SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
BUTEFİN 1% topical spray, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1 ml solution contains;

Active substance:
Butenafine hydrochloride 10 mg

Excipients:
Propylene glycol 343,33 mg/ml
Methyl paraben (E218) 1 mg/ml
Propyl paraben (E216) 0,5 mg/ml

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Solution
Clear, colorless, odorless solution

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
BUTEFİN is indicated for the topical treatment of tinea (pityriasis) versicolor, tinea corporis dermatological infections caused by *M. furfur* (formerly *P. orbiculare*) and tinea cruris dermatological infections caused by *E. floccosum, T.mentagrophytes, T. rubrum* and *T. tonsurans*.

4.2. Posology and method of administration
Posology/frequency of administration and duration of the treatment:
Use in adults:
Patients with tinea (pityriasis) versicolor, tinea corporis, or tinea cruris should apply BUTEFİN once daily for two weeks.

If there is no clinical improvement after the treatment period, the diagnosis and treatment should be reviewed.

Method of Administration:
Adequate amounts of BUTEFİN should be applied to cover the affected area of patients and its immediate surroundings. It is suitable for use on hairy body areas.

Additional information for special populations
Renal/Hepatic Failure:
There is no additional information on use in patients with renal/hepatic failure.

Pediatric population:
Safety and efficacy in pediatric patients under 12 years of age have not been studied as tinea versicolor is not common in patients younger than 12 years of age.

Geriatric population:

There is no special situation regarding the use of BUTEFİN in elderly patients.

4.3. Contraindications
BUTEFİN is contraindicated in people with known or suspected sensitivity to butenafine hydrochloride or any of its ingredients.

It should not be used concurrently with other topical creams or sprays.

It should not be used in children under 12 years of age.

4.4. Special warnings and precautions for use
If irritation or sensitivity develops during use, treatment should be discontinued and appropriate therapy instituted.

The diagnosis of the disease was made by culture in a suitable medium [except *M. furfur* (formerly *P. orbiculare*)] or by direct microscopy of infected superficial epidermal tissue in potassium hydroxide solution.

Patients known to be sensitive to allylamine antifungal agents should use BUTEFİN with caution as cross-reactivity may occur.

BUTEFİN should not come into contact with the eyes or mucous membranes; in case of accidental contact, it should be washed immediately with water.

It is suitable for use on hairy body areas.

The product should never be taken orally. Hands should be washed after applying the product.

Propylene glycol contained in BUTEFİN may cause skin irritation.

Methyl paraben and propyl paraben contained in BUTEFİN may cause allergic reactions (possibly delayed).

4.5. Interactions with other medicinal products and other forms of interaction
There are no known or expected interactions of BUTEFİN with other medicinal products via topical application.

Additional information for special populations:
No interaction studies have been conducted in special populations.

Pediatric population:
No interaction studies have been conducted in the pediatric population.

4.6. Fertility, pregnancy and lactation
General advice:
Pregnancy category: C

Pregnant and lactating mothers can use it under the supervision of a doctor. It should be used in pregnant women after risk/benefit assessment by the doctor.

Women of childbearing potential/Birth control (contraception)
The effect of BUTEFİN on childbearing potential and contraceptive methods is unknown.

Pregnancy
Subcutaneous doses of butenafine (dose levels up to 25 mg/kg/day administered during organogenesis) (equivalent to 0.5 times the maximum recommended human dose for tinea versicolor based on body surface area comparisons) were not teratogenic in rats. In an oral embryofoetal development study in rabbits (dose levels up to 400 mg butenafine HCl/kg/day administered during organogenesis) (equivalent to 16 times the maximum recommended human dose for tinea versicolor based on body surface area comparisons), no treatment-related external, visceral, skeletal malformations or changes were observed.

In an oral peri- and post-natal development study in rats (dose levels up to 125 mg butenafine HCl/kg/day) (equivalent to 2.5 times the maximum recommended human dose for tinea versicolor based on body surface area comparisons), no treatment-related effects on postnatal survival, F1 generation (first generation) development or subsequent maturation, and fertility were observed..

Animal studies are insufficient with respect to pregnancy / and-or / embryonal / fetal growth / and-or /natal / and-or / postnatal development (see section 5.3). Potential risk is not known for human.

BUTEFİN should not be used during pregnancy unless necessary.

Lactation
It is not known whether butenafine is excreted in human milk. The excretion of butenafine in breast milk has not been studied in animals. The benefit of breastfeeding for the child and the benefit of BUTEFİN therapy for the nursing mother should be taken into account when deciding whether to discontinue breast-feeding or to discontinue/avoid BUTEFİN therapy.

Reproductive ability/Fertility
No information is available on the effect on fertility.

4.7. Effects on ability to drive and use machines
No studies on the effects of BUTEFİN on the ability to drive and use machines have been conducted.

4.8. Undesirable effects
The undesirable effects specified are classified according to the following rule:
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); not known (cannot be estimated from the available data).

Skin and subcutaneous tissue disorders:
Common: Burning/stinging, itching, worsening of condition, contact dermatitis, erythema, irritation.

4.9. Overdose and treatment
Overdose is not expected as a result of topical application of BUTEFİN.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Other Topical Antifungals

ATC Code: D01AE23

Butenafine HCl is a benzylamine derivative and its mode of action is similar to allylamine class antifungal drugs. Butenafine HCl is hypothesized to act by inhibiting the epoxidation of squalene and thereby blocking the biosynthesis of ergosterol, an essential component in fungal cell membranes. Benzylamine derivatives, like allylamines, play a role in earlier steps of the ergosterol biosynthesis pathway than the azole class of antifungal drugs. Depending on the drug concentration and the fungal species tested, butenafine HCl may be fungicidal or fungistatic in vitro. However, the clinical significance of these in vitro data is unknown.

Butenafine hydrochloride has been shown to be effective against many strains of the following microorganisms, both in vitro and in clinical infections.

Epidermophyton floccosum

Trichophyton rubrum

Malassezia furfur

Trichophyton tonsurans

Trichophyton mentagrophytes

5.2. Pharmacokinetic properties
General characteristics
Absorption:
Topically applied Butenafine HCl is absorbed in humans in very small amounts, therefore no systemic effects are expected.

Distribution:
The total amount (or percent dose) of butenafine HCl absorbed from the skin into the systemic circulation could not be measured.

Biotransformation:
It was determined that the primary metabolite in urine is formed by hydroxylation in the terminal t-butyl side chain.

Elimination:
It was determined that the primary metabolite in urine is formed by hydroxylation in the terminal t-butyl side chain.

5.3. Preclinical safety data
In the data presentations below, patients with tinea (pityriasis) versicolor were examined. The term **"Negative Mycology"** was defined as the absence of hyphae in KOH preparations prepared from skin rashes, that is, the absence of any fungal forms or the presence of only yeast cells (blastospores). The term **"Effective Treatment"** was defined as a total signs and symptoms score of 1 or less (on a scale of zero to three) for Negative Mycology plus erythema, flaking, and pruritus at 8 weeks. The term **"Complete Cure"** was defined as Negative Mycology plus a sign/symptom score of zero for erythema, flaking, and pruritus.

Two separate studies compared vehicle with 1% butenafine hydrochloride cream applied once daily for 2 weeks for the treatment of tinea (pityriasis) versicolor. Patients were treated for 2 weeks and evaluated at 2 (Week 4) and 6 (Week 8) weeks post-treatment. All subjects with positive baseline KOH and drug delivery were included in the "intent to treat" analysis as shown in the table below. Statistical significance for Effective Treatment (cream and vehicle containing

1% butenafine hydrochloride) was achieved in Study 31, but not for Complete Cure 6 weeks post-treatment. In Study 32, marginal statistical significance (p=0.051) (cream and vehicle containing 1% butenafine hydrochloride) was achieved for Effective Treatment, but not for Complete Cure at 6 weeks post-treatment. Data from these two controlled studies are presented in the table below.

Responders (%) in pivotal clinical trials (all randomized patients)

Patient Response Category	Week@	Study 31		Study 32	
		Butenafine	**Vehicle**	**Butenafine**	**Vehicle**
Complete Cure*	2	41/87 (47%)	11/40 (28%)	29/85 (34%)	12/41 (29%)
	4	43/86 (50%)	15/42 (36%)	36/83 (43%)	13/41 (32%)
	8	44/87 (51%)	15/42 (36%)	30/86 (35%)	10/43 (23%)
Effective Treatment **	2	56/87 (64%)	16/40 (40%)	46/85 (54%)	16/41 (39%)
	4	50/86 (58%)	19/42 (45%)	45/83 (54%)	16/41 (39%)
	8	48/87 (55%)	15/42 (36%)	37/86 (43%)	11/43 (26%)
Negative Mycology ***	2	57/87 (66%)	20/40 (50%)	57/85 (67%)	21/41 (51%)
	4	51/86 (59%)	20/42 (48%)	52/83 (63%)	18/41 (44%)
	8	48/87 (55%)	15/42 (36%)	43/86 (50%)	12/43 (28%)

@ Week 2 (end of treatment), Week 4 (2 weeks after treatment), and Week 8 (6 weeks post treatment)

* Negative Mycology plus absence of erythema, flaking and pruritus
** Negative Mycology plus no or minimal erythema, flaking and pruritus
*** the absence of hyphae in KOH preparations prepared from skin rashes, that is, the absence of any fungal forms or the presence of only yeast cells (blastospores).

Tinea (pityriasis) versicolor is a superficial, chronically recurrent infection of hairless skin caused by *Malassezia furfur* (formerly *Pityrosporum orbiculare*). The commensal organism is part of the normal skin flora. In susceptible individuals, the disease may cause hyperpigmented or hypopigmented patches on the body, which may spread to the neck, arms, and upper thighs.

Treatment of the infection may not immediately improve the pigmentation of the affected areas. After successful treatment, the normalization of pigments may vary depending on the individual's skin type and accidental sun exposure and may take months. The recurrence rate of the infection can vary.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Propylene glycol
Diethylene glycol monoethyl ether
Methyl paraben (E218)
Propyl paraben (E216)
Purified water

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months

6.4. Special precautions for storage
Store at room temperature below 25 °C.

6.5. Nature and contents of container
The primary packaging material is presented in an amber glass bottle (Type III) with PE capillary tube and PP spray cap immersed in the bottle, in packages containing 15 ml and 30 ml solution.

7. MARKETING AUTHORIZATION HOLDER
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8. MARKETING AUTHORIZATION NUMBER(S)
2017/755

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION
Date of the first authorization: 29.09.2017
Date of the renewal of the authorization: -

10. DATE OF REVISION OF THE TEXT
23.05.2019