Actolind®

A new approach for wound care with a smart molecule

Your first choice for burns, chronic wound care and diabetic wound

Irrigation, moisturizing and care products for wound and skin
Modern Wound Care

- Your first choice for burns and chronic wound care
- Irrigation, moisturizing and care products for skin, mucosa and wounds
- “Your first choice” for decontamination of patients or personnel contaminated with antibiotic resistant microorganisms (MRSA, MRE, VRE)

Provide patients with the right antimicrobial agent when needed
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What is a wound?

The word “wound” derived from the Latin word ‘vulnus’ and describes the disturbance of normal continuity (for example skin) with or without tissue loss. It may accidentally happen due to an injury, a traumatic injury or an intentional surgical procedure.

The wounds can be classified according to their point of origin:

- Mechanical
- Thermal
- Chemical
- Radiation
- Skin Ulcer

What should be considered in wound care?

Sterile disposable materials and the products that heal the wound by keeping them moist (instead of the products that dry the wound) should be used in wound care.

If dried wound material is on the wound, it may be removed after soaking.
About Wounds

Which criteria should be considered when choosing wound treatment preparations?

**Products used on wounds on skin and mucous membranes should not do the following:**

- cause inflammation,
- work against human cells that help in wound healing process,
- be absorbed by the wound,
- cross the circulation system.

**But what they should do, is to be effective against all resistant microorganisms.**

What are the most important factors for wound healing?

- Improvement of the general condition of the patient
- Removal of pressure from wound surface
- Moisturizing the wound
- Removal of necrotic tissue with appropriate and sterile dressings, wiping with an antiseptic solution (working from wound center to the edges)
- Fighting infections
- If necessary, cover wounds with gauze or surgical biological bandages.
- Keep the wound temperature constant
- Follow-up blood values
- Assessment of the wound for infection, serosity and hematoma by daily opening
Wound Care Guide

Wounds can be classified by their appearance, source and state of contamination with pathogenic microorganisms. Wound classification facilitates assessment of the wound and enables early identification of potential risks.

<table>
<thead>
<tr>
<th>Wound Types</th>
<th>Description</th>
<th>Product Suggestion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Open wounds</strong></td>
<td>In these wounds cutaneous and subcutaneous tissue are harmed and skin integrity is damaged in different sizes.</td>
<td>Actolind® w Solution + Actolind® w Gel</td>
</tr>
<tr>
<td><strong>Clean wounds</strong></td>
<td>These wounds do not have pathogenic microorganisms. Clean wounds do not have any tissue loss or infection and their edges unite and they have minimal scar tissue.</td>
<td>Actolind® w Solution + Actolind® w Gel</td>
</tr>
<tr>
<td><strong>Contaminated wounds</strong></td>
<td>There are pathogenic microorganisms in the wound, but no indication of infection. Open wounds occurring immediately after traumata become contaminated wounds due to a major problem in the sterile technique which leads to excessive entry of bacteria into normally sterile body segments.</td>
<td>Actolind® w Solution + Actolind® w Gel</td>
</tr>
<tr>
<td><strong>Infected wounds</strong></td>
<td>In these wounds pathogenic microorganisms are present. Skin rash, pain, discharge, bad odor and other infection indications are seen on the wound.</td>
<td>Actolind® w Solution + Actolind® w Gel</td>
</tr>
<tr>
<td><strong>Burns</strong></td>
<td>“Burn” means the tissue damage caused by factors such as heat, electricity, chemicals, boiling water, flame, etc. Extent of the tissue damage depends on the size of burnt area and the continuity of the causing factor.</td>
<td>Actolind® w Solution + Actolind® w Gel</td>
</tr>
<tr>
<td><strong>Chronic wounds</strong></td>
<td>A chronic wound is a wound that does not heal within three months. The wound occurs repeatedly. There is a local or systemic factor that prevents wound healing (e.g., decubitus ulcers).</td>
<td>Actolind® w Solution + Actolind® w Gel</td>
</tr>
</tbody>
</table>

“Do not use any product on the wound that cannot be used on the eyes!”
Prof. Dr. A. Kramer.
Polyhexamethylene Biguanide Hydrochloride (Polyhexanide)

A new approach for wound care with a smart molecule

Polyhexanide (PHMB) is a strong cationic, polymeric biguanide derivative. It shows a broad spectrum of activity and high tissue compatibility.

Polyhexanide is a raw material known since 1959, which is used in cosmetics and food industry. Other capabilities are in cleaning and disinfection of beer plants or as a disinfectant and anti-flock substance in swimming pools (no smell of chlorine).

In 1995 polyhexanide could also be used for the manufacture of wound dressing solutions. The first major application area were surgical wounds. Soon, the solutions produced in the hospital pharmacies were used in the treatment of infected chronic wounds.

It is a new generation smart molecule. It has to be the "first choice" in the treatment of chronic wounds and burns.

Polyhexanide has an incredible advantage over other microbicide substances: it has the highest therapeutic ratio (TB). In other words, the relationship between the benefit and harm is mostly on the benefit side.

Polyhexanide is odorless, colorless and hypoallergenic. It does not cause inflammation on wound or cause wound healing disorders according to current knowledge.

One product - six properties

• Reliable broad-spectrum of antimicrobial effect
• Even effective under high biological load
• Accelerating and supporting effect for wound healing
• High cell and tissue compatibility
• No known resistance development
• Low allergy, anaphylaxis and systemic circulation risk
Polyhexanide has a high tissue compatibility. This property is derived from its selective binding to the acidic phospholipids, in particular phosphatidylglycerol and diphosphatidylglycerol on the pathogenic cell membrane.

When the primary function of a product is to create pharmacological, immunological or metabolic effects during human use, it is considered as a drug. The polyhexanide remaining of the skin surface forms a film layer and directly act mechanical, not physical, immunological or metabolic.

It is applied topically on skin, mucosa and wound. There is no evidence that polyhexanide passes through the systemic circulation as a result of the application. Due to its polymeric structure and high molecular weight, polyhexanide reduces the risk of transition to the systemic circulation.

It shows strong microbicidal effects on gram positive and gram negative bacteria, fungi, HPV (Human papillomavirus), some viruses and amoebas. In vitro studies on gram positive and gram negative bacteria have reported that polyhexanide completely kill Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Enterococcus hirae, Candida albicans, Klebsiella and Enterobacter species in 5-10 minutes.

Polyhexanide does not directly affect the body. It does not accumulate in cells or tissues and is not absorbed by them. Polyhexanide, however, binds tightly to the cell wall of bacteria. It permanently damages and weakens bacteria even at very small concentrations. For example the therapeutic ratio for Staphylococcus aureus is 25’000 in contrast to 500 for the therapeutic ratio for PVP-iodine or Octenidine with 3.2 or for Chlorhexidine with 0.9. (Table I).

Characteristics of Polyhexanide

- Reduces wound pain rapidly and effectively [1,2]
- Reduces wound malodour [2]
- Increases formation of granulation tissue [3]
- Increases keratinocyte and fibroblast activity [4]
- Reduces scurf formation within the wound [3]
- Reduces MMP-induced periwound breakdown [5,6]
- Helps to remove non-viable tissue [7]
- The success of PHMB has resulted in its recommendations as the primary antimicrobial in many European countries [8] and has prompted the publication of a UK consensus review [9]
Keratinocytes are cells which form the largest part of the epidermis and which are responsible for keratin synthesis in the stratum corneum or hair shaft. Keratinocytes occur in the basal layer of the epidermis and reproduce by mitosis. They produce lipids, the 'Natural Moisturizing Factor' (NMF) and keratin when they are located on skin surface. In this process, keratinocytes flatten, lose their nuclei and die. In later stages, these cells are known as corneocytes.

How does it support wound healing?

The basic principle of wound healing is that wound care products should not block cell function in wound healing. However, the feature of many conventional wound care products is the damage to both bacteria and human cells. While polyhexanide damages the bacteria, it does not destroy the structure of healthy human cells and has no toxic effect on them. The basic evidence for this is the investigation of keratinocytes. A study with polyhexanide keratinocytes* showed that keratinocyte production increased at a concentration of 0.2 micrograms/ml. Polyhexanide accelerates wound healing even at very low concentrations.

The basic principle in wound healing is non-blocking of the wound healing cell functions. While polyhexanide damages the bacteria, does not destroy the structure of the healthy cell and does not have any toxic effect on the cell.

The basic proof of that is the study on keratinocytes. In a study of polyhexanide keratinocytes*, it is shown to increase keratinocyte production at a concentration of <0.02. [10]

The most outstanding effect of polyhexanide in performed studies is its antimicrobial activity against resistant bacteria such as multidrug-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE) and Acinetobacter. [11,12]

*Keratinocytes are cells which form the largest part of the epidermis and which are responsible for keratin synthesis in the stratum corneum or hair shaft. Keratinocytes occur in the basal layer of the epidermis and reproduce by mitosis. They produce lipids, the 'Natural Moisturizing Factor' (NMF) and keratin when they are located on skin surface. In this process, keratinocytes flatten, lose their nuclei and die. In later stages, these cells are known as corneocytes.

Table 1: Overview of different therapeutic ratios of different active ingredients.

<table>
<thead>
<tr>
<th>Active Substance</th>
<th>LD$_{50}$ mouse/MIC ratio (exposure time: 5 min.)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Staphylococcus aureus</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>0.9</td>
</tr>
<tr>
<td>Octenidine</td>
<td>0.2</td>
</tr>
<tr>
<td>Benzalkoniumchloride</td>
<td>8.0</td>
</tr>
<tr>
<td>PVP iodine</td>
<td>500.0</td>
</tr>
<tr>
<td>Polyhexanide</td>
<td>25000.0</td>
</tr>
</tbody>
</table>

Support Wound Healing
Poloxamers can be used therapeutically in wound cleaning, irrigation and some pharmaceutical industries such as eye drop formulations and in treatment of kidney stones.

Poloxamers are polyoxyethylene and polyoxypropylene block polymers. The hydrophobic propylene oxides (PO) and the hydrophilic ethylene oxides (EO) comprise more than 50 liquid and solid types of amphiphilic nonionic block polymers.

In dermal irritation and tenderness tests, poloxamers have negative results.

Their removal out of the body is rapid and there is no risk in growth and/or development toxicity and carcinogenesis.

The use of poloxamer-based non-ionic surfactant gels as carriers for antibiotics and antimicrobials has been strongly supported, based both on the sustained localisation of antimicrobial activities (because of the gel's viscosity) and the ease of removal when compared with common clinical clips.\(^{[13]}\)

Poloxamers have an accelerating effect on cell repair processes, regardless of the type of injury. They have been used to reseal thermally injured cells and chaperone the functional recovery of heat denatured proteins. Confirmatory in vivo studies have shown that the application of poloxamers to burn wounds increased blood flow and reduced burn depth.\(^{[14]}\)

**Why is poloxamer used as a surfactant?**

Polyhexanide tends to express its properties only when it is used with the amphoteric and non-ionic surfactants in wound healing conditions.

According to European Union Regulation (EC) no. 66/2010, the usage restrictions are put forward because the recycling of surfactants and their toxic levels on creatures are higher in nature.

According to the current legislation, some problems are emphasized in terms of biodegradability of cationic and amphoteric surfactants (including amphoteric alkali betaines) in aerobic and anaerobic conditions.
Actolind® w Solution/w Gel contain a Polyhexanide-Poloxamer combination that has an excellent cleaning effect and is well tolerated by cells. Due to the modified surface tension, the formulation also reaches areas where water cannot penetrate. In this way, it penetrates the deepest areas and provides much better effect than classical antiseptics. Bacterial residues and other wastes do not remain on the skin in contrast to other antiseptics and they are safely removed from the wound.

### Biofilm effect

Poloxamer reduces the surface activity on wound surface and facilitates the removal and destruction of biofilms, dirt and necrotic tissues.

PHMB is an antimicrobial agent and prevents biofilm formation by inhibiting microbial growth.

In accordance with this information, the formulation of Actolind® w Solution/w Gel prevents biofilm formation due to its formulation containing PHMB and poloxamer.
Actolind® w Solution is a ready-to-use, clear, colorless and odorless wound irrigation solution with Polyhexanide as active substance and Poloxamer as auxiliary substance.

It is used for mechanical cleaning, irrigation and moisturizing of acute, chronic and infected wounds, as well as 1st and 2nd degree burns. It can be applied directly to the wound area, or it can be used by applying on a gauze or bandage as a medical device.

Usage purpose

Cleaning and moisturizing

As long as there are no systemic diseases, wounds usually heal on their own provided they are kept clean and moist. Air contact, but also contamination and dehydration of wound lead to the growth of various microorganisms. Actolind® w Solution cleans and moisturizes the wound, creates a protective film layer that isolates the wound surface from the outside environment. The space between the wound surface and wound compresses is filled in by Actolind® w Solution and serves for faster wound healing by stabilizing the wound. In addition, Actolind® w Solution prevents the dressing from adhering to the wound and the exclusion of air prevents the growth of microorganisms.

Irrigation

Wound coverings consist of cell and tissue debris, necrotic tissue, but also wound exudates and other constituents that lead to the formation of biofilms. Actolind® w Solution is used to irrigate the wound to remove just those ingredients that prevent wound healing.

Use in dressing change

Medical devices, such as bandages, gauze, absorbent materials, compresses, etc., can adhere to the wound and cause secondary wounds thereafter infection. Before the dressings and bandages are changed, they should be soaked with Actolind® w Solution. Due to the moisturizing and cleansing agents in the product composition, the bandage is removed from the wound without causing tissue irritation or tissue damage.
• **Actolind® w Solution** is used to wash and irrigate the wound before applying a bandage.

• **Actolind® w Solution** is suitable to wash and moisten the wound with a bandage.

• **Actolind® w Solution** is used for moistens and decontaminates dressings, gauzes and compresses that have dried and adhere to the wound.

• **Actolind® w Solution** provides gently changes of dressing materials without ripping the wound and prolonging the healing process.

**Actolind® w Solution** is suitable for the following wound types:

• Acute wounds (traumatic wounds as a result of cuts, blisters, abrasions, bruises, bites and stab wounds or surgical wounds)

• Chronic wounds (diabetic ulcers, venous ulcers, bed (pressure) wounds, etc.)

• Thermal or chemical burns and injuries (1<sup>st</sup> and 2<sup>nd</sup> degree burns, chemical burns, etc.)

• Wounds as a result of electric current

• Radiation wounds

• Insertion sites of urological catheters

• Stoma care; cleaning, irrigation and moistening of fistula and abscess

**Actolind® w Solution chemical components**: 1% Poloxamer, Polyhexanide (PHMB), and auxiliary substances

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**Leg Ulcer**

*Before Actolind®*  
*Four months*  
*After Actolind®*

*(Photo: ACTO GmbH)*
From the hygienic point of view, disposable products are used to prevent the passage of microorganisms to the patient, but especially to minimize the exposure of pathogens to medical personnel. The use of disposable products prevents cross infection between patients as these products are discarded after a single use on one patient.

As the importance of complying with health regulations in the world increases, the use of disposable products has become increasingly popular.

Monodose products are the best choice for hygiene as they are personalized for medical officials and users.

It provides usage of correct dosage and prevents excessive consumption of the product.

<table>
<thead>
<tr>
<th>Art. No</th>
<th>Unit</th>
<th>Packing Type</th>
<th>Number in a Package</th>
</tr>
</thead>
<tbody>
<tr>
<td>06.6703.03</td>
<td>3 ml</td>
<td>Monodose Strip</td>
<td>100 x 5</td>
</tr>
<tr>
<td>06.6703.05</td>
<td>5 ml</td>
<td>Monodose Strip</td>
<td>100 x 5</td>
</tr>
<tr>
<td>06.6703.10</td>
<td>10 ml</td>
<td>Monodose Strip</td>
<td>50 x 5</td>
</tr>
<tr>
<td>06.6703.50</td>
<td>50 ml</td>
<td>Bottle with spray cap</td>
<td>200</td>
</tr>
<tr>
<td>06.6703.100</td>
<td>100 ml</td>
<td>Bottle with spray cap</td>
<td>100</td>
</tr>
<tr>
<td>06.6703.250</td>
<td>250 ml</td>
<td>Bottle with spray cap</td>
<td>40</td>
</tr>
<tr>
<td>06.6703.500</td>
<td>500 ml</td>
<td>Bottle</td>
<td>20</td>
</tr>
<tr>
<td>06.6703.1</td>
<td>1000 ml</td>
<td>Bottle</td>
<td>10</td>
</tr>
</tbody>
</table>
Actolind® w Gel is a ready-to-use, clear, colorless and odorless gel. It is ready to use. It contains polyhexanide as active substance and poloxamer as auxiliary substance.

Actolind® w Gel is used for the mechanical cleaning and moisturizing of chronic and infected wounds, also 1st and 2nd degree burns and helps to accelerate the healing. It can be applied directly to the wound area, or it can be applied on a gauze or bandage as a medical device.

### Intended use

#### Cleaning and moisturizing
Actolind® w Gel cleans and moisturizes the wound surface. It stays on the wound surface and prevents an acute wound from becoming a chronic wound through dehydration, contamination or air contact.

#### Wound filling
Actolind® w Gel protects the from external influences by forming a thin protective layer on the wound surface. It fills the gap between wound surface and wound dressing and thus increases the effectiveness of the dressing but also prevents the adhesion of the dressing material to the wound.
• **Actolind® w Gel** keeps the wound clean and moist and stabilizes the wound as a wound filler
• **Actolind® w Gel** ensures a simple dressing change and prevents a renewed rupture of the wound and thus a prolonged healing process

**Actolind® w Gel is suitable for the following wound types:**

• Chronic wounds (diabetic ulcers, venous ulcers, pressure sore, etc.)
• Thermal or chemical wounds (e.g. 1st and 2nd degree burns, chemical burns, etc.)
• Wounds as a result of electric current
• Radiation wounds

*Actolind® w Gel chemical components: 0.1% Polyhexanide (PHMB), Poloxamer, and auxiliary substances*

### Table 3: Selling unit of Actolind® w Gel

<table>
<thead>
<tr>
<th>Art. No</th>
<th>Unit</th>
<th>Packing Type</th>
<th>Number in a Package</th>
</tr>
</thead>
<tbody>
<tr>
<td>06.6803.03</td>
<td>3 ml</td>
<td>Monodose Strip</td>
<td>100 x 5 strip</td>
</tr>
<tr>
<td>06.6803.05</td>
<td>5 ml</td>
<td>Monodose Strip</td>
<td>100 x 5 strip</td>
</tr>
<tr>
<td>06.6803.10</td>
<td>10 ml</td>
<td>Monodose Strip</td>
<td>50 x 5 strip</td>
</tr>
<tr>
<td>06.6803.30</td>
<td>30 ml</td>
<td>Tube</td>
<td>240</td>
</tr>
<tr>
<td>06.6803.50</td>
<td>50 ml</td>
<td>Tube</td>
<td>200</td>
</tr>
</tbody>
</table>

**Biocompatibility**

**Evaluation of biocompatibility:**

- **Irritation** (ISO 10993-10 Biocompatibility Test Report)
- **Cytotoxicity** (ISO 10993-5 Biocompatibility Test Report)
- **Sensitivity** (ISO 10993-10 Biocompatibility Test Report)
<table>
<thead>
<tr>
<th>Wound Type</th>
<th>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution</th>
<th>Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel</th>
<th>Packing Type</th>
<th>Usage</th>
</tr>
</thead>
<tbody>
<tr>
<td>use in acute wounds (e.g. traumatic wounds as a result of cuts, tears, grazing, crushes, bites, stabbing, etc. or surgical wounds)</td>
<td>X</td>
<td></td>
<td>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution 50 ml; 100 ml; 250 ml</td>
<td>Apply directly to the wound. Apply Actolind by pressing the spray head 5 times, leave the wounds open depending on wound conditions or covering it with bandages.</td>
</tr>
<tr>
<td>Use in chronic wounds (e.g. diabetic ulcers, venous ulcers, pressure sores)</td>
<td>X</td>
<td>X</td>
<td>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution 500 ml; 1000 ml Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel 50 ml</td>
<td>Diabetic foot (in case of an amputated foot): A bandage soaked with Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution should be applied once or twice daily. Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel should be applied with gauze and covered with bandages. In this way, the contact between the wound and the air is blocked, preventing wound infection. Chronic wounds: In a chronic wound, it is assessed for depth and size and cleaned with Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution. Then apply Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel and cover the wound with bandages. Before a dressing change, the gauze on the wound is soaked with Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution and removed. The duration and number of applications are assessed by a physician and the appropriate period is determined.</td>
</tr>
<tr>
<td>Use in burns (e.g. thermal or chemical wounds, 1&lt;sup&gt;st&lt;/sup&gt; and 2&lt;sup&gt;nd&lt;/sup&gt; degree burns, chemical burns, etc.)</td>
<td>X</td>
<td>X</td>
<td>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution 500 ml; 1000 ml Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel 50 ml</td>
<td>Depending on the depth, type and size of the burn, the burn is washed with Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution. Subsequently Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel is applied and the wound is left open.</td>
</tr>
<tr>
<td>Use in wounds as a result of electric current.</td>
<td>X</td>
<td>X</td>
<td>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution 500 ml; 1000 ml Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel 50 ml</td>
<td>Depending on the depth, type and size of the burn, the burn is washed with Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution. Subsequently Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel is applied and the wound is left open.</td>
</tr>
<tr>
<td>Use in wounds as a result of radiation.</td>
<td>X</td>
<td>X</td>
<td>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution According to status of the wound 250; 300 ml Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel 50 ml</td>
<td>Depending on the depth, type and size of the burn, the burn is washed with Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution. Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel is applied and the wound is left open.</td>
</tr>
<tr>
<td>Use in cleaning of insertion sites of catheters.</td>
<td>X</td>
<td></td>
<td>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution 50 ml; 100 ml; 250 ml</td>
<td>Before the catheter insertion, while the catheter is inserted or after the catheter is removed, Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution is applied directly to the area by spraying 5 times. Insertion site of catheter is wiped from the center to the periphery with a gauze or compress.</td>
</tr>
<tr>
<td>Stoma care; cleaning, irrigation and moistening of fistula and abscess.</td>
<td>X</td>
<td></td>
<td>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution 50 ml; 100 ml; 250 ml</td>
<td>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution is applied directly to the area by spraying 5 times. It is wiped from the center to the periphery with a gauze or compress.</td>
</tr>
<tr>
<td>Use in the moisturizing of bandage, gauge, compress and wound fillers, etc. before the practice.</td>
<td>X</td>
<td></td>
<td>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution All packaging types according to dressing size Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel 50 ml</td>
<td>Dressings and bandages are wetted with Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution before being replaced. Before the dressing replacement, Actolind&lt;sup&gt;®&lt;/sup&gt; w Gel is applied to the wound and the wound is covered with bandages.</td>
</tr>
<tr>
<td>Use in moisturizing and decontamination of bandages, gauges, compresses and wound fillers which are contaminated, dried and adhered to the wound, before they are removed from wound surface.</td>
<td>X</td>
<td></td>
<td>Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution All packaging types according to dressing size</td>
<td>Before replacing wound dressings, all dressings and bandages are wetted with Actolind&lt;sup&gt;®&lt;/sup&gt; w Solution.</td>
</tr>
</tbody>
</table>
Advantages of using Actolind®

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Actolind®</th>
<th>Saline</th>
<th>Water</th>
<th>Antiseptic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in bio burden</td>
<td>✔</td>
<td>❌</td>
<td>❌</td>
<td>✔</td>
</tr>
<tr>
<td>Safe for long term use</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>❌</td>
</tr>
<tr>
<td>No inhibition of granulation tissue</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>❌</td>
</tr>
<tr>
<td>Clinical evidence in reduction of pain and odor</td>
<td>✔</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
</tr>
<tr>
<td>Can be used up to 8 weeks after opening - cost effective</td>
<td>✔</td>
<td>❌</td>
<td>n/a</td>
<td>❌</td>
</tr>
<tr>
<td>Clinical evidence in reduction of infection rates</td>
<td>✔</td>
<td>❌</td>
<td>❌</td>
<td>✔</td>
</tr>
<tr>
<td>Clinical evidence in improved healing times</td>
<td>✔</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
</tr>
</tbody>
</table>

General hints for usage

- Aseptic techniques must be taken into consideration before using Actolind® group products.

- Actolind® w Solution/w Gel can be applied directly to the area/wound surface to be cleaned, or on the bandages, gauzes, etc. Products such as bandages, gauzes, wipes should not be used again, but be disposed of in hazardous waste.

- Actolind® w Solution/w Gel and has 8-week shelf life after opening. The mouth of bottle/tube must be protected in order not to cause contamination during use. Bottles or tubes that have been in direct contact with the wound or that are contaminated otherwise should be discarded.

- Actolind® w Solution can be heated to body temperature before use.

- If the patient has sensitiveness against any content of the product, the product should not be used.
Clinical Study Examples

Summarized results of positive feedbacks and evaluations about the clinical studies of the product are presented here to your attention.

1. Actolind® experience after Z-plastic application on contracture tapes and burns on arms.

Subject:
A tissue healing case is presented. Actolind® w Solution is used after Z plasty application with the purpose of opening contracture bands resulting from the burns.

Period:
70 days

Result:
Actolind® w Solution/ w Gel is attached to the phospholipids in bacteria cells due to its polyhexanide structure and mechanism of effect. It does not penetrate into healthy cell due to its big molecule structure. This antiseptic feature prevents microorganism reproduction and keeps the wound moist and lets the formation of new tissues. Poloxamer, as its content, effectively cleans the wound and prolongs the action time of Polyhexanide. In this case, the repair process continues although it is on the 70th day.

Starting date of Actolind® w Gel and w Solution usage 10.09.15

70th day of Actolind® w Gel and w Solution usage 19.11.15
2. **Actolind®** Experience in burn treatment

**Subject:**
29-year-old female patient sustained a superficial to deep partial-thickness burn to face and neck

**Period:**
6 weeks

**Result:**
Surgical debridement of the burn wound.
Regular wound cleansing with **Actolind® Solution** and wound coverage with **Actolind® Gel**.
2 weeks (post-burn); no signs of infection, successful epithelialization and no need for grafting.
6 weeks (post-burn); complete wound closure with little scarring.

A new approach for wound care with smart molecule
3. **Actolind® Experience in venous ulcer treatment**

**Subject:**
52-year-old male presented to the wound clinic on 26th Oct 2011 with a large arterial, infected wound with deep necrosis and slough caused by trauma.

A leg ulcer to the left leg measuring approximately 7 cm x 7 cm with 50% necrotic tissue, 30% thick slough and 20% granulation and was punched out in center.

**Period:**
5 months

**Result:**
Dressing is done by using *Actolind® w Solution and Actolind® w Gel* together with commenced dressings twice weekly. *Actolind® w Solution and Actolind® w Gel* reduce pain and facilitate debridement. They are applied a hydro fiber to manage exudate and then a charcoal dressing to manage odor. Complete recovery is achieved in 5 months.

![Image of wound before and after treatment](image_url)

**A new approach for wound care with smart molecule**
Questions / Answers

Q : How does a wound heal?
A : Wound healing is a complex and dynamic process that ideally leads to restoration of anatomic continuity and function. The process begins at the moment of the injury and the wound healing can take month or years. The wound healing process can be divided into three stages: (1) Inflammatory, (2) Proliferation and (3) Remodeling. These three processes are carried out automatically by the personal immune system who does not have any problems with its immune system. That means every wound that is kept clean and moist heals spontaneously over time.

Q : What is the difference between an acute and chronic wound?
A : Acute injuries are usually traumatic or surgical. Generally, these injuries occur suddenly, healing process is fast and normal wound healing ideally processes without any major complication. Examples of acute wounds are ruptures, animal stings or knife wounds. A chronic wound can be defined as a wound that is stuck in one or more of the normal wound healing processes (usually the inflammatory phase). Acute wounds heal quickly and properly when they are compared to chronic wounds which have characteristic features. Most of the chronic wounds can be divided into three categories: venous ulcers, diabetic ulcers and pressure ulcers.

Q : What is wound care? What is its benefit?
A : A qualified wound care is achieved by preventing wound infection, trauma or contract with highly malignant agents and by avoiding from the conditions which may cause another surgical intervention. For this reason, it is necessary to keep the wound clean, moist and to disconnect from the external environment against the infection factors.

Q : How are the products classified?
A : Actolind® w Solution and Actolind® w Gel is categorized as Class III Medical Devices according to European Union Medical Device Directive 2007/47/EC (MDD). Class III device design/clinical trial examinations require the product certificate and an evaluated quality system. All these two documents are examined:
• Wound dressings may be in the form of liquid gels and pastes, etc. (e.g. hydrocolloid and hydrogel)
• It is seen that the products such as irrigation solutions intended for mechanical rinsing (e.g. bladder irrigation solution, ocular irrigation solution etc.) are classified as medical devices.

The main purpose of Actolind® w Solution and Actolind® w Gel is to keep the wound clean and moist. However, the dried crusts adhered to the bandage and dead tissues provide a suitable environment for infection development. Polyhexanide is used as a protective antibacterial substance to prevent that bacteria penetrates from dressing to the wound. The polyhexanide forms a protective film layer between the wound and the dressing. This layer cuts off the connection with the external environment and prevents the penetration of bacteria from outer environment to the wound. Unlike drugs, polyhexanide does not have any medical or immunological effect on the cell or bacteria. The polyhexanide binds to acidic phospholipids of bacteria cell wall through electrostatic interaction. Due to all these reasons, it has been certified as a Class III product and defined as a medical product.

Q : Why are Actolind® w Solution and Actolind® w Gel medical products?
A : When a product is classified, all relevant regulations must be considered. Actolind® w Solution and Actolind® w Gel products remain between the medical device and the drug products when it is evaluated in this context. Manual on Borderline and Classification in the Community Regulatory Framework for Medical Devices - Version 1.18 (12-2017) and Meddev 2.1/3 rev 3 Guidance are based on for the classification of byproducts. When these two documents are examined:

- Filling the gap between the skin and the sticking plaster, compress, gauze and other materials and creating a film layer on the wound surface. Thus, it keeps the wound surface stable.
- Healing process is shorten by keeping the wound always moist and not letting the creation of scabs, which is adhered to the dressing, or rupturing these scabs during the dressing change, or letting its reoccurrence.
- It prevents the adhesion of dressing to the wound by wetting it before changing the bandage during the dressing. Therefore, the dressing is removed more easily and the patient does not have any pain during the dressing change due to the rupture of scabs adhered to the wound.

Q : What are the formulations of Actolind® w Solution and Actolind® w Gel?
A : Actolind® w Solution contains a surfactant, Polyhexanide (PHMB) and pure water. In addition to that, Actolind® w Gel has also moisturizing effect.

Q : What are the advantages of Actolind® w Solution and Actolind® w Gel?
A : Combination of surfactant (Poloxamer) and Polyhexanide
- Shortens the healing period by keeping the wound clean and moist
- Due to the large molecular structure of polyhexanide, the product, which is not absorbed by the skin, forms a protective film layer on the wound surface. Polyhexanide film layer with antibacterial effect cuts off the connection with outer environment and prevents the bacterial growth on wound surface. Thus, it keeps the wound surface stable.
- Filling the gap between the skin and the sticking plaster, compress, gauze and other materials and creating a film layer on the wound surface increase the efficiency of these materials.
- Healing process is shorten by keeping the wound always moist and not letting the creation of scabs, which is adhered to the dressing, or rupturing these scabs during the dressing change, or letting its reoccurrence.
- It prevents the adhesion of dressing to the wound by wetting it before changing the bandage during the dressing. Therefore, the dressing is removed more easily and the patient does not have any pain during the dressing change due to the rupture of scabs adhered to the wound.
Q: Do Actolind® w Solution and Actolind® w Gel help debride ment? If yes, how?

A: Yes. Poloxamer, a surfactant, and the moisturizing agent. Glycerin softens the scab and necrotic tissue on the wound surface. Thus, it helps to remove the necrotic tissue from the wound surface by washing, softening and loosening and then removing the necrotic tissue.

Q: Question: What is the usage procedure/protocol?

A: Actolind® w Solution:
To loosen and remove the wound covers; wet the bandages with the product (compress, bandage, gauze, etc.) and wait for 10-15 minutes to let the scabs soften and loosen. Then, remove the loosened material and wash the wound with Actolind® w Solution. Actolind® w Solution will clean the wound surface and create a protective film layer. Then, replace the bandage and end the dressing procedure.

Actolind® w Gel:
Apply it to the wound after the wound is cleaned with Actolind® w Solution. It is a “leave on” product and will create a protective film layer on wound bed. This lets the scabs and necrotic tissue, which are difficult to remove, to be softened. Leaving the gel on the wound provides a continuous cover. Thus, the connection between the wound and outer environment is cut off. Efficiency of bandage is increased because the wound surface is filled well. Due to this protective later, the wound surface is protected from the infection and the wound is kept stable by preventing bacteria growth on the surface.

In case of small and surface wounds, only use Actolind® w Solution. In case of big and deep wounds, wash the wound surface with Actolind® w Solution and then fill the wound surface with plenty of Actolind® w Gel, and then apply the bandage.

Q: How long are Actolind® w Solution and Actolind® w Gel used on the wound?

A: There is not any limit for the use of Actolind® w Solution and Actolind® w Gel. They are especially designed for the treatment of the wounds which require long healing period.

References

[15] Prontomed GmbH