

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Ulesfia Lotion safely and effectively. See full prescribing information for Ulesfia Lotion.

Ulesfia (benzyl alcohol) Lotion

For topical use only

Initial U.S. Approval: 2009

INDICATIONS AND USAGE

Ulesfia Lotion is a pediculocide indicated for the topical treatment of head lice infestation in patients 6 months of age and older. (1.1)

Ulesfia Lotion does not have ovocidal activity. (1.2)

DOSAGE AND ADMINISTRATION

- Apply Ulesfia Lotion to dry hair, using enough to completely saturate the scalp and hair. (2)
- Rinse off with water after 10 minutes. (2)
- Repeat treatment in 7 days. (2)

Table 1: Ulesfia Lotion Usage Guideline

| Hair Length | | Amount of Ulesfia Lotion per Application |
|-------------|----------------|--|
| Short | 0-2 inches | 4-6 oz. (1/2-3/4 bottle) |
| | 2-4 inches | 6-8 oz (3/4-1 bottle) |
| Medium | 4-8 inches | 8-12 oz (1 – 1 ½ bottles) |
| | 8-16 inches | 12-24 oz (1 ½-3 bottles) |
| Long | 16-22 inches | 24-32 oz (3-4 bottles) |
| | Over 22 inches | 32-48 oz (4-6 bottles) |

DOSAGE FORMS AND STRENGTH

Ulesfia Lotion, 5% in 8 oz. bottles (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Neonatal toxicity: Risk of gasping syndrome if benzyl alcohol is used in neonates. (5.1)
- Eye irritation: Avoid eye exposure. Flush immediately with water if Ulesfia Lotion comes into contact with eyes. (5.2)
- Contact dermatitis: May occur with Ulesfia Lotion. (5.3)
- Use in children: Ulesfia Lotion should only be used on children under the direct supervision of an adult. Keep out of reach of children. (5.4)

ADVERSE REACTIONS

Most common adverse reactions (> 1% and more common than with placebo): ocular irritation, application site irritation, and application site anesthesia and hypoesthesia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Sciele Pharma, Inc. Drug Safety at 1-800-849-9707 ext. 1454 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Drug interaction studies were not conducted. (7)

USE IN SPECIFIC POPULATIONS

Pediatric Use: Safety in pediatric patients under six months of age has not been established. (8.4)

See Section 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised 06/2010

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Indication

Ulesfia Lotion is indicated for the topical treatment of head lice infestation in patients 6 months of age and older.

1.2 Limitation of Use

Ulesfia Lotion does not have ovocidal activity.

1.3 Adjunctive Measures

Ulesfia Lotion should be used in the context of an overall lice management program:

- Wash (in hot water) or dry-clean all recently worn clothing, hats, used bedding, and towels.
- Wash personal care items such as combs, brushes and hair clips in hot water.
- A fine-tooth comb or special nit comb may be used to remove dead lice and nits.

2 DOSAGE AND ADMINISTRATION

Ulesfia Lotion is not for oral, ophthalmic, or intravaginal use.

Using the guidelines in Table 1, apply sufficient Ulesfia Lotion to dry hair to completely saturate the scalp and hair; leave on for 10 minutes, then thoroughly rinse off with water. Repeat treatment after 7 days. Avoid contact with eyes.

Table 1: Ulesfia Lotion Usage Guideline

| Hair Length | | Amount of Ulesfia Lotion per Application |
|-------------|----------------|--|
| Short | 0-2 inches | 4-6 oz (1/2-3/4 bottle) |
| | 2-4 inches | 6-8 oz (3/4-1 bottle) |
| Medium | 4-8 inches | 8-12 oz (1 – 1 ½ bottles) |
| | 8-16 inches | 12-24 oz (1 ½-3 bottles) |
| Long | 16-22 inches | 24-32 oz (3-4 bottles) |
| | Over 22 inches | 32-48 oz (4-6 bottles) |

3 DOSAGE FORM AND STRENGTH

Ulesfia Lotion contains 5% benzyl alcohol and is supplied in 8 ounce polypropylene bottles.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Neonatal Toxicity

Intravenous administration of products containing benzyl alcohol has been associated with neonatal gasping syndrome consisting of severe metabolic acidosis, gasping respirations, progressive hypotension, seizures, central nervous system depression, intraventricular hemorrhage, and death in preterm, low birth weight infants. Neonates (i.e. patients less than 1 month of age or preterm infants with a corrected age of less than 44 weeks) could be at risk for gasping syndrome if treated with Ulesfia Lotion [see Use in Specific Populations (8.4)].

5.2 Eye Irritation

Avoid eye exposure. Ulesfia Lotion may cause eye irritation. If Ulesfia Lotion comes in contact with the eyes, flush them immediately with water. If irritation persists, consult a physician.

5.3 Contact Dermatitis

Ulesfia Lotion may cause allergic or irritant dermatitis.

5.4 Use in Children

Ulesfia Lotion should only be used on children (6 months of age and older) under the direct supervision of an adult. Keep out of reach of children.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

The rates of adverse reactions below were derived from two randomized, multi-center, vehicle-controlled clinical trials and one open-label study in subjects with head lice infestation.

Skin, scalp, and ocular irritation were monitored in the clinical trials. All subjects were queried about the presence of skin and scalp symptoms; the results are presented in Table 2.

Table 2: Monitored Adverse Reactions - Application Site Symptoms

| Event | Ulesfia Lotion | Vehicle |
|--|----------------|------------|
| Application site Irritation | 2% (11/478) | 1% (2/336) |
| Application site anesthesia & hypoesthesia | 2% (10/478) | 0% (0/336) |
| Pain | 1% (5/478) | 0% (1/336) |

The subset of subjects who did not have pruritus, erythema, edema or pyoderma of skin and scalp, or ocular irritation prior to treatment were assessed for these signs and symptoms after treatment; the results are presented in Table 3.

Table 3: Monitored Adverse Reactions - Pruritus, Erythema, Pyoderma and Ocular Irritation with Onset After Treatment

| Signs/Symptoms | Ulesfia Lotion | Vehicle |
|-------------------|----------------|-------------|
| Pruritus | 12% (14/116) | 4% (3/67) |
| Erythema | 10% (32/309) | 9% (19/217) |
| Pyoderma | 7% (22/308) | 4% (10/230) |
| Ocular irritation | 6% (26/428) | 1% (3/313) |

Other less common reactions (less than 1% but more than 0.1%) were, in decreasing order of incidence: application site dryness, application site excoriation, paraesthesia, application site dermatitis, excoriation, thermal burn, dandruff, erythema, rash, and skin exfoliation.

7 DRUG INTERACTIONS

Drug interaction studies were not conducted with Ulesfia Lotion.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B

There are no adequate and well-controlled studies with topical benzyl alcohol in pregnant women. Reproduction studies conducted in rats and rabbits were negative. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

No comparisons of animal exposure with human exposure are provided in this labeling due to the low systemic exposure noted in the clinical pharmacokinetic

study [see *Clinical Pharmacology (12.3)*] which did not allow for the determination of human AUC values that could be used for this calculation.

Pregnant rats were dosed with benzyl alcohol via subcutaneous injection at 100, 250, and 500 mg/kg/day. No teratogenic effects were noted at any dose. Maternal toxicity and decreased fetal weight occurred at 500 mg/kg/day. When pregnant rabbits received subcutaneous injections of benzyl alcohol at 100, 250, and 400 mg/kg/day, there were no teratogenic effects in offspring at any dose. In rabbits, maternal toxicity occurred at the two higher doses and was associated with decreased fetal weight at the highest dose.

8.3 Nursing Mothers

It is not known whether benzyl alcohol is excreted into human milk. Because some systemic absorption of topical benzyl alcohol may occur and because many drugs are excreted in human milk, caution should be exercised when Ulesfia Lotion is administered to a nursing woman.

8.4 Pediatric Use

The safety and effectiveness of Ulesfia Lotion was evaluated in two multicenter, randomized, double-blind, vehicle-controlled studies which were conducted in 628 subjects 6 months of age and older with active head lice infestation [see *Clinical Studies (14)*].

Rates of adverse events in younger children (6 months to 12 years) were similar to those of older children and adults.

Safety in pediatric patients below the age of 6 months has not been established. Ulesfia Lotion is not recommended in pediatric patients under six months of age because of the potential for increased systemic absorption due to a high ratio of skin surface area to body mass and the potential for an immature skin barrier.

Neonates could be at risk for gasping syndrome if treated with Ulesfia Lotion [see *Warnings and Precautions (5.1)*].

Intravenous administration of products containing benzyl alcohol has been associated with neonatal gasping syndrome. The gasping syndrome (characterized by central nervous depression, metabolic acidosis, gasping respirations, and high levels of benzyl alcohol and its metabolites found in the blood and urine) has been associated with benzyl alcohol dosages > 99 mg/kg/day in preterm neonates. Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. Although expected systemic exposure of benzyl alcohol from proper use of Ulesfia Lotion is substantially lower than those reported in association with the gasping syndrome, the minimum amount of benzyl alcohol at which toxicity may occur is not known.

8.5 Geriatric Use

The safety of Ulesfia Lotion in patients over 60 years of age has not been established.

10 OVERDOSAGE

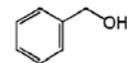
If oral ingestion occurs, seek medical advice immediately.

11 DESCRIPTION

Ulesfia Lotion is supplied as a white topical lotion containing benzyl alcohol, 5%. Inactive ingredients in this formulation are water, mineral oil, sorbitan monooleate, polysorbate 80, carbomer 934P and trolamine.

The active ingredient, benzyl alcohol, is a clear, colorless liquid with a mild aromatic odor. Benzyl alcohol has a molecular mass of 108.14 g/mol. The molecular formula is C₇H₈O.

The chemical structure of benzyl alcohol is



Benzyl Alcohol

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

In vitro studies of the effect of Ulesfia Lotion on native, captured lice suggest that benzyl alcohol inhibits lice from closing their respiratory spiracles, allowing the vehicle to obstruct the spiracles and causing the lice to asphyxiate.

12.3 Pharmacokinetics

The absorption of benzyl alcohol from Ulesfia Lotion was evaluated in 19 subjects with head lice infestation. Subjects were divided into two age groups: 6 months to 3 years and 4 to 11 years. Ulesfia Lotion was applied for an exaggerated exposure period (3 times the normal exposure period). Benzyl alcohol was quantified in a single plasma sample in 4 out of 19 subjects (21%); three subjects in the 6 months to 3 years age group at 0.5 hour post-treatment (ranging from 1.97 to 2.99 mcg/mL) and one subject in the 4 to 11 year age group (1.63 mcg/mL) at 1 hour post-treatment out of a total of 102 samples analyzed.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential of Ulesfia Lotion have not been conducted. No evidence of carcinogenic activity was noted for benzyl alcohol in 2 year oral carcinogenicity studies in rats (doses up to 400 mg/kg benzyl alcohol) or mice (doses up to 200 mg/kg benzyl alcohol) conducted by the National Toxicology Program.

Benzyl alcohol has produced mixed results in genetic testing. Benzyl alcohol was negative in the Ames test with and without metabolic activation, sex-linked recessive lethal assay, and a replicative DNA synthesis assay (conducted in male rats). Negative results were obtained in the mouse lymphoma assay with metabolic activation, but a positive response was noted in the mouse lymphoma assay without metabolic activation at a concentration producing a high level of cellular toxicity. Benzyl alcohol was positive in the Chinese hamster ovary chromosomal aberration assay with metabolic activation.

No fertility studies have been conducted with benzyl alcohol.

14 CLINICAL STUDIES

Two multicenter, randomized, double-blind, vehicle-controlled studies were conducted in 628 subjects 6 months of age and older with active head lice infestation. For the evaluation of efficacy, the youngest subject from each household was enrolled in the Primary Treatment Cohort with Ulesfia Lotion or vehicle. Other infested household members were enrolled in a Secondary Treatment Cohort and received the same treatment as the youngest subjects. The Secondary Treatment Cohort was not included in the efficacy analysis, but was evaluated for all safety parameters.

In Study One, 125 Primary Treatment Cohort Subjects were randomized to Ulesfia Lotion (N=63) and vehicle (N=62). Study Two enrolled 125 Primary Treatment Cohort Subjects: 64 randomized to Ulesfia Lotion and 61 to vehicle. Treatment was applied two times separated by one week.

Efficacy was assessed as the proportion of subjects who were free of live lice 14 days after the final treatment. Subjects with live lice present at any time after first treatment were considered to be treatment failures. Table 4 contains the proportion of subjects who were free of live lice in each of the two trials.

Table 4: Proportion of Subjects Free of Live Lice 14 Days After Last Treatment

| | Ulesfia LOTION | Vehicle |
|---------|----------------------|----------------------|
| Study 1 | (N=63) 48 (76.2%) | (N=62) 3 (4.8%) |
| Study 2 | (N=64) 48 (75.0%) | (N=61) 16 (26.2%) |

16 HOW SUPPLIED/STORAGE AND HANDLING

Ulesfia Lotion 5% is supplied as 8 fl oz (227 g) polypropylene bottles (NDC 59630-780-08). Store at 20° - 25° C (68° - 77° F); excursions permitted to 15° - 30° C (59° - 86° F) [See USP controlled room temperature].

Do not freeze. Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

See 17.3 for FDA-approved patient labeling.

17.1 Instructions to Patients

This medication is to be used as directed by the physician. Use only on scalp and scalp hair. Avoid contact with eyes. As with any topical medication, patients should wash hands after application.

Instruct patients on proper use of Ulesfia Lotion, including the amount to apply, how long to leave it on the hair, and the importance of a second treatment 1 week (7 days) after the initial application.

17.2 Adverse Reactions

Inform patients that Ulesfia Lotion may cause eye irritation, skin irritation, and contact sensitization.

Instruct patients to inform a physician if the area of the application shows signs of irritation and any signs of adverse reactions.

17.3 FDA-Approved Patient Labeling

Patient Information

Ulesfia (Yoo-Les-fee-ah) (benzyl alcohol 5%) Lotion

Read the Patient Information that comes with Ulesfia Lotion before you start using it and each time you get a refill. There may be new information. This leaflet does not take the place of talking to your healthcare provider about your medical condition or treatment.

Note: For use on scalp hair and scalp only

What is Ulesfia Lotion?

Ulesfia Lotion is a prescription medicine used to get rid of lice in scalp hair of children and adults. It is not known if Ulesfia Lotion is safe for children under 6 months of age or in people over age 60.

Once Ulesfia Lotion is washed off, a fine-tooth comb may be used to remove treated lice and nits from the hair and scalp. All personal items exposed to the hair or lice should be washed in hot water or dry-cleaned. See "How do I stop the spread of lice?" at the end of this leaflet.

What should I tell my healthcare provider before I use Ulesfia Lotion?

Tell your healthcare provider if your baby was born

early so your healthcare provider can decide if your infant is old enough for Ulesfia Lotion.

Tell your healthcare provider about all of your medical conditions, including if you:

- have any skin conditions or sensitivities,
- are pregnant or planning to become pregnant. It is not known if Ulesfia Lotion can harm your unborn baby,
- are breastfeeding. It is not known if Ulesfia Lotion passes into your breast milk or if it can harm your baby. You should choose to breastfeed or use Ulesfia Lotion, but not both. Talk to your healthcare provider about other ways to feed your baby while using Ulesfia Lotion.

How should I use Ulesfia Lotion?

- Use Ulesfia Lotion exactly as prescribed. Your healthcare provider will prescribe the treatment that is right for you. Do not change your treatment unless you talk to your healthcare provider.
- Use Ulesfia Lotion in two applications that are one week apart. Ulesfia Lotion gets rid of lice but does not get rid of lice eggs so a second treatment is needed one week (7 days) after the first treatment.
- Ulesfia Lotion coats the lice on your scalp and scalp hair. It is important to use enough Ulesfia Lotion to coat completely every single louse and to leave it on your scalp for the full 10 minutes. See the detailed Patient Instructions for Use at the end of this leaflet.
- Because you need to completely cover all of the lice with Ulesfia Lotion, you may need help in applying Ulesfia Lotion to your scalp and hair. Make sure that you and anyone who helps you apply Ulesfia Lotion reads and understands this leaflet and the Patient Instructions for Use.
- Children need adult help in applying Ulesfia Lotion.
- Do not get into eyes. If Ulesfia Lotion gets in the eye, flush with water right away.
- Do not swallow Ulesfia Lotion. If swallowed, call your healthcare provider right away.
- Wash your hands after you apply Ulesfia Lotion.

What are the possible side effects of Ulesfia Lotion?

People using Ulesfia Lotion may have skin or eye:

- itching,
- redness,
- irritation. If skin or eye irritation happens, rinse with water right away, then call your healthcare provider or go to the emergency department.

These are not all the side effects of Ulesfia Lotion. For more information, ask your healthcare provider.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Ulesfia Lotion?

- Store Ulesfia Lotion in a dry place at room temperature, (59 °to 86° F or 15°to 30° C).
- Do not freeze Ulesfia Lotion.

Keep Ulesfia Lotion and all medicines out of the reach of children.

What are the ingredients in Ulesfia Lotion?

Active ingredient: benzyl alcohol, 5%
Inactive ingredients: purified water, mineral oil, sorbitan monooleate, polysorbate 80, carbomer 934P and trolamine

General Information about Ulesfia Lotion

Medicines are sometimes prescribed for conditions other than those described in the patient information leaflets. Do not use Ulesfia Lotion for any condition for which it was not prescribed by your healthcare provider. Do not give Ulesfia Lotion to other people, even if they have the same symptoms as you. It may harm them.

This leaflet summarizes the most important information about Ulesfia Lotion. If you would like more information, talk to your healthcare provider. You can also ask your healthcare provider for information about Ulesfia Lotion that is written for healthcare professionals.

Patient Instructions for Use

Apply the full amount of Ulesfia Lotion prescribed by your healthcare provider for each of your 2 treatments one week apart. Ulesfia Lotion gets rid of lice but does not get rid of lice eggs so a second treatment is needed one week (7 days) after the first treatment.

For different hair lengths, use the following as a guide for the amount of Ulesfia Lotion you may need to cover the hair and scalp completely.

| Hair Length | Amount of Ulesfia Lotion to apply each time |
|-------------------------|---|
| Short- up to 2 inches | up to ¼ the bottle |
| Short- 2-4 inches | up to 1 bottle |
| Medium- 4-8 inches | up to 1 ½ bottle |
| Medium- 8-16 inches | up to 3 bottles |
| Long- 16-22 inches | up to 4 bottles |
| Long- 22 inches or more | up to 6 bottles |

Step 1



- Cover your face and eyes with a towel and keep your eyes closed tightly.
- Apply Ulesfia Lotion directly to dry hair.
- Ulesfia Lotion must cover your entire scalp and all scalp hair. Have an adult help you apply Ulesfia Lotion.

Step 2



- Massage Ulesfia Lotion into your hair and scalp.
- When your head is completely covered with enough Ulesfia Lotion, *dripping* will happen. Protect your eyes and skin from these drips with your towel.



- Be sure to apply Ulesfia Lotion to the area behind your ears



- Be sure to apply Ulesfia Lotion to the back of your neck.

If not enough Ulesfia Lotion is used, some lice may escape treatment. It is important to use the full amount of Ulesfia Lotion prescribed by your doctor.



Correct application of Ulesfia Lotion

Step 3



- Allow Ulesfia Lotion to stay on your hair for 10 minutes. Use a timer or clock.
- Start timing after you have completely

covered your hair and scalp with Ulesfia Lotion.

Step 4



- After 10 minutes, completely rinse Ulesfia Lotion from your hair and scalp with water.
- You or anyone who helps you apply Ulesfia Lotion should wash your hands after application.
- You can shampoo your hair right after the treatment.
- A lice comb may be used to remove the dead lice after both treatments.

Step 5

One week (7 days) after your first treatment, repeat the steps above to help get rid of lice that hatched from eggs.

How do I stop the spread of lice?

To help prevent the spread of lice from one person to another, here are some steps you can take.

- Avoid head-to-head contact at school, on the playground, in physical education classes, during sports activities, and while playing with other children.
- Do not share combs, brushes, hats, scarves, bandannas, ribbons, barrettes, hair bands, towels, helmets, or other hair-related personal items with anyone else, whether they have lice or not.
- Avoid sleepovers and slumber parties during lice outbreaks. Lice can live in bedding, pillows, and carpets that have recently been used by someone with lice.
- After finishing treatment with lice medicine, check everyone in your family for lice after one week. Be sure to talk to your healthcare provider about treatments for those who have lice.
- Machine-wash any bedding and clothing used by anyone having lice or thought to have been exposed to lice. Machine wash at high temperatures (150°F) and tumble in a hot dryer for 20 minutes.

This Patient Leaflet has been approved by the U.S. Food and Drug Administration.

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