Synactin™ AC: Designed for Treating Acne-affected Skin with Pigmentation Control
What is the ideal acne treatment?

- Should quickly and effectively control acne, have few if any side-effects
- Reduces seborrhoea (excess sebum production)
- Should be acceptable (safety & tolerability) to patients
What is Synactin™ AC?

The composition:

- Ethyl Linoleate
  - >70% pure
- 4-Hexylresorcinol (Synovea® HR)
  - >99% purity with <0.1% resorcinol
- Caprylic/Capric Triglycerides
  - Widely used in personal care
What are the key benefits of Synactin™ AC?

**Effective**
- Shown by in-vitro studies
- To be proven clinically

**Safe**
- Long history of human use
- No skin irritation & No skin sensitization (HRIPT at 10% dilution in corn oil)

**User friendly**
- Liquid
- No dusting problem
How acne develops?

- Acne develops with the negative effects of dihydrotestosterone (DHT) on the oil glands
  - The enzyme 5-α-reductase converts testosterone to DHT
  - DHT binds to androgen receptors on the oil glands
  - DHT stimulation results in excessive oil production
  - Excess oil obstructs the skin pores allowing bacterial growth that causes inflammation, infection and visible acne

Stages of the Common Acne

0 - Normal skin
1 - Whiteheads
2 - Blackheads
3 - Pustules & Nodules
4 - Cysts
How acne can be treated?

- Four major principles presently governing the therapy of acne
  
- Correction of follicular keratinization
  - Linoleic acid deficiency, interleukin 1, retinoids and androgens have been implicated as causative factors in the follicular hyperkeratinization

- Decrease in sebaceous gland activity
  - 5-α-reductase inhibitors

- Decrease the follicular bacterial population of Propionibacterium acne
  - P. acne inhibitors

- Produce an anti-inflammatory effect
  - Anti-inflammatory agents

- Global acne market was worth US $2.8 billion in 2009 and is estimated to reach revenues of $3.02 billion by 2016
Current topical treatments available for acne

- **Exfoliating agents**
  - Salicylic acid, Glycolic acid
    - Skin becomes more sensitive to sun-induced damage

- **Topical bacteriocides**
  - Benzoyl peroxide
    - Reclassified as a category I (generally recognized as safe and effective, GRASE) product from Category III (safety is uncertain) since 2010
  - Antibiotics - Erythromycin, Clindamycin, Stiemycin or Tetracycline
    - Bacterial resistance
    - Contributor to Candida overgrowth

- **Topical retinoids**
  - Retinol, Retinyl palmitate, Retinoic acid
    - Initial flare-up; dry skin; headache & other problems

- **Retinoic acid is effective against all 4 major pathophysiologic features of acne**
  - Has many serious side effects including teratogenecity
  - Occasionally causes depression

Linoleic acid (LA) is an essential fatty acid needed for skin nourishment
- Ethyl linoleate (EL) gets converted to LA by skin lipase
- Reduces redness and scaling of the diseased skin
- Involved in sebocytes functions and differentiation
- LA is the only one fatty acid subjected to β-oxidation leading to the generation of acetyl-CoA


Depletion of LA in sphingolipids has been hypothesized to be involved in the follicular hyperkeratosis, which is a crucial event involved in the comedones formation [D T Downing et al, Essential fatty acids and acne, *J Am Acad Dermatol*, 14(2): 221–225, 1986]

**Why select Ethyl Linoleate in developing Synactin™ AC?**
Why select Synovea® HR? It has superb inhibitory activity against a wide variety of bacteria & fungi

<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>MIC in µg/ml</th>
</tr>
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<tbody>
<tr>
<td>Propionibacterium acne</td>
<td>50/25</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>2.2</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>2.2</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>1.7</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>0.7</td>
</tr>
<tr>
<td>Aspergillus</td>
<td>0.1</td>
</tr>
</tbody>
</table>

1. Acne-affected skin has higher levels *Staphylococcus* & *Candida*

2. Bakuchiol (Sytenol® A) in the management of acne-affected skin
   Chaudhuri & Marchio, *C&T*, July issue 2011
Asyntra™ AC indeed is a synergistic anti-acne blend

<table>
<thead>
<tr>
<th>Product</th>
<th><em>P. Acne</em> (MIC in µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synactin™ AC</td>
<td>50/25</td>
</tr>
<tr>
<td>(Contains only ~25% Synovea® HR)</td>
<td></td>
</tr>
<tr>
<td>Synovea® HR</td>
<td>50/25</td>
</tr>
<tr>
<td>Ethyl linoleate</td>
<td>&gt; 100</td>
</tr>
</tbody>
</table>

Synactin™ AC containing products may require low levels of preservation
Why select Synovea® HR? It has a broad skin protective properties

Cell protection
- Upregulating Glutathione, Glutathione peroxidase, Glutathione reductase

DNA Protection
- Providing long-term protection of DNA; Practically no DNA degradation even under UV-light

Protein Protection
- Protecting Collagen and other proteins by reducing Glycation
Synactin™ AC may be effective in controlling acne-induced (?) pigmentation

Two key ingredients in Synactin™ AC shown to be effective in controlling pigmentation

- Linoleic acid has been demonstrated to lighten UV-induced skin pigmentation

- Linoleic acid lightens skin by accelerating post-translational tyrosinase degradation

- Synovea® HR is four-times more effective than Hydroquinone
  - Proven by human clinical studies
  - Excellent inhibitor of Tyrosinase & Peroxidase enzymes
  - Reduces H₂O₂-induced DNA degradation
  - Stimulates production of Glutathione
    - Competitive binding to Tyrosinase active site

How does Synactin™ AC work?

Correcting follicular keratinization
- Linoleic acid (LA) is significantly reduced in epidermal and comedonal lipids in acne subjects [J Am Acad Dermatol, 14:221–225, 1986]
- Lack of LA – Hyperkeratinization, bacterial proliferation

Decreasing sebaceous gland activity
- Acne-prone sebaceous glands have high level of 5 α-reductase due to low level of linoleic acid → high sebum production
- Linoleic acid is a 5 α-reductase inhibitor [Int J Dermatol, 43:701-702, 2004]

Decreasing the follicular bacterial population
- Synovea® HR has a broad-spectrum antimicrobial activity
- *P. acne* (25 µg/ml); *S. epidermidis* (2.2 µg/ml); *C. albicans* (1.7 µg/ml)

Producing an anti-inflammatory effect
- Synovea® HR is a NF-kappa B inhibitor [J&J report]
Product applications

- **Suggested use level of Synactin™ AC**
  - 2 to 4% w/w
  - For making an anti-acne claim, include Salicylic acid in the formulation

- **Formulation choices**
  - Lotion, crème, gel, serum, spray etc

- **Formulators’ choice**
  - A unique stand alone product for acne-affected skin with pigmentation control
  - Complex formulations targeting for Skin pigmentation control
Formulation guidelines

- Add Synactin™ AC to the oil phase directly or after making the lotion while cooling at ~40 °C.

- For preparation of serum or transparent gel, use non-ionic solubilizers having high HLB values. Use PEG-40 hydrogenated castor oil, Laureth 23, Polysorbate 20 or 80.

- Addition of a small amount of disodium EDTA (~0.1%) resolves the coloration problem, if any, due to the presence of iron or copper.

- The finished product must be acidic, preferably having pH below 6.5.

- Formulations containing Synactin™ AC may cause drop in viscosity. Acidic (such as, Xanthan gum) or neutral thickeners (such as, Cellulosics) are good for maintaining desired viscosity.

- The finished product should be protected from prolong exposure to heat and light.
Product availability

- Commercially available in 4.5 Kg packing size

- Sample size – 50 g

For sample and literature, contact
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Thank you