Pharmaceutical Compounding in Belgium

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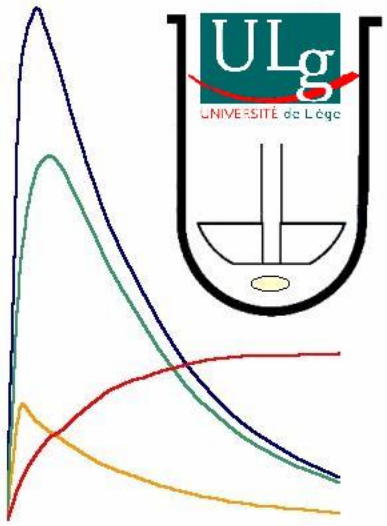


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(NORWAY)
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Greenland Sea
Denmark Strait
Norwegian Sea
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Tromsø
Murmansk
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Arkhangel'sk
Reykjavik
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NORWAY
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Umeå
FINLAND
Trondheim
Tórshavn
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Campine
St-Nicolas
Gand
Escaut
Malines
Meuse
Hasselt
Plaine de Flandre
Roulers
Alost
Louvain
Courtrai
BRUXELLES
ALLEMAGNE
Mouscron
Liège
Hesbaye
Tournai
Verviers
Hautes Fagnes
La Louvière
Namur
Mons
Charleroi
Escaut
Fagne
Plateau de l'Ardenne
FRANCE
LUXEMBOURG
Arlon
Meuse
50 km

FORMULAIRE THERAPEUTIQUE MAGISTRAL

1RE EDITION - PHARMACIENS

2003

Edité sous la direction du
Service Public Fédéral Santé publique, Sécurité de la Chaîne alimentaire et Environnement, Direction Générale de la Protection de la Santé publique: Médicaments

THERAPEUTISCH MAGISTRAAL FORMULARIUM

1STE UITGAVE - APOTHEKERS

2003

Uitgegeven onder de directie van
de Federale Overheidsdienst Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu, Directoraat-Generaal Bescherming Volksgezondheid: Geneesmiddelen

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Elaboration of a new formulary for pharmaceutical compounding in Belgium

In 1997, the Belgian Ministry of Health decided to take the necessary steps to guarantee the quality of compounded products.

A working party responsible for elaborating a new formulary was appointed and subsequently integrated into the Belgian Pharmacopoeia Commission.

The new formulary called « Formulaire Thérapeutique Magistral/Therapeutisch Magistraal Formularium »(FTM/TMF) had to be validated on three aspects:

1. Therapeutic effectiveness and safety
2. Pharmaceutical quality and stability
3. Socioeconomic benefit

FORMULAIRE THERAPEUTIQUE MAGISTRAL
1RE EDITION - PHARMACIENS

Dermatologists often prescribe compounded products due to the importance of the medication vehicle and the unavailability of certain medication combinations. A compounding pharmacist can compound drug products or combinations of drug products in ointments, creams, gels, and pastes based on specific patient needs

FORMULAIRE THERAPEUTIQUE MAGISTRAL
1RE EDITION - PHARMACIENS
(SUITE)

Three main requirements:

1. therapeutic benefit:

   The quality starts with the validation on the therapeutic level: all the formulations described in the FTM were developed in collaboration with experts in pharmacology and clinicians who helped to select the active substances, the vehicles and the preparations based on their therapeutic effectiveness.

Three main requirements(continued):

1. therapeutic benefit,
2. socio-economic benefit

   These formulations were also evaluated with regard to their cost in comparison with the corresponding proprietary products when available.

Three main requirements (continued):

1. therapeutic benefit,
2. socio-economic benefit and
3. top-level pharmaceutical quality of the preparations described in the FTM.

   After the selection of the formulations based on the two above-mentioned criteria, the next step was to validate the formulations by the laboratories of Pharmaceutical Technology and of Drug Analysis of the Belgian universities.

PHARMACEUTICAL QUALITY

The quality of the chemicals: **distributors of raw materials have to submit an analytical dossier to the Belgian Pharmacopoeia Commission with a Certificate of Analysis and samples to be controlled by authorized laboratories.**

The quality of the finished product:

- **validation of the formulations by the laboratories of Pharmaceutical Technology and of Drug Analysis of the Belgian universities.**
- **stability studies if necessary, on preparations stored during 2 months at ambient temperature and at 4°C.**
- **"ring tests" intended to verify the feasibility of the compounding processes and to control the conformity of the preparations to the analytical standards.**

The implementation of a quality system **also belongs to the new trend in pharmaceutical compounding in Belgium: it includes the availability of suitable equipment and premises as well as the traceability.**

I - DERMATOLOGIE
I - A - 1 - a
1

CHLORHEXIDINE DIGLUCONATE (SOLUTION HYDRO-ALCOOLIQUE A 0,5%)

INDICATIONS

Désinfection hygiénique et chirurgicale des mains.
Désinfection rapide de la peau intacte, par exemple avant une intervention chirurgicale, une injection ou le placement d'une sonde.

COMPOSITION

Rp	*Chlorhexidine digluconate solution à 20%*	*2,50 g*
	Alcool dénaturé à l'éther	*70 g*
	Eau purifiée q.s. ad	*100 g*

MODE OPERATOIRE

Tarez un becher.
Pesez séparément les différents constituants.
Dans ce becher, introduisez 2,50 g de solution de chlorhexidine digluconate à 20%.
Ajoutez-y 70 g d'alcool dénaturé à l'éther et complétez à 100 g en tenant compte de la tare, avec de l'eau purifiée fraîchement bouillie et refroidie. Agitez pour homogénéiser.
Conditionnez la préparation dans un flacon en verre brun.

CONSERVATION

A une température comprise entre 15 °C et 25 °C.

DUREE DE CONSERVATION

2 mois.

In every monograph, the following headings can be found:

- **Indications**
- **Composition**
- **Compounding process**
- **Storage**
- **Shelf life**
- **Comments**
- **Dosage and recommendation**

REMARQUES

La solution ne doit pas être diluée avant l'emploi.

COMMENTAIRES

La solution alcoolique de chlorhexidine ne peut pas être appliquée sur une peau lésée et ne peut pas entrer en contact avec l'oreille moyenne.
Elle est incompatible avec les tensio-actifs anioniques (par exemple les savons).

POSOLOGIE USUELLE ET RECOMMANDATION

➤ ***Désinfection hygiénique des mains***
Lavez préalablement les mains et les poignets, puis séchez- les.
Prenez la solution dans la paume des mains et frottez toute la surface des mains et des poignets jusqu'à séchage complet, en portant une attention particulière aux espaces interdigitaux.

➤ ***Désinfection rapide de la peau intacte***
Frottez la peau pendant 30 secondes avec de la gaze imprégnée de solution. Laissez sécher.

CREME AU CETOMACROGOL TAMPONNEE

	Qté 100 g	Autre qté. x g	N° du registre	Pesées
Tare du becher (A)				
Alcool cétostéary-lique	7,2 g			
Cétomacrogol 1000	1,8 g			
Vaseline blanche	15 g			
Paraffine liquide	6 g			
Eau purifiée	60 g			
Phosphate monosodique dihydraté	0,30 g			
Sorbate de potassium	0,27 g			
Eau purifiée	5 g			
Acide phosphorique dilué ou hydroxyde de sodium 1 M q.s.	ad pH 5			
Eau purifiée q.s.	ad 100 g			
Poids total	A + 100 g	A + x g		

Date de préparation	Signature(s)

Remarques personnelles :

Weighing sheet serving as a compounding record which must document the following:

1. The ingredients and amounts or volumes used including the source, lot numbers and expiration dates;

2. The order of the mixing or preparation of the product including the date mixed;

3. The identity of the pharmacist and any staff member involved in each step of the procedure; and

4. The pharmacy's lot or identification number and expiration date for the compounded drug/product if applicable.

BETAMETHASONE DIPROPIONATE FTM (CREME HYDROPHILE A 0,064%)

PRESCRIPTION

Rp/ Crème hydrophile à 0,064% de dipropionate de bétaméthasone FTM dt. x * g

**** Cette quantité doit être limitée à 50 g (voir page 116).***

N.B. La concentration de 0,064% de dipropionate de bétaméthasone dans cette préparation est la concentration maximale recommandée.

COMPOSITION

Bétaméthasone dipropionate 0,064%,
crème au cétomacrogol tamponnée q.s.

PROPRIETES

Préparation topique ayant une activité corticostéroïdienne très puissante.

POSOLOGIE USUELLE

Une ou deux application(s) par jour en couche mince sur toute la surface des lésions à traiter.

RECOMMANDATION

Le traitement sera arrêté dès que les lésions sont contrôlées.

Dans les cas favorables, cet arrêt peut avoir lieu après quelques jours. Il est conseillé de ne pas prolonger le traitement au-delà d'une semaine sans contrôle médical. La quantité de crème appliquée par semaine devrait en tous cas être inférieure à 50 g.

INDICATIONS

Toutes les indications des corticostéroïdes à usage topique.

CONSERVATION

A une température comprise entre 15 °C et 25 °C.

DUREE DE CONSERVATION

2 mois (7 jours sans agent conservateur).

REMARQUES

A la demande expresse du médecin, le pharmacien préparera extemporanément la crème au cétomacrogol tamponnée, sans agent conservateur. La quantité prescrite sera alors limitée en conséquence.

COMMENTAIRES

Voir la fiche I-B-1-a-1, page 124.

Formulary for physicians: abridged version of the formulary for pharmacists: 1 page(2 sides)maximum per monograph with the following headings:

- ***Instructions for prescription***
- ***Composition***
- ***Properties***
- ***Dosage***
- ***Recommendation***
- ***Indications***
- ***Storage and shelf life***
- ***Comments***

Preparations for cutaneous application

E.P. Classification

- Semisolid preparations
- Liquid preparations
- Powders

SELECTION OF ACTIVE SUBSTANCES

- Anti-infectives
- Corticosteroids
- Antipruritics
- Keratolytic agents
- Miscellaneous

CLASSIFICATION

I - DERMATOLOGIE

A. PREPARATIONS ANTI-INFECTIEUSES

CLASSIFICATION

A.Anti-infectives

1.antiseptics and disinfectants

- Chlorhexidine digluconate
- Clioquinol, Iodine, Povidone iodine
- Potassium permanganate

2.antibiotics

- Clindamycin, Erythromycin

3.antifungals

- Econazole nitrate, Miconazole nitrate
- Nystatin

4.Scabicides and Pediculicides

- Benzyl benzoate
- Crotamiton
- Malathion
- Permethrin

G. AUTRES PREPARATIONS

- After the delivery of the FTM/TMF at the end of 2003, organization of many seminars for both pharmacists and dermatologists by continuing education societies.
- To remain efficient, the FTM will be regularly updated by revising the existing formulations, by removing obsolete compositions and by inserting new formulations meeting therapeutic needs.

OTHER THERAPEUTIC CLASSES

- Cardiovascular system
- Gastrointestinal tract
- Respiratory tract
- Analgesic and anti-inflammatory drugs
- Opioids
- CNS drugs
- Hormone therapy
- Anti-infectives
- Minerals and vitamins
- Ear, nose and throat

Appropriate dosage forms for the other therapeutic classes

- Capsules
- Oral solutions and suspensions
- Suppositories and rectal ointments
- Nasal solutions and suspensions
- Auricular solutions
- Oral gels

etc

RING TEST nr 3 – September 2004

130 pharmacists

1. Acetazolamide capsules
2. Colloidal silver suppositories
3. Ergotamin tartrate + Caffein suppositories
4. Ergotamin tartrate + Caffein capsules
5. Erythromycin + Benzoyl peroxide gel
6. Fludrocortisone acetate capsules
7. Hydrocortisone acetate + Lidocaïne HCl oral gel
8. Loperamide capsules
9. Metronidazole benzoate pediatric suspension
10. Scopolamine N-butylbromide capsules
11. Nitrofurantoïne pediatric suspension
12. Triamcinolone acetonide nasal suspension
13. Xylometazolin HCl nasal solution

1. Suppositoires à 150 mg de collargol

Composition

Rp Collargol		0,150 g
Mannitol poudre fine		0,150 g
Adeps solidus H 15		q.s.
pf 1 suppositoire (**de 3 g**)	dt X	

ERGOTAMINE TARTRATE (TRITURATION A 2%)

Rp	Ergotamine tartrate	1,00 g
	Acide tartrique	1,0 g
	Oxyde de fer rouge	50 mg
	Excipient diluant B* q.s. ad	50g

*Mannitol poudre fine 99,5% + Silice colloïdale anhydre 0,5%

Erythromycin 3 % and Benzoyl peroxide 5 % gel

Composition	Theoretical quantities for 50 g	Quantities for 60 g
Erythromycin	1.5 g	2.16 g
Benzoyl peroxide	2.5 g	4.40 g
SDS	0.05 g	0.06 g
Carbomer 974P	0.35 g	0.42 g
Trometamol	0.30 g	0.36 g
Propyleneglycol	5.0 g	6.0 g
Purified water	q.s. ad 50 g	q.s. ad 60 g

Gélules à 0,025 mg d'acétate de fludrocortisone

Composition

_Rp Fludrocortisone acétate	0,025 mg*
Excipient diluant B **	q.s.
pf 1 gélule	dt n° XL

* sous forme de trituration à 0,2%

**Mannitol poudre fine 99,5% - Silice colloïdale anhydre 0,5%

FLUDROCORTISONE ACETATE (TRITURATION A 0,2%)

Rp Fludrocortisone acétate	*100 mg*
Riboflavine	*50 mg*
Excipient diluant B q.s. ad*	*50 g*

Gel buccal contre les aphtes

Composition

Rp	Lidocaïne chlorhydrate	5,0 g
	Hydrocortisone acétate	1,0 g
	Phosphate disodique dihydraté	50 mg
	Glycérol	17 g
	Esprit de menthe	0,50 g
	Saccharine sodique	100 mg
	Hydroxypropylméthylcellulose 4000	3 g
	Eau conservante q.s. ad	100 g

Suspension pédiatrique à 30 mg/ 5 ml de nitrofurantoïne

Suspension pédiatrique de nitrofurantoïne

Composition

Rp	Nitrofurantoïne « macrocristalline »	0,420 g
	Cellulose microcristalline et carmellose sodique*	2,10 g
	Glycérol	7,0 g
	Essence de banane	3 gouttes
	Eau conservante q.s. ad	70 ml (= 71 g)

*52,5 g de dispersion aqueuse à 4% (dispersez au mixer à froid pendant 3 minutes 4 g de cellulose microcristalline et carmellose sodique – AVICEL^{R} RC 581 – dans 96 g d'eau conservante – pesez 52,5 g de cette dispersion pour réaliser la préparation)

FTM/TMF is an official document and a dynamic reference book intended to be complemented and regularly updated in function of the patient/physician expectations and of the advances in medicine and pharmaceutical sciences.

Disposable blades

The disposable mixing blades were designed at the request of practicing pharmacists and laboratory personnel, who work frequently with sensitive preparations and suspensions.
The disposable blades are recommended for formulations, where it is crucial to maintain the "closed" environment after the mixing process.
The disposable blades are made from an inert polymide plastic and attach (clockwise) directly to appropriate blade shaft. Once the preparation is completed, the operator simply disengages (counterclockwise) the disposable blade from the shaft, leaving the blade inside the jar.
Disposable mixing blades provide excellent mixing results with minimal clean-up.

UNGUATOR® - Jars

All Unguator® jars operate on the patented “piston-principle” design, which serves unique functions prior, during, and after the mixing process. The Unguator® system is unique in that all ingredients can be weighed into the mixing jar at the same time. The closed environment achieved in the container eliminates the problems of air intake and contaminations associated with traditional preparations.

The jars serve simultaneously as:

- Measuring Unit
- Mixing Chamber
- Storage Container
- Dispensing Jar

Therefore, all materials and ingredients remain in the closed jar throughout the mixing process. The final product represents a consistent, superior blending result with:

- Extended shelf life
- Significant time, cost savings
- Accurate, specific dispensing
- Minimal clean-up

Unguator® jars are made from a durable polypropylene/polyethylene plastic and can be heated in a hot water bath or microwave oven.

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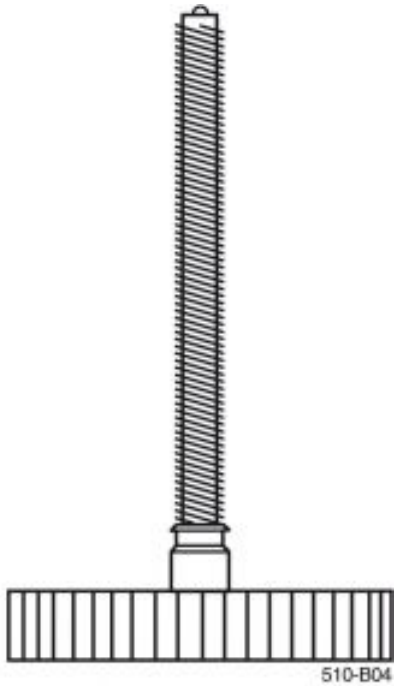


Spindle

The spindle serves as dispensing aid for 300/390ml and 500/600ml jars. **Important!** The jars have the spindle attached to them and have to be removed by rotating to the right, prior to the mixing process.
Prior to administering the finished preparation to the patient, the spindle needs to be inserted through the bottom of the jar by rotating to the left until the spindle has reached its locked position.

(Attention: by rotation counter clockwise, the moveable bottom can be damaged by mistake – these jars can only serve as dispensing jar, but no longer as mixing jar)

AirDynamic® Pump System

The AirDynamic® pump system consists of a pump ball and jar adapter that are connected by a hose.

By pumping air pressure into the bottom of the 300, 500, 1000ml jars, the moveable bottom rises towards the top and allows the easy dispensing of the formulation from the jar. This also allows for the easy transfer of finished materials from one jar to other jars via the jar coupling.

The large Unguator® Jars are particularly well suited as storage and transfer containers of semi-solid materials as problems with evaporation, oxidation, and contamination are largely avoided.

The jars remain closed throughout the mixing process and the variable volume insert ensures that no air can enter the material during storage and dispensing.

Coupling

The UNGUATOR® coupling connects larger and smaller jars to serve as transfer nozzle for hygienic dispensing from bulk preparations in the larger dosage containers.

The coupling is connected at the centre of the jar lid. For dispensing from 300, 500 and 1000ml jars, the spindle or AIR-Dynamik® system may be used.

IMPORTANT! The finished product should be transferred shortly after the mixing process, since the product is often still warmer than room temperature and at a lower viscosity than after the cooling process.

Why has a new method of ointment preparation become necessary?

So far today, ointment preparations according to the GMP (Good Manufacturing Practice) standard are limited in pharmacies. It is important that a validation in the preparation of prescription ointments is guaranteed. Only with such validation will the quality and dependability of the product be reached. For one, the preparation with the conventional method of the mortar and pestle risks microbiotic contamination of the ointment. Secondly, ointments that are sold in the conventional jars, are contaminated with the finger and germs kill the effectiveness of the prescription

Are trial tests for purchase decisions necessary for pharmacists before implementing the UNGUATOR® - Technology?

Generally no. In almost all instances, the use of the UNGUATOR® - technology is specified to the preparation of various prescription ointments. We have experienced that approximately 95% of all ointment formulations sold in pharmacies can be guaranteed with the with the UNGUATOR® - equipment, as well as with the traditional ointment mill. Recommended preparations include:

- Suspension ointments
- Gels
- Emulsion ointments
- Waxes and hydrophilic ointments
- Pastes
- Crystalline substances, such as urea, can be added to the mixing jar, after being crushed down with the traditional mortar and pestle.

Are UNGUATOR® -jars reuseable?

It is advised that individual ointment preparations that are given to the patient, are disposed without the reuse or refill. The threat of germ contamination is too great for the new prescription ointment that is to be prepared in the recycled ointment container. For the mixing in UNGUATOR® -jars in larger quantities, the same container can be reused for the same ointment mixing process that is then dispensed into smaller ointment jars for sale to the patient.

Which UNGUATOR® jar sizes are most commonly used in the pharmacy?

The best selling sizes of ointment jars are generally 50ml and 100ml. Usually, these are the amounts in dosage that doctors prescribe to their patients for treating an infection or other illness.
Additionally, 300ml, 500ml and 1000ml jars are used more often in pharmacies for preparing the ointment in bulk, before dispensing into smaller jars with aid of the UNGUATOR® – coupling.

Which is the difference in use of mortar & pestle, ointment plate and UNGUATOR® - mixing system?

In Germany, appr. 50% of pharmacists use the UNGUATOR® – Technology for the preparation of prescription ointments. Neither, the mortar and pestle nor the ointment plate can even be compared with this new technology. The advantages of fast preparation, few, if any, germ contaminations or air intakes and no cleaning requirements have also convinced pharmacists worldwide. One reason for not choosing the UNGUATOR® – Technology by pharmacists has generally been the limited requirement of actually preparing prescription ointments. With the introduction of the short (ear and nose) and long (rectum and vagina) applicators for injection as well as varionozzles of 1, 2 and 4 mm the UNGUATOR® – Kruken have shown tremendously popular for various purposes.

How does the UNGUATOR® – Spindle work?

For the 300ml and 500ml ointment jars, the spindle serves as the tool to screw the sliding bottom to the very top. It is necessary to review the use of it in the operating manual, before penetrating the sliding bottom after the mixing process. This method of dispensing the ointment has proven very successful by pharmacists and should soon be introduced to the smaller containers as well.

The Unguator is an excellent addition to any compounding pharmacy. It saves time and can greatly improve product quality. The Unguator is very flexible and versatile with the various jars and attachments. It can be used for enhanced packaging, stability and operator/patient safety."

Loyd V. Allen, Jr., Ph.D. – Editor in Chief,
International Journal of Pharmaceutical Compounding (IJPC)

UNGUATOR® Advanced Mixing Technology

Revolutionizing the pharmacy environment has been the main focus of the UNGUATOR® technology. Its aim has been to facilitate the preparation of many pharmacy, cosmetic, veterinary, and other formulations, in a fraction of the time and cost associated with conventional methods.

Its line of advanced sweep – wall mixing systems has accelerated formula developments and has increased overall production efficiency in preparation of compounding prescriptions, such as creams, gels, pastes, powders etc.

The UNGUATOR® product assortment also consists of a unique set of “push-up” jars that work specifically with its mixing devices.

While no single device can accommodate every formulation in the pharmacy, the use of the UNGUATOR® system offers an entire range of new compounds with consistent quality by replacing many of the traditional tools.

The UNGUATOR® 2000 employs four on-board microprocessors, which enable the user to operate the machine as a stand - alone device or, via serial port, with the UNGUATOR® Assist software from the PC.
All general mixing parameters are pre-set in the system, which allow the operator to concentrate more on raw materials and less on recipe specifics, leaving it up to the device to continually adjust the mixing settings.
Whether making creams, gels, ointments, powders, suspensions, emulsions, or other formulations, the UNGUATOR® 2000 fully automates and documents the once cumbersome blending process.
With the introduction of this model, laboratories and pharmacies are now able to prepare everything from the most intricate reaction mixing, at very slow speed, to bulk manufacturing, up to 1000ml. With a speed range starting as slow as 120 rpm and up to 2500 rpm, this model is not limited by low viscosities or other raw material properties.
Fully compatible with all current Unguator® products, the system quickly transforms any pharmacy into a fully capable compounding facility.


UNIGUATOR® 2000

Assist Software

The UNGUATOR 2000® operates efficiently as a stand alone machine by itself or assisted by its newly available, Windows based, UNGUATOR® Assist Software package.

Prepares everything from reaction mixes to high-speed homogenizations thanks to its flexible speed range of 120 rpm to 2,500 rpm.

Pre-programmed mixing parameters automate preparations. Manual programming for formulation mixing is optional.

The computer-assisted design allows for automatic recipe saving, customization, and retrieval. It prints labels, test results, and other types of documentation.

Standard mixing blades

The standard mixing blades used with the Unguator technology are available in (7) seven different sizes for each corresponding jar volume.
Each blade is slightly larger in diameter than the equivalent jar size, which allows the standard blades to "sweep" the inner chamber wall, creating shear and promoting optimal amalgamation.
Further, the blades were designed with a sharp leading edge to both act as a grinding mechanism and ensure product homogeneity. The standard mixing blades achieve the finest results in all formulations.
The shaft of each blade is made of a titanium-hardened NIRO stainless steel (grade 1.4301) and the winged "S" blade is composed of durable Delrin® polyoxymethylene plastic.

Topical DMSO and Dexamethasone for the treatment of the Hand-Foot Syndrome (HFS)in Oncology Patients

Hand-Foot Syndrome (www.chemocare.com/managing/fullstory.sps?iNewsid=23197&itype=1875)

Other terms: Palmar-Plantar Erythrodysesthesia; PPE

What is hand-foot syndrome?

Also called hand-foot syndrome or hand-to-foot syndrome, Palmar-Plantar Erythrodysesthesia is a side effect, which can occur with several types of chemotherapy or biologic therapy drugs used to treat cancer. For example, Capecitabine (Xeloda®), 5-Flurouracil (5FU), continuous-infusion doxorubicin, doxorubicin liposomal (Doxil®), and high-dose Interleukin-2 can cause this skin reaction for some patients. Following administration of chemotherapy, small amounts of drug leak out of very small blood vessels called capillaries in the palms of the hands and soles of the feet. Exposure of your hands and feet to heat as well as friction on your palms and soles increases the amount of drug in the capillaries and increases the amount of drug leakage. This leakage of drug results in redness, tenderness, and possibly peeling of the palms and soles. The redness, also known as Palmer-Plantar erythema, looks like sunburn. The areas affected can become dry and peel, with numbness or tingling developing. Hand-foot syndrome can be uncomfortable and can interfere with your ability to carry out normal activities.

Which drugs cause hand-foot syndrome?

The chemotherapy drugs that have been reported to cause hand-foot syndrome in some patients include:[1]

- Capecitabine (Xeloda®)
- Cytarabine (Cytosar-U®)
- Floxuridine (FUDR®)
- Fluorouracil (5-FU)
- Idarubicin (Idamycin®)
- Liposomal doxorubicin (Doxil®)

How is hand-foot syndrome treated?

Hand-foot syndrome is first treated by reducing the dose or stopping treatment with the chemotherapy drug that is causing it. Other approaches to managing hand-foot syndrome include:

Corticosteroids: Steroids work by reducing inflammation. Your doctor may recommend a systemic corticosteroid (administered in a pill) to help relieve the symptoms of hand-foot syndrome.

Dimethyl-sulfoxide (DMSO): Topical treatment with DMSO has shown activity in treating leakage of chemotherapy drugs into tissues.[2]

Vitamin B6 (pyridoxine): A small clinical trial has shown that treatment with vitamin B6 can reduce the symptoms of hand-foot syndrome.[3]

Lopez AM, Wallace L, Dorr RT, Koff M, et al. Topical DMSO treatment for pegylated liposomal doxorubicin-induced palmar-plantar erythrodysesthesia. Cancer Chemother Pharmacol. 1999; 44(4): 303-6.

Abstract:

Abstract Purpose: Chemotherapeutic regimens that utilize fluorouracil, cytarabine, and doxorubicin have been shown to cause a dermatologic syndrome known as hand-foot syndrome, or palmar-plantar erythrodysesthesia syndrome (PPES). Pegylated liposomal doxorubicin has proven effective in the treatment of AIDS-related Kaposi's sarcoma, ovarian cancer refractory to platinum and paclitaxel therapies, and metastatic breast cancer. In a study of the treatment of refractory epithelial cell ovarian cancers with lipozomal doxorubicin utilizing intravenous doses of 50 mg/m^2 every 3 weeks, grade 3 PPES was observed in 29% of patients (10/35) and required dose reductions and/or dose delay after a median of three therapy cycles. Methods: Current methods to prevent pegylated liposomal doxorubicin-induced PPES include dose reduction, lengthening of the drug administration interval and ultimately, drug withdrawal. Topical 99% dimethylsulfoxide (DMSO) also has shown strong activity in treating tissue extravasation reactions during intravenous administration of doxorubicin. Results: Two patients undergoing chemotherapy with pegylated liposomal doxorubicin, 50 mg/m^2 every 4 weeks, developed grade 3 PPE after three cycles. Their PPES resolved over a period of 1 to 3 weeks while receiving topical 99% DMSO four times daily for 14 days. Conclusions: While these results are promising, patients must be treated in a prospective study of this topical DMSO formulation to definitively document its therapeutic efficacy.

What is hand-foot syndrome?

Hand-foot syndrome is a side effect of some chemotherapy drugs that results when a small amount of drug leaks out of the smallest blood vessels in the palms of the hands and soles of the feet. The amount of drug in the capillaries of the hands and feet increases due to the friction and subsequent heat that is generated in those extremities. As a result, more drug may leak out of capillaries in these areas. Once out of the blood vessels, the chemotherapy drug damages surrounding tissues.

Topical DMSO and Dexamethasone for the treatment of the Hand-Foot Syndrome (HFS)in Oncology Patients

Rp	CARBOPOL 940	0.243
	Glycerol 85%	4.000
	PARABENS 10% in Propyleneglycol	0.400
	Trometamole	0.257
	Purified water	35.050
	DMSO (Dimethylsulfoxide)	50.000
	Dexamethasone	0.050
	Excipial Fettsalbe[R]	10.000
	Total	100.00

Excipial Fettsalbe

SPIRIG PHARMA AG (Cholesterol. - Isopropylium myristic. - Monostearin. - Paraffin. liquid. - Vaselin. album)

Excipial Fettsalbe - eine Fettgrundlage - ist wasserfrei und stark fettend; sie hält die Feuchtigkeit in der Haut zurück und ist mit Wasser abwaschbar. Sie enthält kein Parfum.

- Préparer le gel de Carbopol avec les 5 premiers constituants
- stériliser à 121° C pendant 15 minutes.
- Incorporer aseptiquement au gel stérile le DMSO, la dexaméthasone et l'excipient *EXCIPIAL FETTSALBE*
- Conditionner dans un tube de 50g en Al vernis
- Conservation: température ordinaire

Prescription d’un oncologue de la Clinique des Bruyères

Rp	Gel de Carbopol	40 g
	Dexaméthasone	50 mg
	DMSO	50 g
	EXCIPIAL LIPOCREME	10 g

Excipial Fettcreme (Lipocreme) pflegt trockene, fettarme Haut

Beschreibung:
Excipial Fettcreme (Lipocreme) pflegt und schützt trockene, empfindliche Haut. Anwendung auf kleinen bis mittelgroßen Hautarealen.

Inhaltsstoffe:
Aqua, Paraffinum Liquidum, Paraffin, Sorbitan Isostearate, Petrolatum, Sorbitan Laurate, PEG-25 Hydrogenated Castor Oil, Hydrogenated Castor Oil, Cera Alba, Polysorbate 20, Magnesium Sulfate, Stearic Acid, Triclosan, Chlorhexidine Dihydrochloride, Amyl Cinnamal, Benzyl Benzoate, Benzyl Salicylate, Limonene, Alpha-Isomethyl Ionone, Parfum.

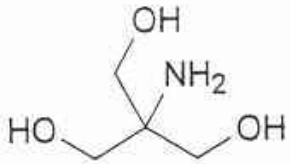
Formule proposée par le LPG ULg

Octobre 2003

Rp	Carbomère 980	2 g
	Trométamol	1,5 g
	Propylèneglycol	10 g
	Nipagine/Nipasol 8:2	0,1 g
	Eau purifiée	q.s. ad 50 g
	DMSO	50 g
	Dexaméthasone	50 mg

TROMÉTAMOL

Trometamolum



$C_4H_{11}NO_3$ M_r 121,1

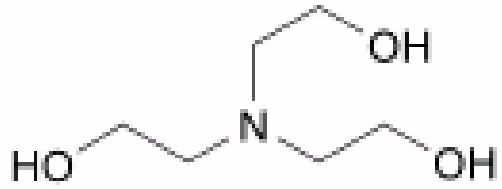
DÉFINITION

Le trométamol contient au minimum 99,0 pour cent et au maximum l'équivalent de 100,5 pour cent d'aminométhylidynetri(méthanol), calculé par rapport à la substance desséchée.

Également appelé tromethamine ou tris(hydroxymethyl)aminomethane

TROLAMINE

Trolaminum



$C_6H_{15}NO_3$ M_r 149,2

PRODUCTION

La méthode de production doit être évaluée de façon à déterminer le potentiel de formation de 2,2.-nitrosoimino(diéthanol) (*N*-nitrosodiéthanolamine). Si nécessaire un essai validé pour la substance doit être effectué (critère d'acceptation d'au maximum 25 ppb) et/ou la méthode de production est validée pour démontrer qu'elle assure une élimination acceptable.

Gel au gluconate Ca contre les brûlures par HF

Rp	Hydroxyéthylcellulose*	17,5 g
	Sol.conc. de parabens	10 g
	Gluconate Ca	25 g
	Eau stérile q.s. ad	1000 ml

*NATROSOL^{R} 250 HEC (utiliser le grade HR à 1,75% ou le grade MR à 3%)

N.B.: dans le Formularium Helveticum, on rajoute 0,5% de digluconate de chlorhexidine (2,5 g de la sol. à 20%)

CLASSIFICATION

A.Anti-infectives(continued)

Les classifications varient dans la littérature essentiellement parce que les critères d'appréciation ne sont pas toujours identiques :

- ➢ tests de vasoconstriction,
- ➢ action antimitotique,
- ➢ activité variable en fonction de l'excipient utilisé,
- ➢ tests thérapeutiques divers effectués dans des dermatoses différentes.

Pour la prescription magistrale, 23 préparations renfermant les molécules actives suivantes sont disponibles :

- ❒ **préparations très puissantes** renfermant :
  0,064%(maximum)de bétaméthasone dipropionate ou
  0,05% (maximum) de clobétasol propionate ou
  0,3% (maximum) de diflucortolone valérate
- ❒ **préparations puissantes** renfermant :
  0,121% (maximum) de bétaméthasone valérate ou
  0,1% (maximum) de diflucortolone valérate
- ❒ **préparations moyennement puissantes** renfermant :
  0,1% (maximum) de triamcinolone acétonide ou
  0,05% (maximum) de clobétasone butyrate
- ❒ **préparations peu puissantes** renfermant :
  1% (maximum) d'hydrocortisone acétate.

La concentration maximale recommandée pour chaque corticostéroïde en préparation magistrale est celle mentionnée ci-dessus.

Toute concentration supérieure pourrait entraîner des effets non contrôlés car n'ayant fait l'objet d'aucune étude clinique préalable sur un nombre suffisant de patients.

En cas de dépassement de la concentration maximale recommandée, le pharmacien doit vérifier l'intention du prescripteur. ***(2)***

En fonction de la puissance de la préparation, les quantités maximales à prescrire devront également être adaptées :

- ➢ **limiter à 50 g la quantité des préparations très puissantes même si on prescrit le corticostéroïde à une concentration plus basse que la concentration maximale recommandée;**
- ➢ **limiter à 100 g la quantité des préparations puissantes et moyennement puissantes.**

There are recommendations with regard to the highest concentration of corticosteroids to incorporate into topical compounded preparations: this highest concentration corresponds to the concentration used in proprietary products. A higher concentration would cause uncontrolled effects in the absence of a preliminary clinical study on enough patients.In case of reception of a prescription exceeding the maximum recommended concentration , pharmacists must check the intention of the prescriber. Depending on the potency of the preparation, the prescription of maximum quantities should be adapted: maximum 50 g of very potent preparations even if the preparation contains a lower concentration than the maximum recommended concentration, maximum 100 g of potent and moderately potent preparations.(except for patients suffering from acute manifestations of severe dermatoses such as acute extensive psoriasis).

En cas d'association avec l'acide salicylique dont la concentration la plus élevée ne doit pas dépasser 3%, la quantité maximale de préparation à délivrer doit être limitée à 50 g car la pénétration du corticostéroïde est augmentée en raison des propriétés kératolytiques de l'acide salicylique.

Les associations de plusieurs corticostéroïdes au sein d'une même préparation ainsi que le mélange de spécialités renfermant des corticostéroïdes différents sont à proscrire car ils n'ont aucune justification thérapeutique et ils augmentent le risque d'allergie de contact.

De même la dilution de spécialités à base de corticostéroïdes peut difficilement se justifier.
L'éventail de puissance de ces dernières est suffisamment large lorsqu'une réduction progressive de la corticothérapie s'avère nécessaire et il est possible de prescrire en préparations magistrales, tous les corticostéroïdes disponibles comme matières premières à des concentrations plus faibles. (7)

L'approche rationnelle consiste donc dans ce cas à prescrire une préparation magistrale ou une spécialité non diluée plutôt que de recourir à la dilution d'une spécialité puissante.

Le choix du corticostéroïde doit être évalué en fonction de l'affection à traiter, de sa localisation et de la durée du traitement.

Pour minimiser les effets secondaires systémiques, il faut se souvenir que la diffusion des principes actifs peut être modifiée par certains facteurs tels que l'âge et les variations ou anomalies de la peau.

La perméabilité de la peau dépend de ses qualités intrinsèques qui varient d'un individu à l'autre mais aussi chez un même sujet, suivant l'endroit à traiter; la voûte plantaire et la paume de la main ont une faible capacité de résorption tandis que le cuir chevelu, les aisselles, le visage ont une capacité de résorption plus importante et le scrotum a un pouvoir de résorption considérable.

Les dermatoses, avec ou sans plaies, modifient aussi la perméabilité de la peau. Un pansement occlusif augmente fortement la résorption; il conviendra donc d'être attentif à l'effet occlusif des langes chez les nourrissons et les incontinents.

L'excipient peut aussi influencer la pénétration percutanée d'un principe actif; le choix de l'excipient sera donc basé sur ses propriétés physiques et sur les symptômes cliniques de l'affection.