LSI

Piroctone olamine

LSI's Newest Antidandruff Active

« LSI is the leading global provider of anti-dandruff solutions »

« As consumers look for new actives, LSI is ready to meet consumer demands for more antidandruff and scalp care solutions »

Key Product Attributes:

- Relieves dandruff
- Relieves itching sensation in consumer testing
- Targets the dandruff-associated yeast *Malassezia* sp.
- Compatible with transparent formulations
- Produced under EFfCI GMP compliance in Switzerland

(Underlying) Causes of Dandruff

Dandruff is a condition of the scalp affecting about half of the adult population.[1] It is characterized by visible flaking of the skin often accompanied by itchiness. Dandruff is not a medically serious condition, but because of its undesirable appearance, it can cause psychological and social stress affecting quality of life. Therefore, effective treatments are highly sought after.

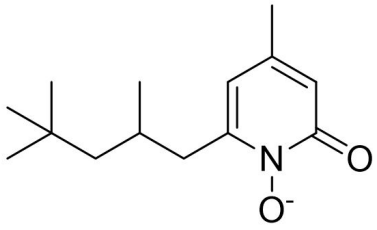
The precise triggers for dandruff are unknown, however it is recognized that *Malassezia* yeasts, sebaceous lipids, and individual susceptibility all contribute to the development of dandruff.[2] In a healthy scalp, *Malassezia* species exist symbiotically with the human host, feeding off of sebaceous secretions as a nutrient source. In scalp affected by dandruff that symbiosis is swept out of balance, with elevated populations of *Malassezia* causing a chain of events leading to the macroscopic symptoms of flaking and itching.

Malassezia species hydrolyze sebaceous triglycerides, releasing a mixture of saturated and unsaturated fatty acids. While the saturated fatty acids act as a nutritional source, the unsaturated fatty acids such as oleic acid are generally thought to be irritating to the scalp.[3] Increased hydrolysis of sebum, either caused by elevated *Malassezia* levels or increased sebum production, will lead to higher levels of unsaturated fatty acids on the scalp, which in turn can cause hyperproliferation of epidermal keratinocytes as part of an irritation response. Epidermal hyperproliferation is known to result in flaking of the skin as well as increased sensitivity to irritants from impaired skin barrier function.[4]

In addition to yeast colonization and sebum production, other factors that can trigger or exacerbate dandruff are cold and dry weather, stress or fatigue, mechanical stress on hair follicles, and the presence of dermal penetration enhancers such as propylene glycol in certain aftercare products.

Treatment of Dandruff with Piroctone olamine

LSI's newest antidandruff active, Piroctone olamine active (Fig.1), works to treat dandruff at the root cause by functioning as a fungicide with specific efficacy against Malassezia.



$H_3N^+CH_2CH_2OH$

Figure 1

Structure of Piroctone Olamine

Although there are a number of antifungals that have been demonstrated to be effective in the treatment of dandruff, Piroctone olamine active carries advantages that make it ideal for use in over-the-counter shampoos and hair treatment products that are both efficacious and have excellent consumer appeal. For instance, azole-based actives work on the cell membrane by inhibiting ergosterol synthesis which results in disrupted membranes and increased permeability of the organism.[5] Exposure to this type of active can lead to adaptations and mutations that change the ergosterol synthesis pathway rendering the cell wall more impervious to the anti-microbials.

Unlike the azole family, Piroctone Olamine active is a hydroxypyridinone antifungal that is thought to work through interference with the active transport of essential macromolecules into the cell. By moving freely in and out of the cell membrane and taking ions with it, these actives work to deplete the organism of essential nutrients needed to survive.[6] Piroctone olamine active penetrates the cell wall, forming complexes with iron(III), thus inhibiting energy metabolism in the mitochondria.[6] This mode of action does not interfere with cell wall enzymes.

LSI's newest antidandruff offering, Piroctone olamine active, is produced in the beautiful Swiss Alps at our Visp location. LSI's Visp site has been producing 1,000+ unique products over the last 45 years with the highest of quality standards. Piroctone olamine active is produced to EffCI GMP standards and offers formulators a versatile active, with proven clinical efficacy, that is easily incorporated, even into clear formulations.

Antifungal Efficacy

The antifungal potential of Piroctone olamine active against *Malassezia furfur* was evaluated using standard methodology, showing a minimum inhibitory concentration (MIC) against *M. furfur* of 16 ppm. Further, suspension-based tests were performed to evaluate the performance of Piroctone olamine in several common surfactant systems.[7] Results show quick kill in a standard SLES shampoo surfactant system (Fig. 2). There is an approximately 5 log10 reduction in the *M. furfur* population within 4 hours contact time.

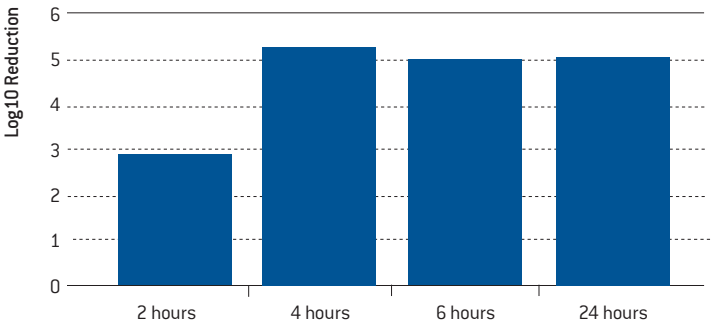


Figure 2

Efficacy of 1% Piroctone olamine in an SLES surfactant system. Kill rate of *M. furfur* calculated as Log10 reduction in population after 2-24 hours contact time.

Clinical Efficacy

Efficacy of Piroctone olamine active was further assessed *in vivo* over a period of 28 days, in a double-blind, randomized study. A group of 32 subjects, male and female, with ages ranging from 25 to 59, were included in the study if their total dandruff score was ≥4 on a scale of 0-10. They applied a shampoo containing 1% Piroctone olamine active at least 3 times per week, and their dandruff was clinically assessed once per week.

The formulation containing Piroctone olamine active was well tolerated, and no sensations of discomfort were reported by the study subjects. Clinical assessment of total dandruff showed a significant decrease, versus the baseline (D1) evaluation, starting at day 8, and continuing through the length of the study. This significant decrease was also evident when examining non-adherent and adherent dandruff separately (Fig. 3).

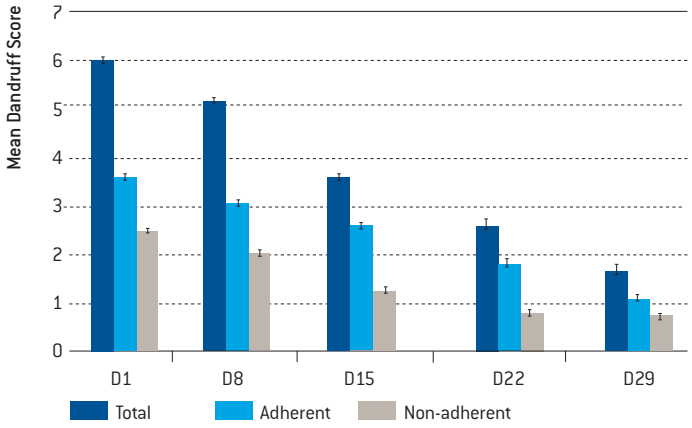


Figure 3

In vivo efficacy of Piroctone olamine active shampoo. The mean scores for total, adherent and non-adherent dandruff are shown. Significance was calculated using a Dunnett t (2 sided) comparison and differences were considered significant at $p<0.05$.

The clinical results were mirrored by subject self-assessment of their dandruff (Fig. 4). Subjects were asked to assess their dandruff on a scale from 1 to 10. A significant effect on dandruff was perceived by the panelists beginning with day 8, the first evaluation after study initiation. As in the clinical assessment, the self-perceived amount of dandruff continued to decrease through the duration of the study.as well as a significant decrease in self-assessed dandruff and itching scores that persisted through the end of the study.

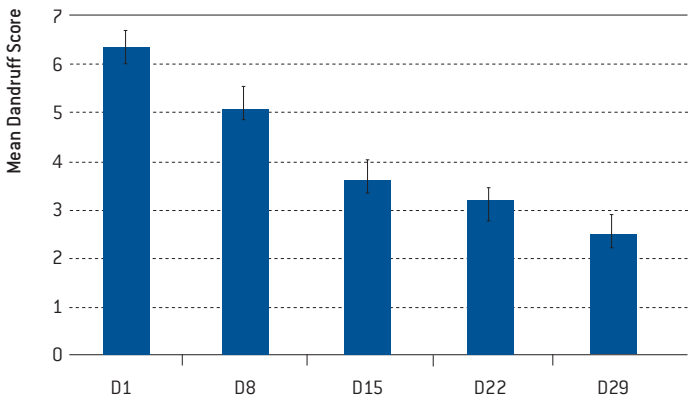


Figure 4

Self-assessment of dandruff and efficacy of 1% Piroctone olamine active shampoo. Assessment on an ordinal scale of 1 (no dandruff) to 10 (very abundant dandruff). The mean scores for dandruff are shown. Significance was calculated using a Dunnett t (2 sided) comparison and differences were considered significant at $p<0.05$.

Subjects were also asked to assess scalp itch during the study, on a scale of 1 to 10. A significant decrease in itch, versus study start, was observed starting with the first assessment date on D8 of the study (Fig. 5). The mean itch level continued to decrease through the length of the study.

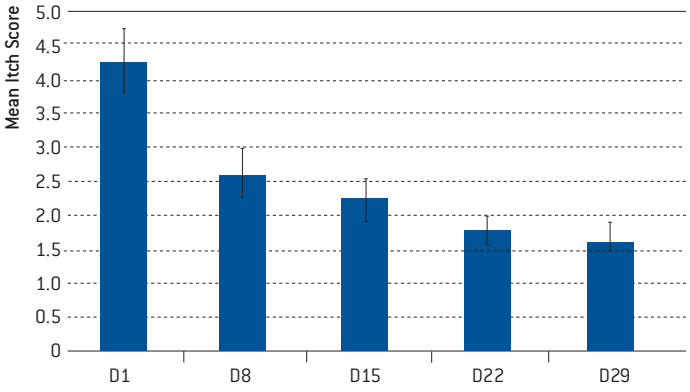


Figure 5
Self-assessment of itch with application of 1% Piroctone olamine active shampoo. Assessment on an ordinal scale of 1 (no itching) to 10 (very strong itching). The mean scores for itch are shown. Significance was calculated using a Dunnett t (2 sided) comparison and differences were considered significant at $p<0.05$.

Regular application of a shampoo containing 1% Piroctone olamine active was well tolerated and showed clinical efficacy against total, non-adherent and adherent dandruff. This efficacy was perceivable by study subjects in dandruff level as well as scalp itch.

Formulation Tips

- Recommended use levels
  - Rinse-off products – 1.0% max
  - Leave-in products – 0.3% max
- Suitable for shampoos, conditioners, creams, lotions and gels including clear shampoos formulations and solid shampoo bars
- Piroctone olamine can lead to viscosity increases
- Incompatbilities
- Metal ions, particularly iron ions should be avoided
- Final products should be stored in an opaque container to avoid degradation by UV

Product Information

INCI Name	Piroctone Olamine
CAS#	68890-66-4
Appearance	White to pale yellow powder
Assay %	98.0 – 101.5
2-aminoethanol %	20.1 – 20.9
Melting point	130.0 – 136.0
pH (1% aq.)	8.5 – 10.0
Residual Solvents	≤ 0.3
Shelf Life	36 months
Available Pack Size	25 kg boxes
Manufacturing Location	Switzerland

Regulatory

Chemical Inventory Compliance:
Listed or exempt (cosmetic use exemption) from listing:

- Australia
- China
- EU (REACH Registered)
- Japan
- Korea
- New Zealand
- Philippines
- Thailand
- Vietnam

Other

- EU: Use for non-preservative applications is supported by the opinion (SCCNPF/0525/01) of the SCCNFP (now superceded by the SCCS).

References

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