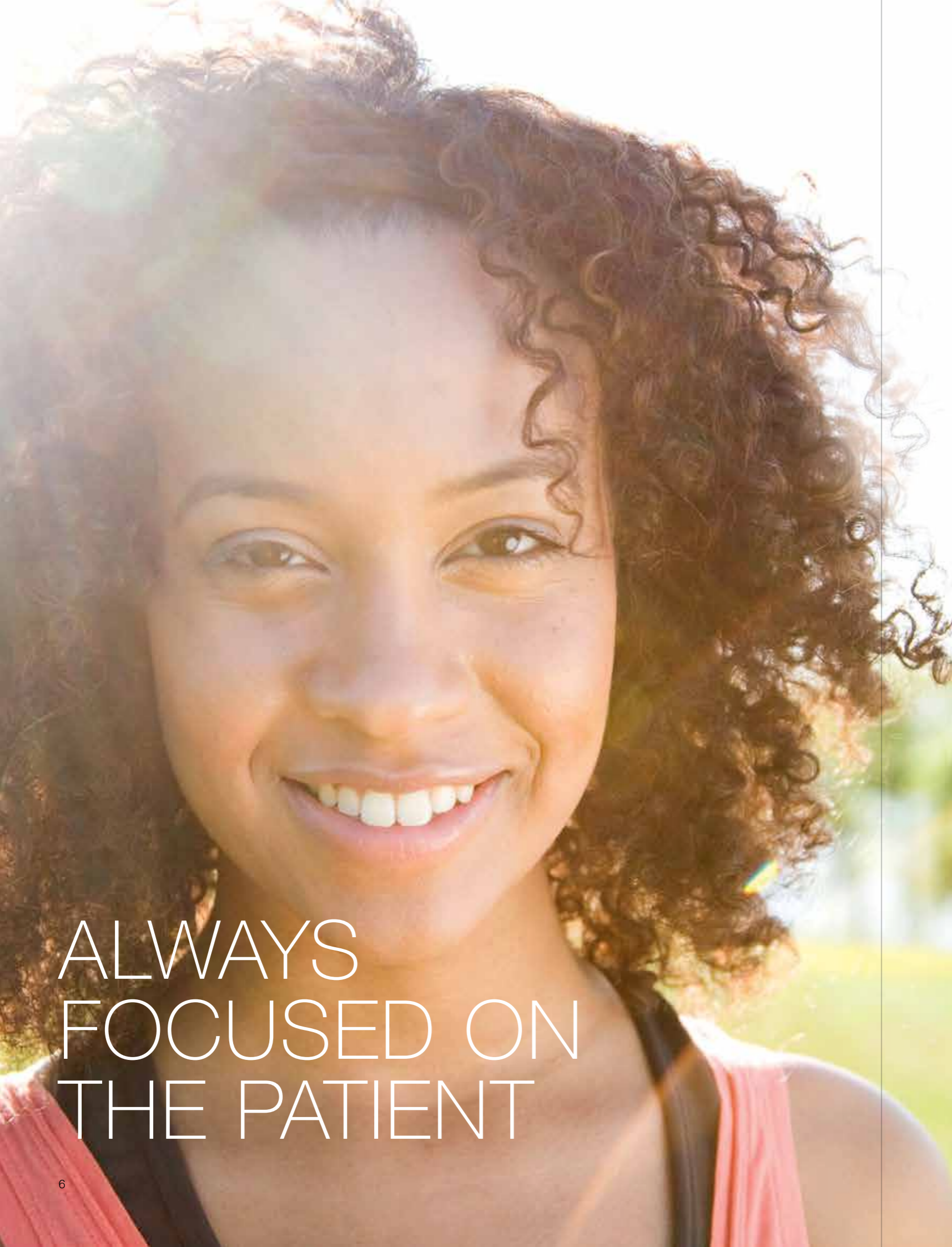
LTS produces patches and oral wafers in any batch size for all global markets, thus offering a comprehensive full service, including packaging development and support in the drug approval process as required.



LTS – YOUR PARTNER FOR INNOVATIVE SOLUTIONS

The development of new pharmaceutical drugs is a lengthy and complex process in which not every highly promising active substance eventually becomes a successful drug. This is often because developers only think to develop tablets, capsules or solutions.

With transdermal therapeutic system (TTS) and oral thin films (OTF), LTS has created several innovative drug delivery systems. We combine your active substances with cutting-edge applications that make patients' lives easier. This is why alternative delivery systems such as LTS TTS and LTS OTF should also be taken into account.



ALWAYS
FOCUSED ON
THE PATIENT

Together with our partners, we have set ourselves the goal of making therapy as effective as possible for the patient and, at the same time, minimising undesirable side effects.



Many patients suffer from gastrointestinal problems due to side effects of tablets or capsules. We sought solutions that would allow us to avoid the gastrointestinal area and, with transdermal application systems, have found a way to administer the active substance directly into the bloodstream. With this method, we are able to go some way to improving patients' quality of life. For multi-morbid patients in particular – a growing group in society due to the age structure of the population – any

medication that avoids the gastrointestinal area represents a major relief. With transdermal systems, we are also able to provide patients with active substances that would have no effect if taken orally. This allows us to make a significant contribution to expanding the range of therapy options for the patient.



LTS – TTS THE PATCH AS A THERAPEUTIC SYSTEM

Transdermal patches or transdermal therapeutic systems (TTS) are drug delivery systems that are applied directly to the skin. The active substance is absorbed by the skin and distributed through the body via the bloodstream.

A patch as an alternative to tablets, capsules or drops.

TTS are drug delivery systems that can be applied to the human skin to release a variety of active substances. TTS enable substances to be absorbed by the skin, whereupon they enter the tissue beneath and into the bloodstream. The primary function of the skin is to protect the body from foreign objects and microorganisms, yet it is not completely impermeable. Relatively small drug molecules can pene-

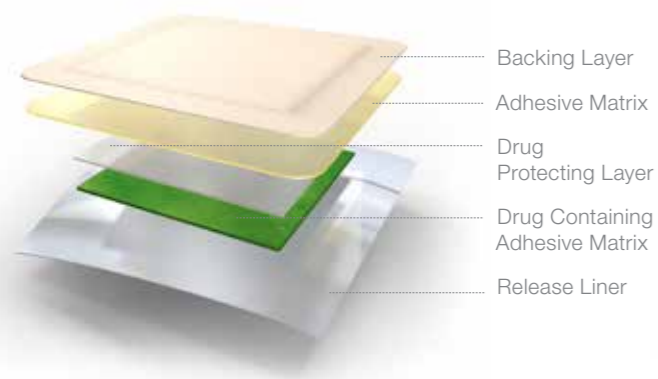
trate the skin, and this is how transdermal patches work. In contrast to drugs taken orally TTS have the advantage that the substance does not have to be digested first. This means that the substance remains chemically unchanged and directly accesses the part of the body where it needs to take effect via the bloodstream. As a result, this also avoids filtration and initial metabolism by the liver, or the 'first-pass effect'. Another advantage of LTS patches is that they release the substance constantly and continuously over a long period of time.

DIVERSE TECHNOLOGIES FOR WIDE-RANGING APPLICATIONS

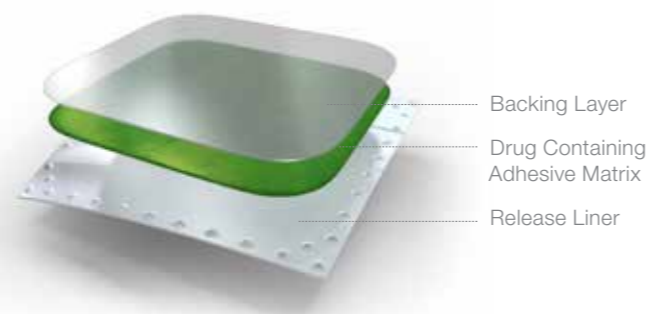


A wide range of TTS technologies from LTS make it easy to ensure the ideal dose for any active substance. The drug molecule should not exceed a certain size (approx. 500 g/mol) so that it can penetrate the skin effectively. To date, there are 20 active substances known to fulfil this requirement. LTS processes twelve of these for its various partners in the pharmaceuticals industry. Experts have predicted that there are at least 30 other active substances that could be suited to transdermal delivery.

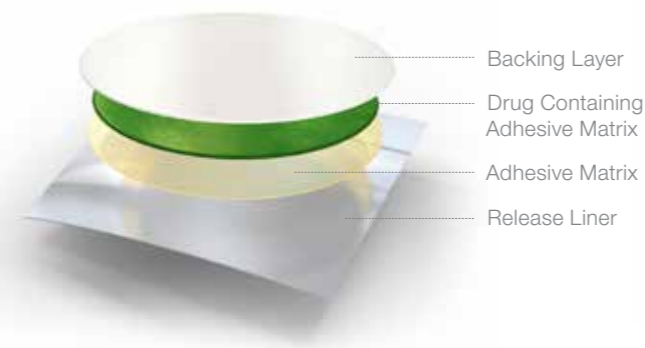
Matrix-TTS with Overlapping Backing layer



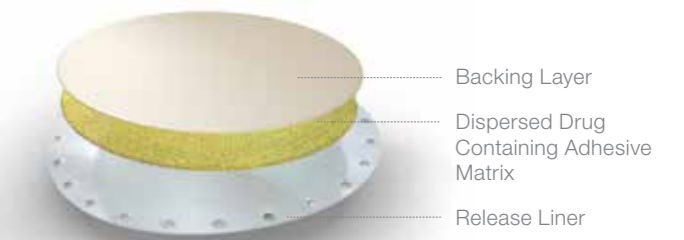
Monolithic Matrix-TTS



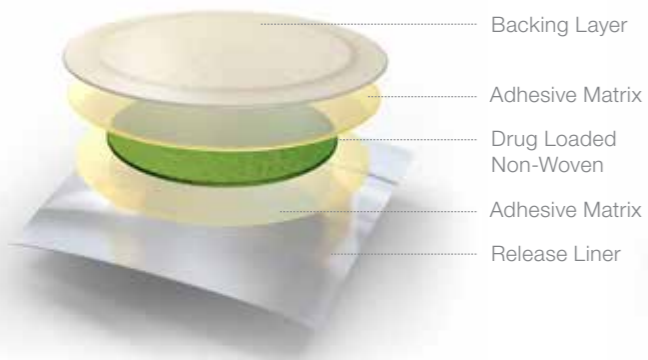
Multilayer Matrix-TTS



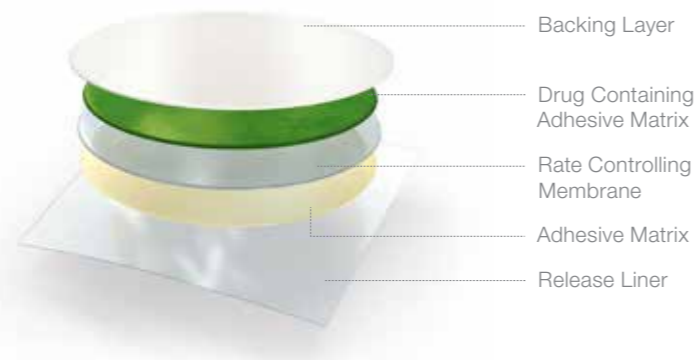
Mikroreservoir-Matrix-TTS



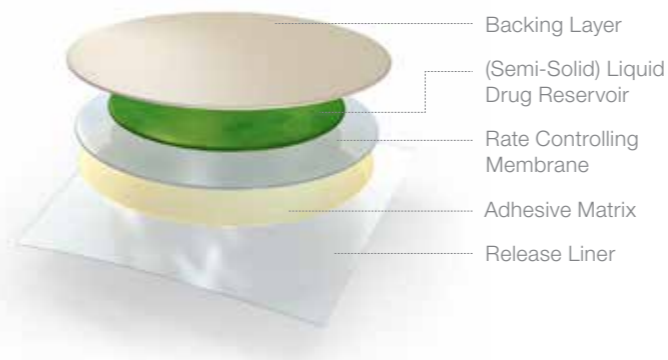
Modified TTS for Volatile Drug Substances



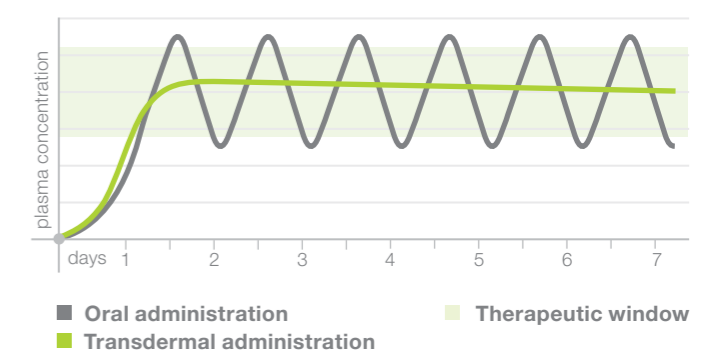
Matrix-TTS with Rate Controlling Membrane



Reservoir-Matrix-TTS



TTS technology makes exact dosing possible



THE ADVANTAGES OF LTS PATCHES



For patients:

- ▶ Safe, reliable, precise and pain-free application
- ▶ Easier to treat children, as well as older patients and patients requiring complex care
- ▶ Ideal for patients who have difficulty swallowing
- ▶ Longer intervals between doses, particularly with multi-day patches

For pharmaceutical companies:

- ▶ Efficacy of active substances with low oral bioavailability
- ▶ Controlled, even application – no peak concentration
- ▶ Easy to manage dosage by varying the area of the patch
- ▶ No loss of active substance due to avoidance of first-pass metabolism by the liver
- ▶ Potentially requires significantly lower amounts of active pharmaceutical ingredients (active substances) than for tablets or solutions
- ▶ No breakdown of the active substance in the gastrointestinal tract
- ▶ Improved compliance on the part of patients
- ▶ Additional options for differentiating a product range





ORAL THIN FILMS – A NEW EVOLUTION STEP FOR ACTIVE SUBSTANCES

Oral thin films are loaded with active substances. The thin films are taken orally and dissolve immediately in the mouth or are applied to the mucosa.

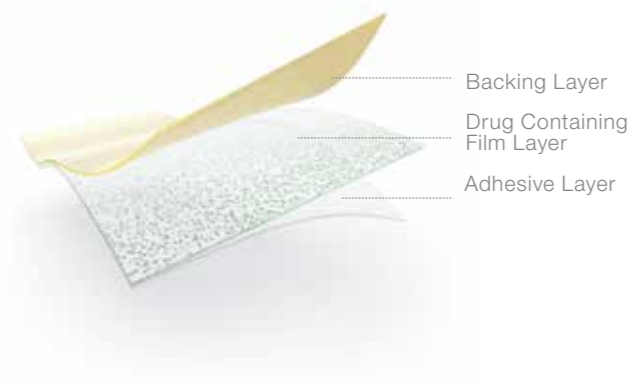


Oral thin films (OTF) are thin, flexible films for drug delivery. They are placed on or under the tongue, where they then dissolve. Transmucosal films are absorbed by the body directly via the oral mucosa. The excellent blood supply to the oral mucosa means the active substance enters the bloodstream immediately bypassing the liver's first-pass-effect.

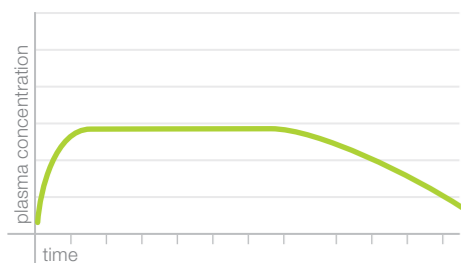
DIVERSE TECHNOLOGIES FOR WIDE-RANGING APPLICATIONS

Various LTS OTF technologies enable fast or sustained release of the active substance, thus ensuring the ideal dosage. LTS OTFs measure between 2 and 10 cm² and are extremely thin (20 to 500 μm). These thin films can take the form of a single-layer or multi-layer system. The active substance can be dissolved in the matrix, emulsified or dispersed. If necessary, it can also be bound as a complex in order to mask taste, for example.

Non-Disintegrating Buccal Film



Long-acting release formulation

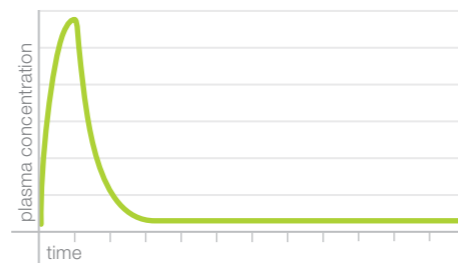


Dissolution/ release:
several hours
Resorption site:
gums
Effect:
systemic

Fast Disintegrating Buccal Film

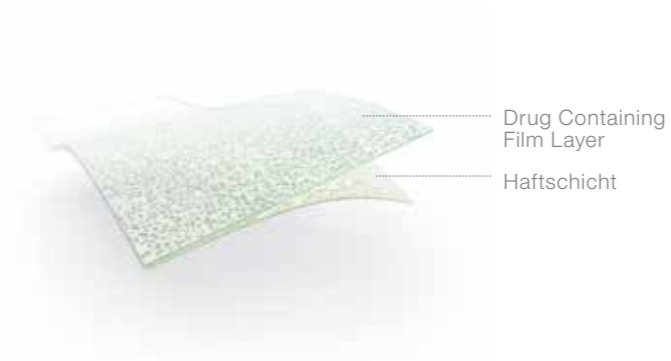


Rapid release formulation, fast onset of action

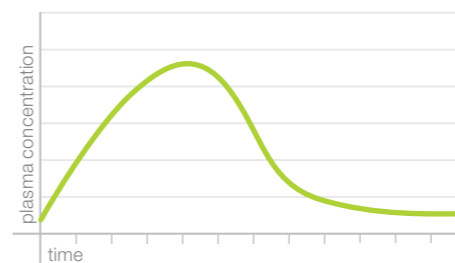


Dissolution/ release:
maximum of 30 seconds until complete dissolution
Resorption:
oral mucosa or gastrointestinal tract
Effect:
systemic odr local

Melt Away Film



Intermediate dissolution at application site, high local drug concentration



Dissolution/ release:
5-30 minutes, formation of gel-like depot
Resorption:
oral mucosa
Effect:
systemic odr local



LTS as a partner for healthcare innovations

LTS covers in a single source all the relevant technical steps in drug development – from feasibility studies for your drug up to the market launch and subsequent large scale manufacturing. LTS manufactures for the global markets of your choice.

LTS has at its disposal exceptionally well-equipped research, development and production facilities covering all areas – from drug development to the production for the global market. Feasibility studies, technical and clinical development (up to phase II) of novel agents, drug delivery systems, production and quality control.

The expertise of our experienced pharmacists and engineers enables us to respond to the requirements of each and every customer. This results in customised production systems and facilities. In addition, LTS can react quickly and flexibly to new requirements in the global pharmaceuticals markets and adapt its production processes to comply with them.

Full-service partner for phases I to IV

LTS' Clinical Research Services (CRS) is part of the LTS Group and has been conducting phase I and II clinical trials for over 35 years. The institute has 230 beds and a large medical department featuring

leading-edge equipment for non-invasive analysis. With its highly qualified employees, CRS has everything it needs to successfully complete any clinical trial within the shortest possible time period. CRS also manages phase III and IV trials.

Tailored production facilities at two locations

One of LTS's major strengths is its production expertise. From small- laboratory scale to fulfilling all the production requirements for sales on the global market – we provide our customers with what you need. From a pilot plant, our research department

develops high-tech production facilities that can cope with global production to exacting laboratory specifications. If required, LTS can also construct with its engineering capabilities completely new production lines in order to realise new product designs, for example.

LTS can also manufacture everything it develops

A major advantage of working with LTS is its experience and reliability. Our diverse experience with active substances, products and manufacturing processes simplifies drug development and ensures we can provide cost-effective solutions. LTS does not sell products under its own-brand but focuses

exclusively on research, development and production for its partners in the pharmaceutical industry. Integrated, one-stop solutions from LTS guarantee a seamless transition between the individual stages in the development project. Thanks to its extensive expertise, LTS can respond to every customer request and adapt its work to the results desired by the customer.

Five steps of success

1	Theoretical tests and benchmarking
2	Practical feasibility study, including prototypes
3	Complete pharmaceutical development programme, including clinical trial
4	Creation of the production line or the adaptation of existing production facilities
5	Production for its partners as contract manufacturer

► For every partnership, LTS adapts its research and development, technological expertise and production capacity to the requirements and expectations of the client company.



TWO LOCATIONS: EUROPE AND THE USA

The roots of LTS may lie in Germany, but we are internationally oriented. The USA is the world's largest pharmaceuticals market and thus represents attractive market potential for our partners.

That's why we established a location in the USA as early as the 1990s, allowing us to offer our partners a direct link to the US market. Optimisation of transport costs and the time to market for orders are the immediate advantages.

With almost identical machinery at both locations, we can also guarantee a switching of production locations where required. This allows LTS to actively minimise the risk of production stoppages for our partners.

GOOD REASONS FOR CHOOSING LTS

The path from the developed substance to the successful transdermal therapeutic system (TTS) or oral thin film (OTF) is a long and labour-intensive one. As such, you need a strong, experienced and committed partner at your side. LTS as the market leader fulfils all these requirements.

- ▶ **LTS leads the way globally** in transdermal therapeutic systems LTS TTS and oral thin films LTS OTF.
- ▶ **With its partners from the pharmaceutical industry**, LTS has developed the most TTS products onto the market. These transdermal patches make treatment much easier for a large number of patients.
- ▶ **LTS has the experience and expertise** to develop and manufacture successful products right up to market approval.
- ▶ **LTS has sufficient capacity** to manufacture the batch sizes required for global sales and high-volume products. Two identical production facilities in Andernach (Germany) and West Caldwell (USA) secure supply chain reliability even in crisis periods.

- ▶ **LTS has production capabilities** of varying sizes to operate all demands from early drug development to large-scale production campaigns. As such, LTS matches its manufacturing processes for its products customer specific to the ideal equipment.
- ▶ **LTS is recognised** by all major health authorities the world over.
- ▶ **LTS has broad experience** in the field of hormone therapy and with anaesthetics narcotic substances. LTS systematically separates the production of hormone products from non-hormone products. As the only manufacturer in the world to do so, LTS has completely separated hormone products avoiding any risk of possible cross - contamination.
- ▶ **LTS offers all services** from a single source – from feasibility studies and clinical trials (up to phase II) to production and packaging.
- ▶ **A global market leader** and also a solid, traditional company deeply rooted in the German Mittelstand, LTS offers an international scope paired with the highest quality standards.
- ▶ **LTS supports each client** with its very own development team, which can also be integrated into a client's research team comprising employees from the client company.
- ▶ **On the basis of mutual trust**, LTS offers its customers complete transparency in all project phases.

YOUR CONTACT



Place for
businesscard.

Germany:

LTS Lohmann Therapie-Systeme AG
Lohmannstraße 2
D-56626 Andernach
Telefon: (0 26 32) 99-0
Telefax: (0 26 32) 99 22 00
E-Mail: info@ltslohmann.de
Internet: www.ltslohmann.de

USA:

LTS Lohmann Therapy Systems Corp.
15 Henderson Drive
West Caldwell 07006
New Jersey, USA
Tel.: 1- 800 5871872 (only from USA)
Tel.: +1 973 396-5345
Fax: +1 973 575 5174
Email: info@ltslohmann.de
Internet: www.ltslohmann.com

