SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Vaniqa 11.5% cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of cream contains 115 mg of eflornithine (as hydrochloride monohydrate).

Excipients with known effect:

Each gram of cream contains 47.2 mg of cetostearyl alcohol, 14.2 mg of stearyl alcohol, 0.8 mg of methyl parahydroxybenzoate and 0.32 mg of propyl parahydroxybenzoate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream.

White to off white cream

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of facial hirsutism in women.

4.2 Posology and method of administration

Posology

Vaniqa cream should be applied to the affected area twice daily, at least eight hours apart. Efficacy has only been demonstrated for affected areas of the face and under the chin. Application should be limited to these areas. Maximal applied doses used safely in clinical trials were up to 30 grams per month.

Improvement in the condition may be noticed within eight weeks of starting treatment.

Continued treatment may result in further improvement and is necessary to maintain beneficial effects. The condition may return to pre-treatment levels within eight weeks following discontinuation of treatment.

Use should be discontinued if no beneficial effects are noticed within four months of commencing therapy.

Patients may need to continue to use a hair removal method (e.g. shaving or plucking) in conjunction with Vaniqa. In that case, the cream should be applied no sooner than five minutes after shaving or use of other hair removal methods, as increased stinging or burning may otherwise occur.

Special population

Elderly: (> 65 years) no dosage adjustment is necessary.

Paediatric population:

The safety and efficacy of Vaniqa in children aged 0 to 18 years has not been established. There is no data available to support use in this age group.

Hepatic/renal impairment: the safety and efficacy of Vaniqa in women with hepatic or renal impairment have not been established. As the safety of Vaniqa has not been studied in patients with severe renal impairment, caution should be used when prescribing Vaniqa for these patients. No data are available.

Method of administration

A thin layer of the cream should be applied to clean and dry affected areas. The cream should be rubbed in thoroughly. The medicinal product should be applied such that no visual residual product remains on the treated areas after rub-in. Hands should be washed after applying this medicinal product. For maximal efficacy, the treated area should not be cleansed within four hours of application. Cosmetics (including sunscreens) can be applied over the treated areas, but no sooner than five minutes after application.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Excessive hair growth can result from serious underlying disorders (e.g. polycystic ovary syndrome, androgen secreting neoplasm) or certain active substances (e.g. cyclosporin, glucocorticoids, minoxidil, phenobarbitone, phenytoin, combined oestrogen-androgen hormone replacement therapy). These factors should be considered in the overall medical treatment of patients who might be prescribed Vaniqa.

Vaniqa is for cutaneous use only. Contact with eyes or mucous membranes (e.g. nose or mouth) should be avoided. Transient stinging or burning may occur when the cream is applied to abraded or broken skin.

If skin irritation or intolerance develops, the frequency of application should be reduced temporarily to once a day. If irritation continues, treatment should be discontinued and the physician consulted.

This medicinal product contains cetostearyl alcohol and stearyl alcohol which may cause local skin reactions (e.g. contact dermatitis) as well as methyl parahydroxybenzoate and propyl parahydroxybenzoate which may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

Throughout clinical trials data from a limited number of exposed pregnancies (22) indicate that there is no clinical evidence that treatment with Vaniqa adversely affects mothers or foetuses. Among the 22 pregnancies that occurred during the trials, only 19 pregnancies occurred while the patient was using Vaniqa. Of these 19 pregnancies, there were 9 healthy infants, 5 elective abortions, 4 spontaneous abortions and 1 birth defect (Down's Syndrome to a 35 year old). To date, no other relevant epidemiological data are available. Animal studies have shown reproductive toxicity (see section 5.3). The potential risk to humans is unknown. Therefore, women who are pregnant or planning pregnancy should use an alternative means to manage facial hair.

Breast-feeding

It is not known whether eflornithine/metabolites are excreted in human milk. Women should not use Vaniqa whilst breastfeeding.

Fertility

There are no data available.

4.7 Effects on ability to drive and use machines

Vaniqa has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The mostly skin related adverse reactions reported were primarily mild in intensity and resolved without discontinuation of Vaniqa or initiation of medical treatment. The most frequently reported adverse reaction was acne, which was generally mild. In the vehicle-controlled trials (n= 596), acne was observed in 41% of patients at baseline; 7% of patients treated with Vaniqa and 8% treated with vehicle experienced a worsening of their condition. Of those with no acne at baseline, similar percentages (14%) reported acne following treatment with Vaniqa or vehicle.
The following listing notes the frequency of adverse skin reactions seen in clinical trials, according to MedDRA convention. MedDRA conventions for frequency are very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), or not known (cannot be estimated from the available data) including isolated reports. Note that over 1350 patients were treated with Vaniqa in these trials for 6 months to one year, while only slightly more than 200 patients were treated with vehicle for 6 months. Most events were reported at similar rates between Vaniqa and vehicle. The skin effects of burning, stinging, tingling, rash and erythema were reported at higher levels in Vaniqa treated patients compared to vehicle, as indicated by the asterisk (*).

Frequency of adverse skin reactions seen in Vaniqa clinical trials, (according to MedDRA frequency convention).

Skin and subcutaneous tissue disorders

Very common (≥1/10)	Acne
Common (≥1/100 to <1/10)	Pseudofolliculitis barbae, alopecia, stinging skin*, burning skin*, dry skin, pruritus, erythema*, tingling skin*, irritated skin, rash*, folliculitis
Uncommon (≥1/1,000 to <1/100)	Ingrown hair, oedema face, dermatitis, oedema mouth, papular rash, bleeding skin, herpes simplex, eczema, cheilitis, furunculosis, contact dermatitis, abnormal hair texture and abnormal hair growth, hypopigmentation, flushing skin, lip numbness, skin soreness
Rare (≥1/10,000 to <1/1,000)	Rosacea, seborrheic dermatitis, skin neoplasm, maculopapular rash, skin cysts, vesiculobullous rash, skin disorder, hirsutism, skin tightness

Paediatric population
The adverse reactions observed in adolescents are similar to the ones observed in adults.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Given the minimal cutaneous penetration of eflornithine (see section 5.2), overdose is highly unlikely. However, should very high dose cutaneous administration or accidental oral ingestion occur, attention should be paid to the effects seen with therapeutic doses of intravenous eflornithine (400 mg/kg/day or approximately 24 g/day) used in the treatment of *Trypanosoma brucei gambiense* infection (African sleeping sickness): hair loss, facial swelling, seizures, hearing impairment, gastrointestinal disturbance, loss of appetite, headache, weakness, dizziness, anaemia, thrombocytopenia and leucopenia.

If symptoms of overdose occur the use of the medicinal product should be stopped.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: other dermatological preparations, ATC code: D11AX16.

Mechanism of action

Eflornithine irreversibly inhibits ornithine decarboxylase, an enzyme involved in the production of the hair shaft by the hair follicle. Vaniqa has been shown to reduce the rate of hair growth.

Clinical efficacy and safety

The safety and efficacy of Vaniqa was evaluated in two double-blind, randomised, vehicle-controlled clinical trials involving 596 women of skin types I-VI (395 on Vaniqa, 201 on vehicle) treated for up to 24 weeks. Physicians assessed the change from baseline on a 4-point scale, 48 hours after women had shaved the treated areas of the affected areas of the face and under the chin, considering parameters such as hair length and density, and darkening of the skin associated with the presence of terminal hair. Improvement was seen as early as 8 weeks after initiation of treatment.

The combined results of these two trials are presented below:

Outcome*	Vaniqa 11.5% cream	Vehicle
Clear / almost clear	6%	0%
Marked improvement	29%	9%
Improved	35%	33%
No improvement / worse	30%	58%

* At end of therapy (Week 24). For patients who discontinued therapy during the trial last observations were carried forward to Week 24.

Statistically significant ($p \leq 0.001$) improvement for Vaniqa versus vehicle was seen in each of these studies for women with marked improvement and clear/almost clear responses. These improvements resulted in a corresponding reduction in the darkening appearance of the facial skin associated with the presence of terminal hair. Subgroup analysis revealed a difference in treatment success where 27% of non-white women and 39% of white women showed a marked or better improvement. Subgroup analysis also showed that 29% of obese women (BMI ≥ 30) and 43% of normal weight women (BMI < 30) showed a marked or better improvement. About 12% of women in the clinical trials were postmenopausal. Significant improvement ($p < 0.001$) versus vehicle was seen in postmenopausal women.

Patient self-assessments demonstrated a significantly reduced psychological discomfort with the condition, as measured by responses to 6 questions on a visual analogue scale. Vaniqa significantly reduced how bothered patients felt by their facial hair and by the time spent removing, treating, or concealing facial hair. Patient comfort in various social and work settings was also improved. Patient self-assessments were found to correlate with physician observations of efficacy. These patient-observable differences were seen 8 weeks after initiating treatment.

The condition returned to pre-treatment levels within eight weeks after discontinuation of treatment.

5.2 Pharmacokinetic properties

Steady state cutaneous penetration of eflornithine in women from Vaniqa on facial skin of shaving women was 0.8%.

The steady state plasma half-life of eflornithine was approximately 8 hours. Steady state was reached within four days. The steady state peak and trough plasma concentrations of eflornithine were approximately 10 ng/ml and 5 ng/ml, respectively. The steady state 12-hour area under the plasma concentration versus time curve was 92.5 ng.hr/ml.

Eflornithine is not known to be metabolised and is eliminated primarily in the urine.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeat dose toxicity, genotoxicity and carcinogenic potential, including one photocarcinogenicity study in mice.

In a dermal fertility study in rats, no adverse effects on fertility were observed at up to 180 times the human dose. In dermal teratology studies, no teratogenic effects were observed in rats and rabbits at doses up to 180 and 36 times the human dose, respectively. Higher doses resulted in maternal and foetal toxicity without evidence of teratogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetostearyl alcohol;

Macrogol cetostearyl ether;

Dimeticone;

Glyceryl stearate;

Macrogol stearate;

Methyl parahydroxybenzoate (E218);

Liquid paraffin;

Phenoxyethanol;

Propyl parahydroxybenzoate (E216);

Purified water;

Stearyl alcohol;

Sodium hydroxide (E524) (to adjust pH)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

Shelf-life after first opening: 6 months.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

High density polyethylene tube with a polypropylene screw cap containing 15 g, 30 g or 60 g of cream. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Almirall, S.A.
Ronda General Mitre, 151,
08022 Barcelona,
Spain.

8 MARKETING AUTHORISATION NUMBER(S)

PLGB 16973/0041

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/01/2021

10 DATE OF REVISION OF THE TEXT

04/05/2022