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Regulatory background for the IOI Oleo site in Witten:

EU GMP-certified
last recurrent inspection: May 2015

US FDA-approved
last recurrent inspection: February 2015

DIN ISO 9001/14001-certified
last recurrent inspection: April 2016

EMAS
Registered

CEP
Certificate of Suitability of Monographs of the European Pharmacopoeia, granted for MIGLYCOL® 812 N

US Drug Master Files
Type II: MIGLYCOL® 812 N
Type IV: MIGLYCOL® 810 N/812 N, 829
SOFTIGEN® 76/7
SOFTISAN® 378, 649
WITEPSOL®s
Injectables – IV, SC and IM

C8/C10 triglycerides (MCT oils) and propylene glycol ester, used as a carrier:

**MIGLYOL® 810 N**
Medium Chain Triglycerides (ratio ~ 70:30%)

**MIGLYOL® 812 N**
Medium Chain Triglycerides (ratio ~ 60:40%)

**MIGLYOL® 840**
Propylene Glycol Diisostearate

Application examples:
- Narcotics (Propofol)
- Malaria (Artemether, Lumefantrin)
- Muscle relaxants (Etomidate)
- Veterinary injection suspension (Amoxicillin, Cefiofur)

Injectables – enteral and parenteral nutrition

C8/C10 triglycerides (MCT oils)

**MIGLYOL® 812 N** – Medium Chain Triglycerides (ratio ~ 60:40%)

Dosage forms: enteral and parenteral nutrition

IOI is the holder of the first CEP (Certificate of Suitability) ever granted for a Medium Chain Triglyceride and has filed US-DMF Type II.

**MIGLYOL® 812 N** has been used in enteral and parenteral nutrition for decades. From a regulatory point of view, the ingredients in some of these formulations are classified as API.
**Topical/dermal applications**

**Self-emulsifying ready-to-use cream base**

**O/W base SOFTISAN® 601**
Suitable for the preparation of skin-compatible, wash-off O/W creams, exhibiting a water content of up to 65%. Not sensitive to ion-active APIs.

**Application examples:** Heparin and steroidal creams, wound care

**Emulsifier O/W**

**IMWITOR® 372 P – Glyceryl Stearate Citrate**
Powerful non-ionic emulsifiers, excellent compatibility with skin and mucosa

**Application examples:** antibacterial creams

**IMWITOR® 960 K – self-emulsifying Glyceryl Monostearate**
Emulsions with IMWITOR® 960 K are compatible with a wide range of APIs and therefore an excellent basis for stable formulations.

**SOFTISAN® 354 – Hydrogenated Palm Oil**
Triglyceride of blends of natural, saturated, even-numbered and unbranched vegetable fatty acids of mainly C16 and C18.

It contains no additives, such as antioxidants or stabilizers.

**Solubilizer and refatting agent**

**SOFTIGEN® 767 – Macrogol 6 Glycerolcaprylocaprate**
Acts as a solubilizer, e.g. for essential oils and as a refatting agent, shows good skin tolerance. Even on eczematous skin its tolerance is exceptional, and it is therefore used in psoriasis treatment.

**Application examples:** Antihistamine balms; corticosteroid gels and psoriasis lotions

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**Topical formulations**

**Emulsifier W/O**

**IMWITOR® 600 – Polyglyceryl-3 Polyricinoleate**
Especially suitable for soft to low-viscosity W/O emulsions and lotions; excellent stability of formulations even with high water content.

**IMWITOR® 618 – Triglycerol Diisostearate**
Slightly yellowish, viscous liquid. Suitable for use in dermatitis preparations and lip care products.

**Solubilizer and refatting agent**

**SOFTIGEN® 767 – Macrogol 6 Glycerolcaprylocaprate**
Acts as a solubilizer, e.g. for essential oils and as a refatting agent, shows good skin tolerance. Even on eczematous skin its tolerance is exceptional, and it is therefore used in psoriasis treatment.

**Application examples:** Antihistamine balms; corticosteroid gels and psoriasis lotions
Topical formulations

Skin protection

**SOFTIGEN® 701** – Glyceryl Ricinoleate

It is attracted to the adsorption sites on the skin’s surface due to the free hydroxyl group. Therefore, it protects the skin from being attacked by damaging substances. After long-term use in pharmaceutical preparations and in an epicutaneous skin test, **SOFTIGEN® 701** showed excellent tolerability.

Penetration enhancer

**IMWITOR® 742** – Glycerol Monocaprylocaprate, Type I

**IMWITOR® 988** – Glycerol Monocaprylate, Type I

Several scientific tests illustrate their ability to enhance the skin penetration of poorly soluble APIs. Both excipients are used in various dosage forms in amounts of 3–15%, depending on the kind and amount of active substance.

Oleogels for consistency regulation

**MIGLYOL® Gel B**

Manufactured by jellifying **MIGLYOL® 812 N** neutral oil, using an inorganic and chemically modified hectorite clay.

**MIGLYOL® Gel T**

W/O emulsions containing this oleogel reduce phase separation even after short heating up to approx. 90 °C.

**MIGLYOL® 840 Gel B**

Manufactured by jellifying **MIGLYOL® 840** oil with an inorganic chemically modified hectorite clay.

These specialties are recommended for use as consistency regulators in pharmaceutical preparations where it is important to maintain the viscosity over a wide temperature range (occlusion).

The above may give you a general idea. For more information about applications, properties and quality of our specialties, please ask our experts.
SOFTISAN® 649 – the compliant and modern alternative to lanolin

Applications
- Wound dressing
- Wound care (ointments, creams, lotions, emulsions)
- Protective baby skin treatment
- Ophthalmic formulations
- Nasal preparations
- Powder additive
- Transdermal drug delivery systems

Characteristics
- Based on pure vegetable and synthetic raw materials (Bio-Diglyceryl Polyacyladipate-2)
- Non-occlusive
- Superior adhesion to skin and mucosae
- Low water content ≤ 0.25% (m/m)
- High water binding capacity of more than 200% (m/m)
- Free of additives such as antioxidants, preservatives or stabilizers

WITEPSOL® – well-established hard fats for suppository/ovule production

Expertise in hard fats for decades
- Production in Witten since mid 1950s
- 18 different grades

State-of-the-art production
- Production through de novo synthesis
- Modern Sandvik pastillation belt
- Clean room class D environment
- Automatic packing process
- Full GMP compliance

The above may give you a general idea. For more information about applications, properties and quality of our specialties, please ask our experts.
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WITEPSOL® – well-established hard fats for suppository/ovule production

Our WITEPSOL® grades

- **W** Series (5 types)
- **H** Series (7 types)
- **E** Series (3 types)
- **S** Series (3 types)

GMP-certified production

- US: FDA-approved
- EU: GMP-certified

State-of-the-art production

- Production through de novo synthesis
- Modern Sandvik pastillation belt
- Clean room class D environment
- Automatic packing process
- Full GMP compliance

Regulatory aspects

- US-DMF No. 420
- GRAS (CFR § 178.161)
- Ph. Eur., USP and JPE monograph compliant

Mucosa and skin protection

Rectal irritations caused by suppositories may be due to various reasons. The use of coarse crystalline substances or subsequent recrystallization on the surface of the suppositories as well as many plant extracts – e.g. Echinacea extract – can cause irritations of the rectal mucosa. Such irritations can be reduced by using certain WITEPSOL® grades (WITEPSOL® H 19 and WITEPSOL® S 58). These hard fats contain our excipient SOFTIGEN® 701, which is able to protect the mucosa and also encapsulates the drug by forming a slight gel.

Therefore, these hard fat grades are especially recommended for use in hemorrhoidal suppository applications or for ovule usage.
Hard fats – application beyond suppositories

In addition to our WITEPSOL® types, we also offer SOFTISAN® 378, a fat with a consistency similar to natural lard. SOFTISAN® 378 complies with the requirements of the Ph. Eur. monograph „Hard Fat“.

WITEPSOL®s and SOFTISAN® 378 are used in pharmaceutical dosage forms like:
- Chewable tablets, e.g. anticancer formulations
- Creams, e.g. formulations containing corticosteroids
- Soft gel capsules, e.g. vitamin capsules, anti-cancer formulations

Hot Melt Coating

SOFTISAN® 154 – Hydrogenated Palm Oil
Triglyceride of blends of natural, saturated, even-numbered and unbranched vegetable fatty acids of mainly C16 and C18. Off-white to ebony-coloured solid mass with a faint fatty odour. SOFTISAN® 154 is characterized by its exceptional hardness at room temperature and its sharp melting range. The small interval between melting point and solidification point allows rapid and economic processing.

DYNASAN® 118 – Glycerol Tristearate
A pure, monounsaturated triglyceride, white microfine powder, based on stearic acid of plant origin, odourless and tasteless. It contains no additives, such as antioxidants or stabilizers.

Application examples:
- Taste masking for APIs with an unpleasant taste, e.g. scopolamine, coating to protect API from GI medium (enteric coating), e.g. Diclofenac, coating of granules, e.g. stick pack solutions.

DYNASAN® P 60 – Hydrogenated Palm Oil
A white hydrogenated fat powder, based on palm oil, odourless and with a neutral flavour. It contains no additives, such as antioxidants or stabilizers.

DYNASAN® 118 – Glycerol Tristearate
A pure, monounsaturated triglyceride, white microfine powder, based on stearic acid of plant origin, odourless and tasteless. It contains no additives, such as antioxidants or stabilizers.

Application examples:
- Taste masking for APIs with an unpleasant taste, e.g. scopolamine, coating to protect API from GI medium (enteric coating), e.g. Diclofenac, coating of granules, e.g. stick pack solutions.
Solid dosage forms

DYNASAN®'s 110®, 112®, 114, 116, 118, 122®

These pure monoacyl triglycerides are glycerin esters of selected saturated, even-numbered and unbranched single fatty acids of plant origin. They are free from antioxidants and other stabilizers.

Typical applications are in tablet production where the DYNASAN®s are used as lubricants and to increase the tablet fracture stability. Depending on the concentration, DYNASAN®s can also be used as a controlled release component.

Application examples:
- Osteoporosis prophylaxis and supportive treatment, in tablet form. Treatment of colds and influenza, in hard capsules. For use in dosage forms such as SLN, SEDDS, SMEDDS, Hot Melt Coating (taste masking), Hot Melt Extrusion.

Soft gel capsules

MIGLYOL® 812 N – Medium Chain Triglycerides (ratio ~ 60:40%)

Due to the nature of the product, it acts as a low-viscosity carrier oil.

IMWITOR® 742 – Glycerol Monocaprylocaprate, Type I

Acts as a solubilizer and penetration enhancer for poorly soluble drugs in oral administration forms.

Application examples:
- Various formulations, e.g. treatment of chronic hand eczema, benign prostatic hyperplasia, HIV/antiretroviral, vitamins.
- Osteoporosis prophylaxis and supportive treatment, in tablet form. Treatment of colds and influenza, in hard capsules. For use in dosage forms such as SLN, SEDDS, SMEDDS, Hot Melt Coating (taste masking), Hot Melt Extrusion.

* Not in continuous commercial production, available on demand only, but can be offered in sample volumes.
Veterinary formulations

C8/C10 triglycerides (MCT oils)

MIGLYOL® 810 N – Medium Chain Triglycerides
(ratio ~ 70:30%)

MIGLYOL® 812 N – Medium Chain Triglycerides
(ratio ~ 80:20%)

Application examples:
Veterinary injection suspension (Amoxicillin, Ceftriaxone)

MIGLYOL® 840 – Propylene Glycol Dicaprylocaprate

Application examples:
Pour-on formulation for treatment against internal and external parasites (e.g. Ivermectin, Moxidectin)

Notes

18 | Scope of application

The above may give you a general idea. For more information about applications, properties and quality of our specialties, please ask our experts.

19 | Scope of application
Contact

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