

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**202736Orig1s000**

**LABELING**

## HIGHLIGHTS OF PRESCRIBING INFORMATION

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

### SKLICE (ivermectin) Lotion, 0.5%, for topical use

Initial U.S. Approval: 1996

#### INDICATIONS AND USAGE

SKLICE Lotion is a pediculicide indicated for the topical treatment of head lice infestations in patients 6 months of age and older. (1)

#### DOSAGE AND ADMINISTRATION

- For topical use only. Not for oral, ophthalmic or intravaginal use.(2)
- Apply SKLICE Lotion to dry hair in an amount sufficient (up to 1 tube) to thoroughly coat the hair and scalp. (2)
- After 10 minutes, rinse off with water. (2)
- For single use. Discard any unused portion. (2)

#### DOSAGE FORMS AND STRENGTHS

Lotion: 0.5% (3)

#### CONTRAINDICATIONS

None. (4)

#### WARNINGS AND PRECAUTIONS

Accidental ingestion in pediatric patients may occur: Administer only under direct adult supervision. (5.1)

#### ADVERSE REACTIONS

Most common adverse reactions (incidence <1%) are conjunctivitis, ocular hyperemia, eye irritation, dandruff, dry skin, and skin burning sensation.(6)

To report SUSPECTED ADVERSE REACTIONS, contact Sanofi Pasteur, Inc. at 1-800-835-3592 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

#### USE IN SPECIFIC POPULATIONS

Safety and effectiveness in pediatric patients below the age of 6 months have not been established. (8.4)

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

Revised: 02/2012

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\*Sections or subsections omitted from the full prescribing information are not listed.

## **FULL PRESCRIBING INFORMATION**

### **1 INDICATIONS AND USAGE**

#### **1.1 Indication**

SKLICE™ Lotion is indicated for the topical treatment of head lice infestations in patients 6 months of age and older.

#### **1.2 Adjunctive Measures**

SKLICE 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**

For topical use only. SKLICE Lotion is not for oral, ophthalmic, or intravaginal use.

Apply SKLICE Lotion to dry hair in an amount sufficient (up to 1 tube) to thoroughly coat the hair and scalp. Leave SKLICE Lotion on the hair and scalp for 10 minutes, and then rinse off with water.

The tube is intended for single use; discard any unused portion.

Avoid contact with eyes.

### **3 DOSAGE FORMS AND STRENGTHS**

Lotion: 0.5%; each gram of lotion contains 5 mg of ivermectin. SKLICE Lotion is an off-white to tan lotion.

### **4 CONTRAINDICATIONS**

None.

### **5 WARNINGS AND PRECAUTIONS**

#### **5.1 Ingestion in Pediatric Patients**

In order to prevent ingestion, SKLICE Lotion should only be administered to pediatric patients under the direct supervision of an adult.

## **6 ADVERSE REACTIONS**

### **6.1 Clinical Trials Experience**

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

The data described below reflect exposure to a single 10 minute treatment of SKLICE Lotion in 379 patients, ages 6 months and older, in placebo-controlled trials. Of these subjects, 47 subjects were age 6 months to 4 years, 179 subjects were age 4 to 12 years, 56 subjects were age 12 to 16 years and 97 subjects were age 16 or older. Adverse reactions, reported in less than 1% of subjects treated with SKLICE Lotion, include conjunctivitis, ocular hyperemia, eye irritation, dandruff, dry skin, and skin burning sensation.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Pregnancy Category C

There are no adequate and well-controlled studies with SKLICE Lotion in pregnant women. SKLICE Lotion should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

No comparisons of animal exposure with human exposure are provided due to the low systemic exposure noted in the clinical pharmacokinetic study [*see Clinical Pharmacology (12.3)*].

#### Human Data

There are published reports of oral ivermectin use during human pregnancy. In an open label study, 397 women in their second trimester of pregnancy were treated with ivermectin tablets and albendazole at the labeled dose rate for soil-transmitted helminths and compared with a pregnant, non-treated population. No differences in pregnancy outcomes were observed between treated and untreated populations.

#### Animal Data

Systemic embryofetal development studies were conducted in mice, rats and rabbits. Oral doses of 0.1, 0.2, 0.4, 0.8, and 1.6 mg/kg/day ivermectin were administered during the period of organogenesis (gestational days 6–15) to pregnant female mice. Maternal death occurred at 0.4 mg/kg/day and above. Cleft palate occurred in the fetuses from the 0.4, 0.8, and 1.6 mg/kg/day groups. Exencephaly was seen in the fetuses from the 0.8 mg/kg group. Oral doses of 2.5, 5, and 10 mg/kg/day ivermectin were administered during the period of organogenesis (gestational days 6–17) to pregnant female rats. Maternal death and pre-implantation loss occurred at 10 mg/kg/day. Cleft palate and wavy ribs were seen in fetuses from the 10 mg/kg/day group. Oral doses of 1.5, 3, and 6 mg/kg/day ivermectin were administered during the period of organogenesis (gestational days 6–18) to pregnant female rabbits. Maternal toxicity and abortion occurred at 6 mg/kg/day. Cleft palate and clubbed forepaws occurred in the fetuses from the 3

and 6 mg/kg groups. These teratogenic effects were found only at or near doses that were maternally toxic to the pregnant female. Therefore, ivermectin does not appear to be selectively fetotoxic to the developing fetus.

### **8.3 Nursing Mothers**

Following oral administration, ivermectin is excreted in human milk in low concentrations. This has not been evaluated following topical administration. Caution should be exercised when SKLICE Lotion is administered to a nursing woman.

### **8.4 Pediatric Use**

The safety and effectiveness of SKLICE Lotion have been established for pediatric patients 6 months of age and older [*See Clinical Pharmacology (12.3) and Clinical Studies (14.1)*]

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

### **8.5 Geriatric Use**

Clinical studies of SKLICE Lotion did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

## **10 OVERDOSAGE**

In accidental or significant exposure to unknown quantities of veterinary formulations of ivermectin in humans, either by ingestion, inhalation, injection, or exposure to body surfaces, the following adverse effects have been reported most frequently: rash, edema, headache, dizziness, asthenia, nausea, vomiting, and diarrhea. Other adverse effects that have been reported include: seizure, ataxia, dyspnea, abdominal pain, paresthesia, urticaria, and contact dermatitis.

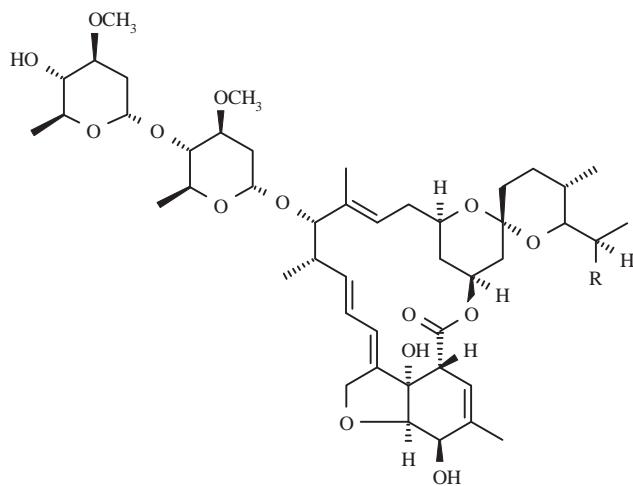
In case of accidental poisoning, supportive therapy, if indicated, should include parenteral fluids and electrolytes, respiratory support (oxygen and mechanical ventilation if necessary) and pressor agents if clinically significant hypotension is present. Induction of emesis and/or gastric lavage as soon as possible, followed by purgatives and other routine anti-poison measures, may be indicated if needed to prevent absorption of ingested material.

## 11 DESCRIPTION

SKLICE (ivermectin) Lotion, for topical administration, is an off-white/tan lotion containing 0.5% ivermectin.

Ivermectin, the active ingredient, is a pediculicide, derived from the fermentation of a soil dwelling actinomycete, *Streptomyces avermitilis*.

Ivermectin is a mixture containing at least 90% 5-*O*-demethyl-22,23-dihydroavermectin A<sub>1a</sub> and less than 10% 5-*O*-demethyl-25-de(1-methylpropyl)-22,23-dihydro-25-(1-methylethyl) avermectin A<sub>1a</sub>, generally referred to as 22,23-dihydroavermectin B<sub>1a</sub> and B<sub>1b</sub>, or H<sub>2</sub>B<sub>1a</sub> and H<sub>2</sub>B<sub>1b</sub>, respectively. The respective empirical formulas are C<sub>48</sub>H<sub>74</sub>O<sub>14</sub> and C<sub>47</sub>H<sub>72</sub>O<sub>14</sub>, with molecular weights of 875.10 and 861.07, respectively. The structural formulas are:



Component H<sub>2</sub>B<sub>1a</sub>: R = CH<sub>2</sub>CH<sub>3</sub> Component H<sub>2</sub>B<sub>1b</sub>: R = CH<sub>3</sub>

SKLICE Lotion contains the following inactive ingredients: water, olive oil, oleyl alcohol, Crodalan AWS, lanolin alcohol, cyclomethicone, shea butter, sodium citrate, sorbitan tristearate, methylparaben, propylparaben, and citric acid.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Ivermectin, a member of the avermectin class, causes death of parasites, primarily through binding selectively and with high affinity to glutamate-gated chloride channels, which occur in invertebrate nerve and muscle cells. This leads to an increase in the permeability of the cell membrane to chloride ions with hyperpolarization of the nerve or muscle cell, resulting in paralysis and death of the parasite. Compounds of this class may also interact with other ligand-gated chloride channels, such as those gated by the neurotransmitter gamma-aminobutyric acid (GABA). The selective activity of compounds of this class is attributable to the fact that some mammals do not have glutamate-gated chloride channels, the avermectins have a low affinity for mammalian ligand-gated chloride channels, and ivermectin does not readily cross the blood-brain barrier in humans.

## **12.2 Pharmacodynamics**

The pharmacodynamics of SKLICE Lotion are unknown.

## **12.3 Pharmacokinetics**

The absorption of ivermectin from SKLICE Lotion was evaluated in a clinical study in subjects aged from 6 months to 3 years. This study evaluated pharmacokinetics in 20 lice infested subjects, and 13 of these subjects weighed 15 kg or less (overall weight range 8.5-23.9 kg). All enrolled subjects received a single treatment with SKLICE Lotion. The systemic ivermectin exposure was evaluated using an assay with a lower limit of quantitation of 0.05 ng/mL. The mean ( $\pm$  standard deviation) plasma maximum concentration (C<sub>max</sub>) and area under the concentration-time curve from 0 to time of last measurable concentration (AUC<sub>0-t<sub>last</sub></sub>) were 0.24  $\pm$  0.23 ng/ml and 6.7  $\pm$  11.2 hr\*ng/ml respectively. These levels are much lower than those observed following oral administration of 165 mcg/kg dose of ivermectin.

# **13 NONCLINICAL TOXICOLOGY**

## **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Long-term studies in animals have not been performed to evaluate the carcinogenic potential of SKLICE Lotion or ivermectin.

Ivermectin was not genotoxic *in vitro* in the Ames test, the mouse lymphoma assay, or the unscheduled DNA synthesis assay in human fibroblasts.

Ivermectin had no adverse effects on fertility in rats at repeated oral doses of up to 3.6 mg/kg/day.

# **14 CLINICAL STUDIES**

Two identical multi-center, randomized, double-blind, vehicle-controlled studies were conducted in subjects 6 months of age and older with head lice infestation. All subjects received a single application of either SKLICE Lotion or vehicle control with instructions not to use a nit comb. For the evaluation of efficacy, the youngest subject from each household was considered to be the index subject of the household (N=289). Other enrolled infested household members received the same treatment as the youngest subject, and were evaluated for all safety parameters [see *Adverse Reactions (6.1)*].

The primary efficacy was assessed as the proportion of index subjects who were free of live lice at day 2 and through day 8 to the final evaluation 14 (+2) days following a single application. Subjects with live lice present at any time up to the final evaluation were considered treatment failures. Table 1 contains the proportion of subjects who were free of live lice in each of the two trials.

**Table 1: Proportion of Subjects Free of Live Lice 14 Days After Treatment**

Study	Vehicle % (n/N)	SKLICE Lotion % (n/N)
Study 1	16.2% (12/74)	76.1% (54/71)
Study 2	18.9% (14/74)	71.4% (50/70)

## 16 HOW SUPPLIED/STORAGE AND HANDLING

SKLICE Lotion, 0.5% is supplied in a 4 oz (117g) laminate tube (NDC 49281-183-71).

Store at room temperature 20°C to 25°C (68°F to 77°F); excursions permitted to 15° to 30° C (59° to 86° F) [See USP controlled room temperature]. Do not freeze.

## 17 PATIENT COUNSELING INFORMATION

“See FDA-approved patient labeling (Patient Information)”.

Inform the patient and caregiver of the following instructions:

- Apply SKLICE Lotion to dry scalp and dry scalp hair.
- Avoid contact with eyes.
- Do not swallow SKLICE Lotion.
- Keep out of reach of children. Use on children should be under the direct supervision of an adult.
- For single use only; do not retreat.
- Discard tube after use.
- Wash hands after applying SKLICE Lotion.

## Patient Information

### **SKLICE™ (sklice) (ivermectin) Lotion, 0.5%**

**Important: For use on scalp hair and scalp only. Do not use SKLICE Lotion in your eyes, mouth or vagina.**

Read the Patient Information that comes with SKLICE Lotion. This leaflet does not take the place of talking to your healthcare provider about your medical condition or treatment.

#### **What is SKLICE Lotion?**

SKLICE Lotion is a prescription medicine for topical use on the hair and scalp only. SKLICE Lotion is used to treat head lice in people 6 months of age and older.

It is not known if SKLICE Lotion is safe and effective for children under 6 months of age.

#### **What should I tell my healthcare provider before using SKLICE Lotion?**

Before using SKLICE Lotion, tell your healthcare provider if you or your child:

- have any skin conditions or sensitivities,
- have any other medical conditions,
- are pregnant or plan to become pregnant. It is not known if SKLICE Lotion can harm your unborn baby, and
- are breastfeeding or plan to breastfeed. It is not known if SKLICE Lotion passes into your breast milk. Talk to your health care provider if you are breastfeeding.

## **How should I use SKLICE Lotion?**

- Use SKLICE 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 SKLICE Lotion when your hair is dry.
- It is important to use enough SKLICE Lotion to completely coat all of your hair and scalp. Leave SKLICE Lotion on your hair and scalp for a full 10 minutes. **See the detailed “Patient Instructions for Use” at the end of this leaflet.**
- You need to completely cover all the scalp and hair with lotion. Make sure that you and anyone who helps you apply SKLICE Lotion reads and understands this leaflet and the Instructions for Use.
- Children will need an adult to apply SKLICE Lotion for them.
- Do not swallow SKLICE Lotion. If swallowed, call your healthcare provider or go to the nearest emergency room right away.
- Do not get SKLICE Lotion into your eyes. If SKLICE Lotion gets in your eye, gently flush with water.
- Wash your hands after applying SKLICE Lotion.

When you complete your dose of SKLICE Lotion, do not use SKLICE Lotion again without talking to your healthcare provider first.

## **What are the possible side effects of SKLICE Lotion?**

**The most common side effects of SKLICE Lotion include:**

- eye redness or soreness
- eye irritation
- dandruff
- dry skin
- burning sensation of the skin

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of SKLICE Lotion. For more information, ask your healthcare provider or pharmacist.

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

### **How should I store SKLICE Lotion:**

- Store SKLICE Lotion at room temperature between 68°F to 77°F (20°C to 25°C).
- Do not freeze SKLICE Lotion.
- Safely throw away any unused SKLICE Lotion.

**Keep SKLICE Lotion and all medicines out of reach of children.**

### **What are the ingredients in SKLICE Lotion?**

Active ingredient: ivermectin

Inactive ingredients: water, olive oil, oleyl alcohol, Crodalan AWS, lanolin alcohol, cyclomethicone, shea butter, sodium citrate, sorbitan tristearate, methylparaben, propylparaben, and citric acid

General information about SKLICE Lotion

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use SKLICE Lotion for a condition for which it was not prescribed. Do not give SKLICE Lotion to other people, even if they have the same symptoms you have. It may harm them. This Patient Information leaflet summarizes the most important information about SKLICE Lotion. If you would like more information, talk to your healthcare provider. You can also ask your healthcare provider or pharmacist for information about SKLICE Lotion that is written for health professionals.

### **Instructions for Use**

Before you use SKLICE Lotion, it is important that you read the Patient Information and these Instructions for Use. Be sure that you read, understand, and follow these Instructions for Use so that you use SKLICE Lotion the right way. Ask your healthcare provider or pharmacist if you have questions about the right way to use SKLICE Lotion.

- Your hair and scalp must be dry before applying SKLICE Lotion.

#### **Figure A**



- Use the top of cap to break the tamper seal on the tube.(See Figure A)

**Figure B**



**Figure C**



**Figure D**



- Apply SKLICE Lotion directly to **dry hair** and **scalp**. (See Figure B)
- Completely cover your scalp and hair closest to the scalp first, and then apply outwards towards the ends of your hair. (See Figure C)
- Rub SKLICE Lotion throughout your hair. (See Figure D)
- It is important to completely cover your entire head so that all lice and eggs are exposed to the lotion. Be sure that each hair is coated from the scalp to the tip.
- Use up to 1 entire tube (4 oz) to completely cover hair and scalp.

**Figure E**



**Figure F**



- Allow SKLICE Lotion to stay on your hair and scalp for 10 minutes after it has been applied. Use a timer or clock. Start timing after you have completely covered your hair and scalp with SKLICE Lotion. (See Figure E)
- After 10 minutes, completely rinse SKLICE Lotion from your hair and scalp using only water. (See Figure F)
- You or anyone who helps you apply SKLICE Lotion should wash their hands after application.
- Do not use SKLICE Lotion again without talking to your healthcare provider first.

### **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 direct head-to-head contact with anyone known to have live, crawling lice.
- 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. Machine wash at high temperatures (150°F) and tumble in a hot dryer for 20 minutes.

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

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Swiftwater, PA 18370

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San Antonio, TX 78215

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U.S. Patent No. 6,103,248 and other patents pending.



Sklice Tube Carton



Sklice Tube Label