TECHNICAL DATA

ANTISEPTIC
2% CHLORHEXIDINE
GLUCONATE
SOLUTION

ANTISEPTIC
4% CHLORHEXIDINE
GLUCONATE
SOLUTION

Antimicrobial Skin Cleansers

Manufactured by:
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Aplicare®, is a registered trademark of Aplicare, Inc.
Hibiclens® is a registered trademark of Mölnlycke Health Care
BACKGROUND
Chlorhexidine Gluconate (CHG) has been used in a variety of pharmaceutical applications for over 40 years. CHG-containing products have been extensively studied and are widely regarded as most effective for hand washing, surgical scrubbing, and preoperative prepping procedures. Its use in the medical, dental, veterinary and dairy industry is widespread and growing. Chemically distinct from other skin disinfectants, this cationic biguanide is effective against a broad spectrum of gram-positive and gram-negative bacteria at concentrations between 0.1% and 4%.

The mode of action of CHG has been shown to differ at high and low concentrations. Concentrations below 100 ppm have bacteriostatic properties that act on cell membrane components. Concentrations above this level have bactericidal effects due to rapid action on the cytoplasm.

CHG’s exceptionally persistent and broad spectrum antimicrobial properties have led to its recognition as the most effective agent available for surgical scrubbing, hand washing, patient preoperative prepping, and skin wound cleansing.

REGULATORY STATUS
CHG is classified by the FDA as a “New Drug”. Use of it as an active ingredient in original formulations for human use requires approval of a New Drug Application (NDA).

SAFETY
Extensive clinical testing in Europe, Canada, and the United States, plus worldwide use has demonstrated the safety of CHG. The compound has been shown to have negligible potential for skin absorption through intact skin. When used as directed, it is safe and typically does not produce clinically significant irritation or sensitization problems.

To date, there is no evidence that susceptible organisms develop a resistance to CHG.

THE APLICARE® ADVANTAGE
Now available in both 2% and 4% concentrations, the APLICARE CHG formulations are both approved by the FDA for use as a:

- Surgical Hand Scrub
- Patient Preoperative Skin Preparation
- Health Care Personnel Handwash (15 sec)
- Skin Wound and General Cleansing

Formulated in a relatively high-sudsing, truly emollient base, the APLICARE 2% and 4% CHG formulations have been pH adjusted for optimal antiseptic activity and stability as well as compatibility with the normal acid pH of the skin.

Designed to be the preferred antiseptic cleanser of healthcare personnel, APLICARE 2% and 4% CHG formulations combine the effectiveness of CHG with superior cosmetic acceptability.

EFFICACY DATA
Decades of research, published articles and clinical use have clearly established Chlorhexidine Gluconate’s superiority to iodine, PCMX (chloroxylenol), alcohol, and other antimicrobials available to the healthcare market. CHG has the following advantages.

- BROAD SPECTRUM: CHG is effective against gram negative and gram positive bacteria as well as fungi and yeasts.
- FAST ACTING: CHG acts quickly; a property that is critical for effective infection control.
- SUBSTANTIVE: CHG achieves an exceptionally high reduction in microbial counts on the skin.
- PERSISTENT: CHG chemically binds to the epithelial surfaces of the skin; thus creating a persistent and residual effect not seen in alcohols, iodine, or other skin disinfectants.
MINIMUM INHIBITORY CONCENTRATION (MIC)

The MIC ranges for APLICARE 4% CHG scrub formulation are tabulated below.

**SPECIES** | **MIC (ppm)**
---|---
**Gram-Negative Bacteria** | |
*Escherichia coli* | 4.0 – 5.0
*Klebsiella pneumoniae* | 4.0 – 10
*Neisseria species* | 2.0 – 4.0
*Proteus vulgaris* | 10
*Pseudomonas species* | 10 – 40
*Serratia marcescens* | 40 – 50

**Gram-Positive Bacteria** | |
*Bacillus subtilis* | 4.0
*Corynebacterium species* | 1.0 – 2.0
*Micrococcus species* | 4.0 – 5.0
*Mycobacterium species* | 1.0 – 2.0
*Sarcina species* | 4.0
*Staphylococcus albus* | 1.0 – 2.0
*Staphylococcus aureus* | 0.4 – 4.0
*Staphylococcus epidermidis* | 0.2 – 5.0
*Streptococcus pyogenes* | 4.0 – 6.8

**Fungi** | |
*Allescheria boydii* | 40
*Aspergillus niger* | 500
*Candida species* | 10 – 40
*Cladosporium species* | 100
*Cryptococcus species* | 20
*Deparyomyces species* | 10
*Microsporum species* | 10 – 20
*Nocardia species* | 100
*Pityrosporum species* | 20
*Streptomyces species* | 40
*Tolypoclados species* | 10
*Trichophyton species* | 20
*Trichosporon species* | 20 – 40

Both APLICARE 2% and 4% CHG formulations are effective against Methicillin-Resistant Staph aureus (MSRA).

CLINICAL STUDIES

Because of the limited value of *in vitro* studies in assessing the efficacy of antimicrobial products in a health care setting, the following FDA recommended *in vivo* studies, intended to simulate actual use conditions, were conducted:

**GLOVE JUICE STUDY**

The FDA-recommended Glove Juice Study measures the immediate, persistent, and residual effects of the product tested. Spanning a five-day period of repeated usage to assess the residual capabilities of the product, bacterial counts are measured immediately, 3 hours, and 6 hours after scrubbing. Both APLICARE 2% and 4% CHG scrub formulations consistently pass this demanding test.

APLICARE 2% and 4% CHG scrub formulations were tested against Hibiclens® 4% CHG at an independent laboratory using the FDA recommended glove juice protocol.

**GLOVE JUICE TEST COMPARISON OF APLICARE 2% AND 4% CHG vs. HIBICLENS**

<table>
<thead>
<tr>
<th>Log10 Reduction Data</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product</strong></td>
<td><strong>0 hr</strong></td>
<td><strong>3 hr</strong></td>
<td><strong>6 hr</strong></td>
</tr>
<tr>
<td>APLICARE 2%</td>
<td>1.10</td>
<td>1.52</td>
<td>1.47</td>
</tr>
<tr>
<td>APLICARE 4%</td>
<td>2.80</td>
<td>1.94</td>
<td>2.59</td>
</tr>
<tr>
<td>Hibiclens 4%</td>
<td>0.00</td>
<td>0.57</td>
<td>0.08</td>
</tr>
</tbody>
</table>

**Comparable Percent Reduction Data**

<table>
<thead>
<tr>
<th>Comparable Percent Reduction Data</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product</strong></td>
<td><strong>0 hr</strong></td>
<td><strong>3 hr</strong></td>
<td><strong>6 hr</strong></td>
</tr>
<tr>
<td>APLICARE 2%</td>
<td>96.56</td>
<td>97.53</td>
<td>98.26</td>
</tr>
<tr>
<td>Hibiclens 4%</td>
<td>45.64</td>
<td>80.29</td>
<td>72.55</td>
</tr>
</tbody>
</table>

**Conclusion:**

APLICARE 4% CHG performed significantly better than Hibiclens 4% CHG. The performance of APLICARE 2% CHG was statistically equivalent to Hibiclens 4% CHG.
HEALTHCARE PERSONNEL HANDWASH STUDY
In the FDA-recommended protocol to assess efficacy of a healthcare personnel handwash, subjects’ hands are contaminated with *Serratia marcescens* or *Bacillus subtilis* var. *niger* (globigii) and a baseline count is taken. This contamination followed by a handwash is carried out 25 consecutive times. Log₁₀ and percent microbial reduction is measured after the 1ˢᵗ, 4ᵗʰ, 7ᵗʰ, and 10ᵗʰ washes and compared to the baseline count. The 11ᵗʰ and 25ᵗʰ washes are carried out to assess irritancy potential.

Performance of APLICARE 2% and 4% CHG products vs. Hibiclens, as a 15 second wash is summarized below.

15 SECOND HANDWASH STUDY

<table>
<thead>
<tr>
<th>Product</th>
<th>1ˢᵗ Wash Log₁₀</th>
<th>1ˢᵗ Wash Percent Log₁₀</th>
<th>4ᵗʰ Wash Log₁₀</th>
<th>4ᵗʰ Wash Percent Log₁₀</th>
<th>7ᵗʰ Wash Log₁₀</th>
<th>7ᵗʰ Wash Percent Log₁₀</th>
<th>10ᵗʰ Wash Log₁₀</th>
<th>10ᵗʰ Wash Percent Log₁₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>APLICARE 2%</td>
<td>1.882</td>
<td>98.69</td>
<td>2.389</td>
<td>99.59</td>
<td>2.770</td>
<td>99.83</td>
<td>3.307</td>
<td>99.95</td>
</tr>
<tr>
<td>APLICARE 4%</td>
<td>2.050</td>
<td>99.11</td>
<td>2.563</td>
<td>99.73</td>
<td>2.696</td>
<td>99.80</td>
<td>3.289</td>
<td>99.95</td>
</tr>
<tr>
<td>Hibiclens 4%</td>
<td>1.629</td>
<td>97.65</td>
<td>2.097</td>
<td>99.20</td>
<td>2.501</td>
<td>99.68</td>
<td>3.115</td>
<td>99.92</td>
</tr>
</tbody>
</table>

PATIENT PREOPERATIVE PREP STUDY
The preoperative patient prep study measures the immediate and persistent effect of the product at two (2) different anatomical sites (abdomen and inner thigh). Baseline counts are taken. Both sites are prepped according to label directions and microbial counts measured at 10 minutes, 30 minutes, and four (4) hours.

APLICARE 2% and 4% CHG formulations were directly tested against Hibiclens 4% CHG. Both APLICARE formulations achieved reductions equivalent to Hibiclens 4% CHG, both immediately and over the four (4) hour time period.

COMPARISON OF APLICARE 2% CHG AND HIBICLENS IRRITATION POTENTIAL
The irritation potential of APLICARE 2% and Hibiclens was compared under use conditions. At least 12 subjects were randomly assigned to each product. There were a total of 10 washes per day with one to two hour intervals between washes. The onset of irritation and the cumulative irritation scoring, after equal numbers of washes, are presented in the table below.

<table>
<thead>
<tr>
<th>Product</th>
<th>Onset of Irritation at Wash</th>
<th>Cumulative Irritation Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>APLICARE 2%</td>
<td>19</td>
<td>33</td>
</tr>
<tr>
<td>Hibiclens</td>
<td>14</td>
<td>45</td>
</tr>
</tbody>
</table>

The study indicates the relative irritation potential of APLICARE 2% CHG to be lower than Hibiclens.

The advent of APLICARE 2% and 4% CHG scrub formulations sets new standards for skin disinfection products.

The choice of APLICARE 2% CHG now enables the Health Care market to realize significant cost savings and lower irritation potential without sacrificing clinical efficacy.
### Drug Facts

<table>
<thead>
<tr>
<th>Active ingredient</th>
<th>Purposes</th>
</tr>
</thead>
<tbody>
<tr>
<td>chlorhexidine gluconate 4% solution</td>
<td>Surgical hand scrub</td>
</tr>
<tr>
<td></td>
<td>Healthcare personnel handwash</td>
</tr>
<tr>
<td></td>
<td>Patient preoperative skin preparation</td>
</tr>
<tr>
<td></td>
<td>Skin wound and general skin cleansing</td>
</tr>
</tbody>
</table>

**Uses**
- Surgical hand scrub: significantly reduces the number of microorganisms on the hands and forearms prior to surgery or patient care
- Healthcare personnel handwash: handwash to help reduce bacteria that potentially can cause disease
- Patient preoperative skin preparation: for the preparation of the patient’s skin prior to surgery
- Skin wound and general skin cleansing

**Warnings**
For external use only

- **Do not use**
  - If you are allergic to chlorhexidine gluconate or any other ingredients
  - In contact with meninges
  - In the genital area
  - As a preoperative skin preparation of the head or face

**Directions**

**Surgical hand scrub**
- Wet hands and forearms under running water for 30 seconds
- Scrub for 3 minutes with about 5 ml of product with or without a wet brush, paying close attention to the nails, cuticles, and interdigital spaces
- Rinse thoroughly under running water for 30 seconds
- Dry thoroughly

**Healthcare personnel handwash**
- Wet hands with water
- Dispense about 5 ml of product into cupped hands and wash in a vigorous manner for 15 seconds
- Rinse and dry thoroughly

**Patient preoperative skin preparation**
- Apply product liberally to surgical site and swab for at least 2 minutes
- Repeat procedure for an additional 2 minutes and dry with a sterile towel

**Skin wound and general skin cleansing**
- Thoroughly rinse the area to be cleaned with water
- Apply the minimum amount of product necessary to cover the skin wound area and wash gently
- Rinse again thoroughly

**Other information**
- Store at 20–25°C (68–77°F)
- Avoid excessive heat above 40 °C (104 °F)

**Inactive ingredients**
- Cocamide DEA, Fragrance POFL 147,
- Glucono-delta-lactone, hydroxyethylcellulose, isopropyl alcohol, lauramine oxide, PEG-75 lanolin, purified water, tridecyl alcohol

**Questions or comments?**
- 1-800-760-3236 (Monday – Friday 8:30 AM – 5:00 PM EST)