VANIQA® (eflornithine hydrochloride) Cream, 13.9%

For topical dermal use only. Not for ophthalmic, oral or intravenous use.

DESCRIPTION
VANIQA is a cream containing 13.9% (139 mg/ml) of anhydrous eflornithine hydrochloride as eflornithine hydrochloride monohydrate (150 mg/g). Chemically, eflornithine hydrochloride is C₂₀H₂₉ClN₅O₃ (molecular weight 411.9), the empirical formula C₂₀H₂₉ClN₅O₃.HCl · H₂O, a molecular weight of 218.85 and the following structural formula:

![Chemical Structure](image)

Anhydrous eflornithine hydrochloride has an empirical formula C₂₀H₂₉ClN₅O₃ , HCl · H₂O and a molecular weight of 218.85. Other ingredients include: cetarati-20, cetomipramide, glycerol stearate, methylparaben, mineral oil, PEG-100 stearete, phenoxyethanol, propylparaben, stearyl alcohol and water.

CLINICAL PHARMACOLOGY

Pharmacodynamics
There are no studies examining the inhibition of the enzyme ornithine decarboxylase (ODC) in human skin following the application of topical eflornithine. However, there are studies in the literature that report the inhibition of ODC activity in skin following oral eflornithine. It has been postulated that topical eflornithine hydrochloride inhibits cell division and synthetic functions, which result in the rate of hair growth, an effect due to changes in the rate of hair growth in non-clinical and clinical studies.

Pharmacokinetics
The mean percutaneous absorption of eflornithine in women with unwanted facial hair, from a 13.3% cream formulation, is less than 1% of the radioactive dose, following either single or multiple doses under conditions of clinical use, that studied Shirley’s use of the product before radioisotope dose application in addition to other forms of cutting or plucking and tweezing to remove facial hair. Steady state was reached within four days of twice-daily application. The apparent steady-state plasma t₁/₂: 15 days. Following twice-daily application of 0.5 g of the cream (total dose 1.0 g/day), 139 mg as anhydrous eflornithine hydrochloride), under conditions of clinical use in women with unwanted facial hair (t₁/₂: 10 days), the steady-state C₀: 42 ng/ml and AUC₀-∞: approximately 12200 ng/ml, 99 ng/ml, respectively, expressed in terms of the anhydrous free base of eflornithine hydrochloride. At steady state, the dose-normalized peak concentrations (C₀) and the area under the plasma concentration vs time exposure (AUC) of eflornithine following twice-daily application of 0.5 g of the cream (total dose 1.0 g/day) is estimated to be approximately 100- and 60-400 ng/ml, when compared to 370 mg/kg/day of a single oral dose. This compound is not known to be metabolized and is primarily excreted unchanged in the urine.

INDICATIONS AND USAGE
VANIQA (eflornithine hydrochloride) Cream, 13.9% is indicated for the reduction of unwanted facial hair in women. VANIQA has only been studied on the face and adjacent involved area and not on non-face affected individuals. Usage should be limited to these areas of involvement.

CLINICAL TRIALS
Rationale
Topical dermal studies for contact sensitization, phototoxic sensitization, and phototoxic irritation reveal that under conditions of clinical use, VANIQA is not reversibly sensitizing. In contrast, VANIQA may cause contact sensitization, phototoxic, or phototoxic sensitization reactions. Results of the topical dermal study for contact sensitization reveal that VANIQA could cause irritation reactions in clinical use. Individual or under conditions of exaggerated use.

Two randomized double-blind studies involving 20% female patients (379 patients total with VANIQA, 20% with vehicle) treated twice daily, for up to 24 weeks evaluated the efficacy of VANIQA in the reduction of unwanted facial hair in women. Women in the trial had a customarily temporary frequency of removal of facial hair two or more times per week. Women with facial conditions such as severe inflammatory acne, women with other rag and nursing mothers were excluded from the study. Physicians assessed the improvement or worsening from the baseline condition (Physician’s Global Assessment [PGA]), 48 hours after shaving, of all treated areas. Statistically significant improvement for VANIQA (eflornithine hydrochloride) Cream, 13.9% versus vehicle was seen in each of these studies for marked improvement or greater response (24-week time point; p=0.0013). Marked improvement was seen consistently at 8 weeks after initiation of treatment and continued throughout the 24 weeks of treatment. Hair growth approached pretreatment levels within 8 weeks of treatment withdrawal. The success rate over time is graphically presented below for each pivotal trial.

Physician’s Global Assessment
Success Defined as Marked or Better Improvement

Approximately 32% of patients showed marked improvement or greater (photographic definition of clinical success) after 12 weeks of treatment with VANIQA (eflornithine hydrochloride) Cream, 13.9%, compared to 8% with the vehicle. Combined results of these two trials through 24 weeks are presented below.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Marked Improvement</th>
<th>P-value</th>
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<tbody>
<tr>
<td>VANIQA cream</td>
<td>27%</td>
<td>0.0001</td>
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<tr>
<td>Vehicle</td>
<td>8%</td>
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</table>

 subgroup analyses showed to suggest greater benefit for White than non-White (37% vs. 22% success, respectively; p=0.0071). However, non-White, mostly Black subjects, did have significant treatment benefit with 22% graded as success on VANIQA compared to 5% on vehicle.

About 12% of women in the clinical trials were postmenopausal. Significant improvement in PGA outcome versus vehicle was seen in postmenopausal women (38% compared to 0%, p<0.001).

VANIQA statistically significantly reduced how bothered patients felt by their facial hair and by the time spent removing, treating or concealing facial hair. These patient-observable differences were seen as early as 4 weeks after initiating treatment. Hair growth approached pretreatment levels within 8 weeks of treatment withdrawal.

Clinical trials with VANIQA involved over 1700 women with unwanted facial hair of skin types I-VI, of whom 64% were White, 17% Black, 11% Hispanic-Latino, 2% Asian-Pacific Islander, 0.6% Native American, and 1.3% other.

CONTRAINDICATIONS
VANIQA is contraindicated in patients with a history of sensitivity to any components of the product.

WARNINGS
Discontinue use if hypersensitivity occurs.

PRECAUTIONS
General
For external use only.

Topical irritation or burning may occur when applied to abraded or broken skin.

Information For Patients
Patients using VANIQA should receive the following information and instructions.

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<thead>
<tr>
<th>Instruction</th>
<th>Duration</th>
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<tr>
<td>Continue on reverse side</td>
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