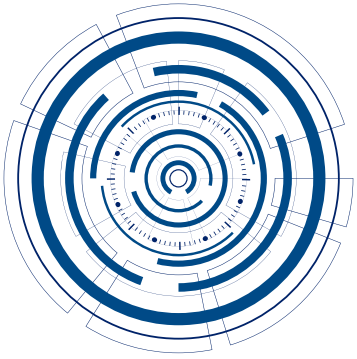


CHEMOEXFOLIATION

ENERPEEL® EL

• INSTRUCTION MANUAL •

CE

TEBITECH
Technologies and Biotechnologies
for dermatology and plastic surgery

ENGLISH

MEDICAL DEVICE FOR THE CHEMOEXFOLIATION AND CUTANEOUS REMODELLING OF THE PERIOCULAR AND PERIORAL AREA

***WARNINGS**

In order to use ENERPEEL® EL (Device) correctly, you must read this instruction manual carefully, so as to work properly and safely.
The ENERPEEL® EL Medical Device is constituted as a single-phase gel with very low acidity values (~ 0.90). For this reason strictly follow the warnings and information contained in this manual, in order to protect yourself and others against lesions or material damage.

IMPORTANT

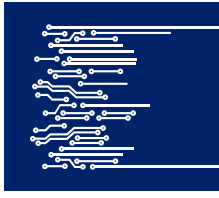
*The * symbol represents a warning sign and is applied next to safety information.*

GENERAL PRECAUTIONS

- Do not leave the Device within reach of children.
- Keep the Device in a safe place, protected against light and store in a cool, dry place.
- Handle with care, follow the indications concerning the preparation and execution procedures of the Device.
- During the preparation and execution phases, keep the Device and its accessories in a safe place, never leaving them close to the patient in order to avoid possible risks resulting in accidental and undesired contact with the patient.
- Immediately after use, close the Device by replacing the top.
- During the Device's preparation and execution phases, always wear appropriate protection.
- When the procedure is completed, dispose of used and no longer reusable Device and components in

accordance with specific national and local environmental protection and waste disposal regulations.

- The Device contains a mixture of acids (Lactic Acid and Trichloracetic Acid) and has an extremely acidic pH value; for this reason, follow the first-aid instructions below in the event of accidental and undesired contact with the Device.
  - In the case of accidental contact with untreated skin, neutralise by means of a 7% sodium bicarbonate solution and wash repeatedly and thoroughly with water for at least 15 minutes; remove any contaminated clothing and shoes.
  - In the case of accidental contact with the ocular conjunctiva, rinse thoroughly with water for at least 15 minutes, keeping the eyelids wide open. Then apply a suitable therapy.
  - In the case of accidental contact with oral mucosa, rinse thoroughly with water for at least 10 minutes.
  - In case of accidental ingestion, rinse mouth with water if the subject is conscious.
- Measures in case of accidental spillage: wash the area which may be contaminated using an abundant 7% sodium bicarbonate solution, and then rinse thoroughly with water.
- The manufacturing company declines all responsibility for any damage to property or persons resulting from incorrect or improper use of the Device.



1. DEFINITIONS, RATIONALE AND SCOPE OF THE DEVICE

ENERPEEL® EL is a Medical Device indicated for cutaneous exfoliation and remodelling (chemical peeling) of the periocular (including the eyelids) and perioral (not including the vermillion) areas. The Device has been designed to obtain results while controlling risks, both through the physiochemical form used and its unique dispensing and application system.

Chemoexfoliation is mainly indicated for the treatment of some dermatological forms characterized by actinic damage. Further to this it also acts as a factor of prevention from the consequences induced by photo exposure, including the development of potentially pre cancerous keratotic lesions.

Actinic damage (classified, by some authors as photo ageing) comprises a series of pathological conditions, such as actinic keratosis (in some cases these may have a pre cancerous potential), cutaneous elastosis & cutaneous dyschromias. Chemo exfoliation, that is, the removal of epidermal cells, followed by their renewal, results in a specific preventive action against the formation of cutaneous lesions (for example actinic keratosis).

The medical device ENERPEEL® EL is intended to be used to cause a superficial chemo exfoliation (removal of the horny layer and the superficial layer of the vital epidermis) of the periocular and perioral area. It should be applied onto intact skin with the aim of preventing some skin pathologies, such as actinic damage and in a broader sense damage induced by chronic photo exposure.

What is chemoexfoliation

Chemo-exfoliation (chemical “peeling”) is a medical procedure which constitutes controlled damage of the skin, performed through the use of organic acids. This procedure is used to improve the specific cutaneous conditions through the removal of dead cells from the horny layer and the regeneration and remodelling of the vital portion of the epidermis and/or dermis, with the ability to physiologically modify aesthetic appearance.
In particular, the chemical “peeling” of the periocular and perioral area must be performed carefully, taking into consideration the special morphology of these particular cutaneous areas.

How is chemoexfoliation classified

The chemical-exfoliation (chemical peeling) classification depends on the chemical agent used, its application time on the skin before neutralization or washing (when required) and the depth reached in the skin, is classified as very superficial (effecting the horny layer), superficial (which can reach the vital portion of the epidermis, down to the basal layer), medium-depth (which effects the papillary portion of the dermis) and deep (which can reach the reticular dermis). During the chemical peeling process a whitening of the skin may occur, a phenomenon also known as “frosting”.

What is “frosting”

“Frosting” is the visible appearance resulting from the denaturing of the epidermic and/or dermic proteins (keratin) which can be divided into 3 levels, depending on the depth reached by the acid:

Level I.

This chemical-exfoliation occurs at the superficial layer of the skin and/or on the entire epidermis. It appears as small sized white splotches, scattered about with medium intensity erythema or, in the case of a deeper action, as a more homogenous whitish surface through which a medium intensity erythema can be seen.

Level II.

This chemical-exfoliation occurs at the level of the papillary dermis. It appears as a homogenous white “lamella” in

which it is difficult to perceive the intensity of the erythema.

Level III.
This occurs as a result of chemical exfoliation carried out at the dermal reticular level. It manifests in the form of a greyish colour.

Definitions: *Procedure - Session - Cycle*

Procedure: The single treatment performed.

Session: The number of pre-defined procedures (treatments).

Cycle: The number of sessions performed per year.

ENERPEEL® EL is a Device made up by a single-phase gel (pH ~ 0.90) with a specially formulated acid blend base (lactic acid and trichloroacetic acid) indicated for the cutaneous exfoliation and remodelling (chemical peeling) of the periocular (including the eyelids) and perioral (not including the vermillion) areas.

The ENERPEEL® EL Device is designed to perform multi-layer applications (a maximum of 4 layers are recommended) in a single treatment on each cutaneous area *(see the definition of the cutaneous area in the following point 1.1.)*.

Based on the desired results and obviously on the type of patient, we recommend performing a yearly cycle made up of two sessions, each one composed by four procedures. The time interval between each procedure (within a single session).

The time interval between each procedure (within a single session) may range from 7 to 14 days, based on the type of patient and the desired result *(See chapter 2)*.

ENERPEEL® EL is a Device that can perform chemical-exfoliation (chemical "peeling") which can be defined as superficial (which involves the horny layer and the vital portion of the epidermis down to the basal layer) in relation to the exposure time before the neutralization process and the subjective response of each individual patient. However, it cannot be ruled out that it may become a medium-depth peel (involving the papillary portion of the dermis) depending on the number of layers applied, the contact time, the number of treatment procedures previously performed, the time interval between one treatment procedure and another, the patient's genetic- ethnic characteristics, phototype and skin type.

ENERPEEL® EL - percentage composition (w/w) of acids: Trichloracetic Acid 3,75%, Lactic Acid 15%.

IMPORTANT WARNINGS*

a. *In case of "frosting" formation, depending on the number of layers applied, the contact time, the number of treatment procedures previously performed, the time interval between one procedure and another, the genetic-ethnic characteristics, the phototype and skin type, proceed immediately with the neutralization using the appropriate NEU Neutralizer wipes.*

b. *The delivery Device (TebiPen™) comes with disposable Applicator tips, intended for a single patient and for a single session. The package contains 20 disposable Applicator tips to be used for up to the same number of procedures (see "Definition of the cutaneous area, physiochemical form and characteristics of the delivery device, preparation and delivery system" in the following point 1.1.).*

c. *The Device can only be used within the expiry date shown on the packaging.*

1.1. Definition of the cutaneous area, physiochemical form and characteristics of the delivery device, preparation and delivery system

Cutaneous area

The periocular and perioral application areas have been arbitrarily divided into the following cutaneous portions. *(See Figure 1)*:

CUTANEOUS UNIT	DESCRIPTION
A	Patient's right periocular area
B	Patient's left periocular area
C	Perioral area

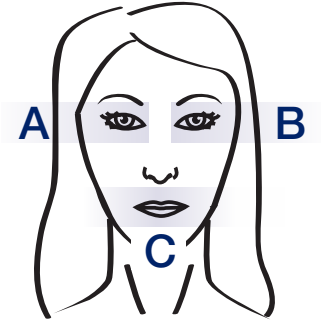


Figure 1

Physicochemical form

The physicochemical form is made up by a single-phase gel with controlled viscosity that reduces the risk of the Device spreading out and/or coming in direct contact with the ocular conjunctiva and/or the vermillion.

The Device contains a concentration of Lactic Acid of 15% (w/w) and Trichloracetic Acid in a concentration of 3.75% (w/w).

Characteristics of the delivery device, preparation and delivery system

TebiPen™ application device has been specifically conceived and designed taking into account the chemical-physical consistency of the Eyes&Lips exfoliating gel, the application area (periocular and perioral portion) and the safety and precision of the application.

TebiPen™ application device allows a precise dosage of the exfoliating gel and its specific Applicator tip grants a controlled, precise and safe application.

TebiPen™ application system is composed of the following components:

- a **Cartridge** containing the exfoliating gel protected by a re-sealable **Safety cap**;
- a **Syringe-shaped delivery device** also protected by a re-sealable **Safety cap**;
- a disposable **Applicator tip** which fits onto the nozzle of the **Syringe-shaped delivery device**.

The cartridge is contained in an individually sealed aluminium pouch.

How to prepare the TebiPen™ device for use:

1. *Take the **Cartridge** out of its aluminum pouch;*
2. *Remove the **Safety cap** from the head of the **Cartridge**;*
3. *Insert the **Cartridge** inside the **Syringe-shaped delivery device** (3-a) by aligning the guidance system until it locks (3-b);*
4. *Remove the **Safety cap** from the head of the **Syringe-shaped delivery device** and fit one disposable **Applicator tip** by gently pushing it all the way down.*

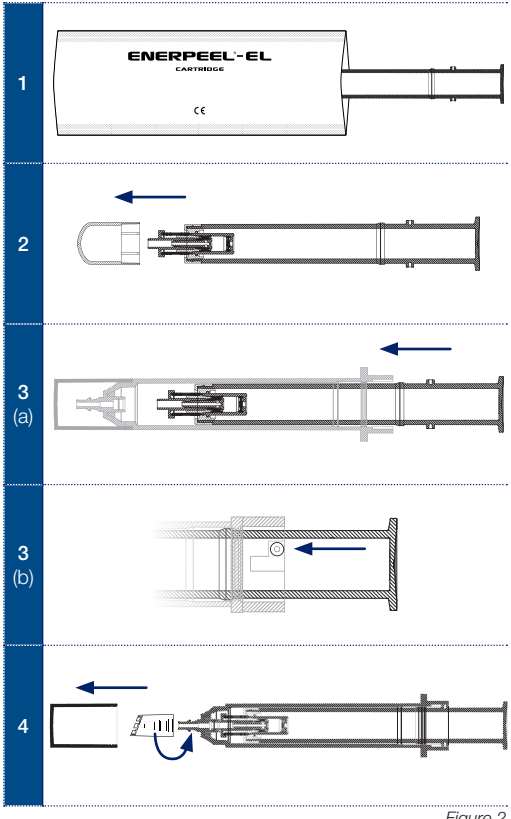


Figure 2

The TebiPen™ Device is now ready for use, according to the instructions provided in point 7.3 hereof.

SUMMARY TABLE OF THE DISPENSED AMOUNTS	
Quantity of gel dispensed after a “click”	~ 0,15 ml ± 0,02
Average surface area of each single cutaneous area	~ 10 cm^2
Quantity of Lactic Acid delivered with a “click”	~ 0,0225 g
Quantity of Trichloracetic Acid delivered with a “click”	~ 0,0056 g

Table 2

IMPORTANT INFORMATION

The application of the exfoliating gel has been conceived to allow the doctor to manage more safely the patient’s reaction to the chemical “peeling”.

WARNING*: *the stated surface areas of the various cutaneous areas (see Figure 1), and the dispensed amounts, are considered to be indicative and valid within a certain margin of variability and are supplied in order to assist the doctor in his/ her evaluation and to help in more precise control during application of the Device.* ***However, the doctor must keep in mind that the chemical effect (even if controlled) may vary from patient to patient.***

2. INSTRUCTIONS AND FREQUENCY OF USE

ENERPEEL® EL is indicated to perform chemoexfoliation able to eliminate damaged keratinocytes, promote the formation of new epidermis and therefore preventing photo-exposure-related pathologies (actinic damage, actinic keratosis, etc.).

Each ENERPEEL® EL course is composed of 4 sessions (treatments), to be performed at 7-14 day intervals. We recommend a yearly cycle of two courses.

Each treatment procedure performed using ENERPEEL® EL normally requires the application of 4 layers onto each cutaneous area. The quantity of acid dispensed with each “click” corresponds to approximately 0.15 ml, which is the correct volume required for one complete layer for each cutaneous area as specified in point 1.1 above.

After the application of each layer, use the applicator in continuous mode to distribute the exfoliating gel on each cutaneous area. After approximately 1-2 minutes, apply the second layer, then the third and the fourth. When the fourth layer has been applied, wait 3-5 minutes and then neutralise with the specific NEU Neutralizer wipe.

Each procedure (composed of up to four layers of exfoliating gel on each cutaneous area) requires a quantity of approximately 0.60 ml for each cutaneous area.

In case of frosting appearance, proceed immediately with the neutralization.

Altogether, when considering the following cutaneous areas:

A. Right periocular area (upper eyelid, lower eyelid and external canthus).

B. Left periocular area (upper eyelid, lower eyelid and external canthus).

C. Perioral area (not including the vermillion).

The quantity of exfoliating gel (4 layers) used on a multiple layer application corresponds to approximately 1.8 ml of product.

Each Cartridge of ENERPEEL® EL contains enough gel for 83 applications of 0.15 ml each. The content of each cartridge is enough for 7 complete procedures.

The doctor must always keep in mind that the cutaneous response to the chemical "peeling" treatment may increase between the first and last treatment session.

WARNING*: ENERPEEL® EL MUST ONLY BE APPLIED TO UNBROKEN SKIN.

3. USER REQUIREMENTS AND SPECIFIC KNOW-HOW

ENERPEEL® EL is a Device to perform chemical-exfoliation (chemical "peeling") for use directly by the doctor, who has to have suitable experience in the "peeling" field, in remodelling of the epidermis and dermis and who has to have specific knowledge of the skin andsubcutaneous tissues, such as:

1. structural, morphological and functional differences in the periocular zone, including the eyelids, and the perioral zone (not including the vermillion);
2. pathology and the natural history of the photo exposure damage;
3. aspects connected to cicatrization formation following "peeling" and cutaneous remodelling, such as:
    a. coagulation and inflammation;
    b. angiogenesis;
    c. the formation of granular tissue;
    d. reepithelialization;
    e. remodelling of collagen;
4. knowledge of the various types of chemical "peeling":
    a. very superficial;
    b. superficial;
    c. medium-depth;
    d. deep;
5. knowledge of the photo-type scale (Fitzpatrick);
6. knowledge of the response to chemical peeling in relation to the various genetic-ethnic characteristics;
7. knowledge of the photo-ageing scale (Glogau);
8. knowledge of possible undesired effects after chemical "peeling".

4. PRELIMINARY INFORMATION

4.1. Exclusion criteria - when not to perform chemical “peeling”

- Incidence and/or history of viral infections caused by Herpes simplex in the area to be treated.
- Recent (in the last 6 months) surgery (blepharoplasty, eyelid lifting, etc.).
- Immuno-depressive diseases and treatments in progress.
- Previous radiation therapy of the portion of the skin to be treated that could compromise the physiological regeneration of the skin.
- Family history with the development of keloids and/or hypertrophic scars.
- Family history with the development of post-inflammatory hyperpigmentation.
- Pregnancy.
- Breastfeeding.
- Allergy and/or known hypersensitivity or any other known and/or probable incompatibility to one or more of the components.
- Other medical considerations.

IMPORTANT WARNINGS*

(1) Smoking can influence the result of the treatment, it increases the risk of scars and accelerates the formation of lines.

(2) Phototypes IV, V and VI on the Fitzpatrick scale are at a higher risk of developing hyperpigmentation in the treated areas. Phototypes I, II, III are more susceptible to developing erythema and scars.

(3) Herpes infections are more likely to develop, especially in the perioral area.

(4) Injectable, fillers and botox based treatments should be performed only after the complete cycle of treatments with the Device.

4.2. Phototype classification according to the Fitzpatrick scale

A photo-type identifies the kind of skin response to solar radiation on the basis of several characteristics such as the colour of the hair, eyes, skin, the presence of freckles and lentigo and on the individual's reaction to solar radiation.
There are 6 photo-types, distinguished by the following characteristics *(See Table 4):*

PHOTOTYPE	DESCRIPTION
Phototype I	Subjects with very pale skin, often with freckles, blond or red hair, light-coloured eyes. They generally develop obvious erythema on any unprotected exposure to the sun. Tanning is very slight or nonexistent. There is extreme reaction to the sun's rays, with high risk of permanent damage.
Phototype II	Subjects with pale skin, dark blond or light brown hair. They tend to get sunburnt easily. They develop a light (golden) tan.
Phototype III	Subjects with fairly dark skin, brown hair. They only get sunburnt after prolonged exposure. They develop a deep, even tan.
Phototype IV	Subjects with olive complexion, dark eyes and black hair. They rarely get sunburnt. They quickly develop a very deep, chocolate-coloured tan.
Phototype V	Subjects with very dark complexion, dark eyes and black hair. They very rarely get sunburnt.
Phototype VI	Subjects with black complexion, dark eyes and black hair.

Table 4

** **Warning:** Phototypes IV, V and VI on the Fitzpatrick scale are at a higher risk of developing hyperpigmentation in the treated areas. Phototypes I, II, III are more susceptible to developing erythema and scars.*

4.3. Racial–genetic classification and the relative cutaneous reactions with respect to chemical exfoliation

The various reactions of the skin from different racial origin to chemical exfoliation (chemical peeling) may be divided into 6 categories, in which the colour of the skin is correlated to the somatic characteristics. These categories are based on geographic distribution and are described in the *Table 5* here below:

RACIAL CATEGORIES	ORIGINAL GEOGRAPHIC HABITAT	CHARACTERISTICS OF SKIN AND FEATURES	COMPLICATIONS SIDE EFFECTS	CANDIDATE RATING
Nordics (Swedish, Irish, English, etc)	Northern Europe	Light to very light color. Skin and features are very fine.	Erythema +++ Teleangiectasia Scarring	Very good
Europeans (French, Italian, Germans, etc)	Mid-Europe Southern Europe	Average color and coarseness of skin and features.	Low incidence	Excellent
Mediterraneans (Spanish, Greek, etc)	Northern Africa and Western Asia	Darker and coarser than the Europeans.	Hyper-pigmentation + / ++ Erythema	Very good
Indo-Pakistan (Pakistanis, Thais, etc)	Upper-Middle Africa and Lower Western Asia	Coarser and darker than the Mediterraneans with thick oily skin and hair.	Hyper-pigmentation +++ Hypo-pigmentation +	Passable for peels
Africans (Black Americans, Sudanese, Nigerians etc)	Middle and Lower Africa	Black to deep black color. Features and skin are coarse to very coarse.	Hypo-pigmentation + Hyper-pigmentation ++	Passable for peels
Asians (Japanese, Koreans, etc)	Eastern Asia	A separate classification color varies from light to medium dark. Skin and features are coarse to very coarse.	Hyper-pigmentation +++ Erythema +++ turning to hyper-pigmentation	Good

Table 5

WARNING*: *the correlation between the Fitzpatrick scale and the genetic-ethnic classification can be useful in predicting the skin's response to chemical peeling, both for evaluating its effectiveness and for determining possible side effects.*

4.4. Photo-ageing classification according to the Glogau scale

Photo-aging conditions can be described according to the scale developed by Glogau, as follows:

DEGREE	AGE	DESCRIPTION
Slight	from 28 to 35 years	Characterized by small wrinkles, without keratosis
Moderate	from 35 to 50 years	Characterized by small wrinkles, sallow complexion with presence of actinic keratosis
Advanced	from 50 to 65 years	Characterized by deep wrinkles, presence of teleangiectasis, pigmented lesions and actinic keratosis
Severe	from 60 to 75 years	Characterized by dynamic and gravitational wrinkles, photo-ageing and actinic keratosis

Table 6

5. IDENTIFICATION OF THE COMPONENTS

Each kit of ENERPEEL® EL contains the following components:

(1) N° 2 **Cartridges** with 12.5 ml of exfoliating gel each;

(2) N° 1 **Syringe-shaped delivery device** into which the **Cartridge** with the exfoliating gel has to be inserted;

(3) N° 20 single use wipes of PS Preparatory Solution - 3 ml

(4) N° 20 single use wipes of NEU Neutralizer - 3 ml

(5) N° 20 disposable **Applicator tips;**

Documentation accessible via QR code: The QR code included in the packaging provides access to the instruction manual, the patient record card, and the informed consent form

6. TECHNICAL DATA

6.1. ENERPEEL® EL Medical Device

Single-phase gel with a controlled viscosity, a density of ~ 1,03 and a pH of ~ 0,90 contained in a **Cartridge** to be inserted into a **Syringe-shaped delivery device**; a single-use **Applicator tip** will be fitted onto the nozzle of the **Syringe-shaped delivery device**.

6.2. PS Preparatory Solution

Single use wipes saturated with a solution formulated to prepare the skin for the chemical exfoliation. It exerts a specific action of delipidation, useful to obtain a more uniform, effective and efficient chemical exfoliation.

6.3. NEU Neutralizer

Single use wipes saturated with a basic solution containing arginine with an approximate pH ~10. It exerts a specific action for the neutralization of acidic exfoliating agents. It helps in modulating the process of chemoexfoliation.

7. DEVICE INSTRUCTIONS

7.1. Preliminary operations

The preliminary operations should be considered as a fundamental stage on which the subsequent procedures and consequently correct use of the Device depend; they can be summarised as follows:

1. compilation of the patient record card;
2. completing the informed consent form.

7.1.1. Patient record card

The patient record card shall describe and identify:

1. patient information;
2. exclusion criteria – when not to perform the chemical "peeling";
3. usage procedures;
4. photo-type classification according to the Fitzpatrick scale (point 4.2.);
5. photo-ageing assessment according to the Glogau scale (point 4.4.);
6. genetic-ethnic classification and related response to chemical "peeling" (point 4.3.);
7. definition of the cutaneous area;
8. estimated number of treatment sessions;
9. Medical Device's layers and application times;
10. any medical notes.

7.1.2. Informed consent form

With the informed consent form, the patient is informed about:

1. introduction;
2. definitions;
3. purpose of the treatment using the ENERPEEL® EL Medical Device;
4. usage procedures;
5. exclusion criteria – when not to perform the chemical "peeling";
6. treatment procedures using the ENERPEEL® EL Medical Device and warnings;
7. duration of a single treatment;
8. estimated number of procedures necessary to reach the purpose of the treatment;
9. possible side effects;
10. procedures during and after the treatment.

7.2. Initial procedure – preparation phase

In order to use the Device correctly and safely, we recommend strictly abiding by the procedures shown here below:

1. position the patient on the bed in a supine position;
2. wear protective rubber gloves or ones of an equivalent material;
3. wear clothing suitable for the medical operation;
4. prepare the envelope of PS Preparatory Solution;
5. prepare the viscous Vaseline;
6. prepare the ENERPEEL® EL Device *(see Definition of the cutaneous area, physiochemical form and characteristics of the delivery device, preparation and delivery system in point 1.1 above);*
7. place the envelope of NEU Neutralizer, still sealed, within hand reach, close to the ENERPEEL® EL Device.

***IMPORTANT WARNING:** make sure that the patient is not wearing makeup and/or contact lenses.*

7.3. Application procedure – execution phase

In order to use the Device correctly and safely, we recommend strictly abiding by the procedures shown here below:

1. Apply a sufficient layer of viscous Vaseline to the patient's lips spreading it to 1-2 mm from the external border of the vermillion.
2. Open the PS Preparatory Solution envelope, take out the wipe and apply the solution rubbing gently on the skin unit/s to treat*(1).
   (See Figure 3).

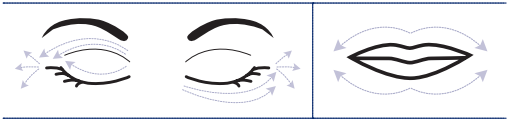


Figure 3

3. Prepare the Device as specified in point 1.1 above; (See Figure 4)
4. Unlock TebiPen™ by turning the Cartridge anti-clockwise.
5. Position TebiPen™ so that the flat part of the Applicator tip is facing upwards, then press the cartridge all the way up to dispense the pre-measured amount of gel onto the Applicator tip (the Applicator tip has been designed with tiny wings to hold the drop of gel and provide the treated cutaneous areas with a specific massage at the same time). *(See Figure 5)*

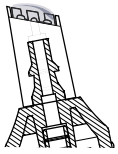
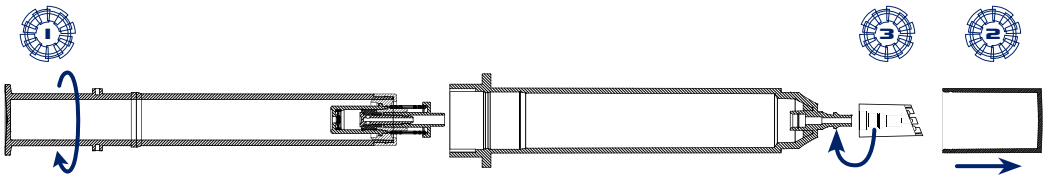


Figure 5

6. Turn TebiPen™ holding it close to the skin (away from eyes and vermillion) and start using the Device.

Note: *at first use you will need to "click" it once or twice to make the exfoliating gel fill the cannula of the head of the Syringe-shaped delivery device. When some exfoliating gel appears on the applicator, remove any excess with a*



1.
Insert the Cartridge by aligning the guidance system

2.
Remove the safety cap from the head of the Syringe-shaped delivery device

3.
Fit one disposable Applicator tip onto the nozzle of the Syringe-shaped delivery device

Figure 4

gauze pad and then, to start, "click" it once more so that the pre-measured amount of exfoliating gel is laid onto the Applicator tip.

7. Apply the first layer of ENERPEEL® EL to each cutaneous area to be treated, starting from cutaneous unit A; repeat the operation for each of the following cutaneous areas B and C (according to the classification listed in point 1.1), following the directions shown in *Figure 6* *(2);

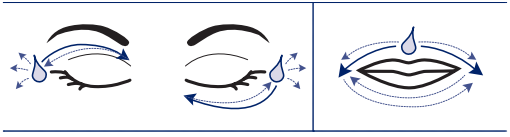


Figure 6

8. Leave for ~ 1 - 2 minutes being sure to spread the gel uniformly onto the treated cutaneous area, using the Applicator tip *(3);
9. Repeat the operation until a maximum of 4 recommended layers of gel are applied, in intervals of time as listed in *Table 7* *(4);

LAYERS	APPLICATION TIMES SUGGESTED
1st Layer	~ 1-2 minutes
2nd Layer	~ 1-2 minutes
3rd Layer	~ 1-2 minutes
4th Layer	~ 3-5 minutes
Total time for a single session	~ 6-11 minutes

Table 7

10. After the last application, wait ~ 3-5 minutes (depending on skin reactivity of the single patient) and in the mean time spread the gel uniformly onto the treated cutaneous area *(5);
11. Gently remove any excess gel, eventually still unabsorbed, with a gauze pad;
12. Carefully perform the neutralization process *(6) using the NEU Neutralizer wipe, applying it carefully, delicately and repeatedly to the skin according to the directions as shown in *Figure 7*;

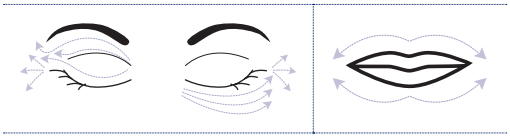


Figure 7

13. After the session *(7), dispose of all the material used and of the material that can be no longer used according to the specific European, national and local standards governing environmental protection.

***GENERAL WARNING:** depending on the patient's skin type, photo-type, the genetic-ethnic characteristics, the number of previously performed sessions, the contact time of the gel and the individual's response, during the application phases of the Device, "frosting" may occur: in order to modulate the desired depth of treatment, the area must be neutralized immediately after the appearance of the first whitish spots. The pre-treatment of the skin with the preparations based on alpha-hydroxy-acids (AHA), beta-hydroxy-acids (BHA) and/or substances with keratolytic activity could determine an increased irritative response of the skin to the Medical Device ENERPEEL® EL.*

***(1) WARNING:** advise the patient to keep his/her eyes always closed during the entire treatment.*

*(2) ***WARNING:*** *apply the gel being sure to maintain a distance of 1-2 mm from the edge of the upper and lower eyelashes and from the edge of the vermillion.*

*(3) ***WARNING:*** *throughout every application phase involving the spreading of the gel, it is very important to distribute the gel evenly; this can be performed using the applicator with which possible accumulations of gel are spread in a uniform way onto the entire cutaneous unit.*

*(4) ***WARNING:*** *each procedure should consist of up to 4 layers of gel. However, it is up to the doctor to decide whether or not to apply all 4 layers of gel, depending on the patient's different cutaneous reactions.*

*(5) ***WARNING:*** *during the application the intervals of time between one layer and another and the contact time of the gel with the skin after the last application, before the neutralization, can be increased at doctor's discretion, keeping in mind their own personal experience in performing the chemical "peeling" process using the ENERPEEL® EL Device, or decreasing the time based on each individual patient's cutaneous reactivity. Whenever the patient feels excessive pricking sensations it is recommended to reduce application times of the exfoliant gel and/or the number of applied layers.*

*(6) ***WARNING:*** *the neutralization procedure is a very important step in controlling the intensity of the chemical "peeling" and must be performed effectively by applying the NEU Neutralizer wipe repeatedly, exerting a perceptible amount of pressure on the treated cutaneous area for a few seconds.*

*(7) ***WARNING:*** *Block the cartridge turning it clockwise, remove the single use applicator and close the TebiPen with the cap after every single use. The cartridge containing the exfoliant gel must not be removed until complete depletion.*

8. USAGE PROCEDURES

The treatment with ENERPEEL® EL is performed in three main steps.

1. **Preparation**

   This procedure, performed with the PS Preparatory Solution, effectively prepares the skin for an even diffusion of the Device.

2. **Application of the Device**
   a. This is the medical procedure in which the chemical "peeling" is performed by applying the Device to the selected skin unit/s.
   b. The intensity of the exfoliation, the depth of the remodelling and the appearance of "frosting" depends on the number of layers of gel applied, the number of previously performed treatments and the contact time of the Device on the selected cutaneous unit/s.
   c. The application times and the number of layers of gel to be applied have been pre-determined; the physician must, anyway, carefully evaluate the skin response based on the skin unit/s, the patient's phototype, the degree of photo-ageing and/or chrono-ageing, the genetic-ethnic characteristics and the patient's relative susceptibility.

3. **Neutralization**

   This procedure, performed with the NEU Neutralizer, reduces the acid strength by modulating the depth of the "peeling" through neutralization.

Each of these three steps are described in detail in chapter 7: Device Instructions.

9. PRECAUTIONS DURING THE PROCEDURES

During the preparation procedure and when applying the Device, check that all the warnings and safety measures have been implemented. The following warnings are particularly important:

1. PS Preparatory Solution wipes are moistened with a quantity of solution so as to reduce the risk of dripping to a minimum. However, the doctor must pay utmost care and advise the patient to keep his/her eyes and lips closed when applying the solution in order to avoid involuntary contact of the solution with the ocular conjunctiva and/or the vermillion.
2. The Device applicator permits a precise application of the gel, so as to reduce the risk of involuntary contact with the ocular conjunctiva and/or the vermillion to a minimum. However, the doctor must pay absolute attention, follow the application instructions in previous point 7.3. *(Figure 6)* and advise the patient to keep his/her eyes and lips closed during the application phase, in order to prevent involuntary contact of the gel with the ocular conjunctiva and/or the vermillion.
3. When removing any excess of unabsorbed gel, pay special attention to avoid dragging traces of gel into the ocular conjunctiva and/or on the vermillion. NEU Neutralizer wipes are moistened with a quantity of the neutralising solution so as to reduce the strength of the acid to modify the depth of the “peeling” by neutralization. In any case, the doctor must pay maximum attention and advise the patient to keep his/her eyes and lips closed during the neutralisation phase, to avoid involuntary contact of the neutralising solution with the ocular conjunctiva and/ or vermillion.

10. POSSIBLE EFFECTS DURING THE TREATMENT

ENERPEEL® EL induces a sensation of prickling/burning that tends to reach a peak of intensity after the first 2-3 minutes and then remains constant during the following minutes until disappearing after neutralization.

11. POSSIBLE EFFECTS AFTER THE TREATMENT

Manifestations that may appear during, immediately after or in the post-treatment phase depend on various variables, such as the depth of the chemical “peeling”, the patient’s phototype, genetic-ethnic characteristics, skin type (thick, thin, keratosic, etc.), the subjective response of each individual subject, and include mainly:

- oedema
- erythema
- flaking
- pigment variations
- other irritating reactions.

12. POST-TREATMENT CONSIDERATIONS

The chemical “peeling” process thins the surface layer of the skin. For this reason, the natural barrier functions of the skin will be altered and the skin response to future treatments could be amplified. The doctor must be particularly careful when performing successive chemical “peeling” procedures.

IMPORTANT WARNING*

Avoid performing the treatment in very sunny seasons. Solar radiation and all artificial tanning procedures may trigger hyper-pigmentation.

Any post-peeling treatment must be carefully assessed by the doctor, as the inappropriate use of drugs, cosmetic products or the application of soothing masks could delay the physiological restoration process of the skin barrier; it is therefore necessary to manage the post-treatment phase on the basis of the doctor’s personal experience in implementing any pharmaceutical or cosmetic intervention. In any case, the post-treatment phase must include the following points:

1. always advise the patient to use suitable protection against solar and artificial radiation (solar protection factor 50+ according to the COLIPA method);
2. recommend the application of products capable of modulating the melanogenesis process;
3. recommend the application of products capable of increasing skin elasticity and hydration for maintenance purposes;
4. inform the patient to clean the treated zone delicately, avoiding any kind of rubbing;
5. inform the patient to avoid the use of pharmaceutical and/or cosmetic products on his/her own initiative, without first consulting the doctor.

13. GLOSSARY

Acid - Chemical substance capable of releasing one or more protons (according to Bronsted and Lowry,1887). The strength of an acid depends on the degree of dissociation in an aqueous solution.

Applicator tip - The removable and disposable part to be fitted onto the nozzle of the Syringe-shaped delivery device and intended for exfoliating gel application. The shape and materials guarantee a controlled and precise application and therefore a safer use of the Device.

Arginine - Basic amino acid present in animal and vegetable proteins.

Base - Chemical substance capable of accepting one or more protons (according to Bronsted and Lowry,1887).

Cartridge – A sealed cylinder containing the single-phase exfoliating gel, to be fitted into the Syringe-shaped delivery device.

Chemoexfoliation (chemical "peeling") – Procedure used to improve specific skin conditions via the removal of dead cells from the horny layer and by remodelling the epidermis and the dermis, depending on the depth reached. It can be classified as very superficial, superficial, medium-depth and deep, depending on the "peeling" agent used and on the application times on the skin before neutralization or washing *(see chap. 1).*

Complications - Secondary reactions that the use of some products may cause along with the main beneficial action.

Cutaneous unit - The portion of the skin that undergoes the chemical "peeling" procedure. The cutaneous units have been arbitrarily classified into the following areas:

A - Right periocular area;
B - Left periocular area;
C – Perioral area (not including the vermillion).
(Point 1.1).

Fitzpatrick scale - This scale identifies photo-types on the basis of hair, eye and skin colour and on individual response to solar radiation.

Glogau scale - This scale identifies the degree of individual photo-ageing on the basis of age and skin damage caused by prolonged exposure to ultraviolet light.

Informed consent form - A written document in which the patient declares to have knowledge of all chemical "peeling" procedures with the Device, all possible correlated risks, post-chemoexfoliation treatment procedures and authorises the doctor to perform the treatment itself.

Lactic Acid - Organic acid (2-hydroxypropanoic acid) - formula CH_3-CH(OH)-COOH present in nature mainly in milk. It performs an important role in diverse biochemical processes. In fact, lactic acid and lactates prove to be efficacious inhibitors in the melanogenesis process.

Layer – A single application of the Device on the treated cutaneous area/s. A maximum of four layers are recommended at each session.

Medical Device - A medical device is any instrument, appliance, system, substance or other product, used alone or in combination, including information technology software used for correct operation, [...], the main desired action of which in the human body is not obtained via pharmacological, immunological means or via metabolism, whereby its function may be assisted by such means *(Ref. Directive 93/42/EEC, 47/2007/EC and subsequent amendments/integrations - concerning medical devices).*

Neutralisation – Process or operation that consists in

adding a base/acid in the form of a pure substance (solid, liquid, or gas), or in the form of an aqueous solution, to adjust the pH value to the physiological value.

Neutralizer – Base/acid added to an acid/basic solution in the form of a pure substance (solid, liquid, or gas), or in the form of an aqueous solution, to adjust the pH value to the physiological value.

Patient record card - A written document concerning one single patient, in which the doctor defines the treatment times and enters all the patient's characteristics necessary for the chemical "peeling" treatment with the Device.

pH - Value that expresses the concentration of hydrogen ions present in solution. It is expressed as the negative algorithm on a scale of 10, of the concentration of hydrogen ions present in aqueous solution, according to the following formula:

$$pH = -\log_{10} [H+ \text{ concentration}]$$

The pH scale is used to express the acidity or alkalinity of an aqueous solution.
pH = 7 indicates neutrality;
pH: 0-7 indicates acidity;
pH: 7-14 indicates basicity.

Photo-ageing - The combination of biochemical and histological modifications to the skin, caused by frequent and prolonged exposure to ultraviolet radiation that determines a particular type of precocious ageing. Ultraviolet rays act directly and partially through the production of free radicals, capable of damaging the DNA, proteins and phospholipids of cell membranes (see point 4.4.).

Frosting - Whitening of the skin caused by the denaturing of the epidermic and/or dermic proteins after a chemical "peeling". Divided into 3 levels (see chapter 1).

Photo-type - The photo-type is a number (from I to VI) that indicates personal sensitivity to solar radiation, in relation to skin pigmentation and eye and hair colour. The photo-type indicates the degree to which the skin manages to protect itself. (see point 4.2.).

Preparatory solution – Solution suitable for preparing the skin subjected to treatment, with the purpose of obtaining the most even diffusion of the exfoliating gel.

Procedure – A single session. A complete treatment course is made up of a maximum of four sessions or treatments on each individual patient.
Several courses in a year make up one cycle.

Syringe-shaped delivery device – The component where the cartridge is fitted into.

Treatment – This is a procedure, namely the medical chemical "peeling" procedure.

Trichloroacetic Acid – An organic acid with CCl_3COOH, formula, derived from acetic acid.
Used in low concentrations it produces the superficial coagulation of proteins and partial epidermal exfoliation.

14. REPORTS

In the case of secondary undesirable effects occurred with the use of ENERPEEL® EL chemical exfoliant Medical Device, it is requested to report promptly the case(s) by calling the following number **+39 0365 529117** and/or by filling the appropriate form **Adverse Event Report** which can be downloaded from the following web address: **ifu.tebitech.com**, and sent via fax to **+39 0365 522619** or via email to the following address: **regulatoryaffairs@general-topics.com**.
A post sales surveillance is activated as well, through which we kindly ask you to report any comments related to the use of the ENERPEEL® EL Medical Device (judgement based on the efficacy and the tolerability, possible collateral effects, observations, etc.) by filling out the special **Post-Sales Surveillance Form**, this form as well can be downloaded from the website: **ifu.tebitech.com** (e-mail: **regulatoryaffairs@general-topics.com**; fax: **+39 0365 522619**).

15. TECHNICAL ASSISTANCE

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