PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PR EUCRISA™

Crisaborole

Ointment, 2 % for topical use

Phosphodiesterase-4 (PDE-4) inhibitor

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

EUCRISA (crisaborole ointment, 2 %) is indicated for topical treatment of mild to moderate atopic dermatitis in patients 2 years of age and older.

1.1 Pediatrics

Pediatrics (2 to <18 years): Based on the data submitted and reviewed by Health Canada, the safety and effectiveness of EUCRISA have been established in pediatric patients age 2 years and older for topical treatment of mild to moderate atopic dermatitis.

Pediatrics (<2 years of age): No data are available to Health Canada, therefore, Health Canada has not authorized an indication for pediatric patients below the age of 2 years.

1.2 Geriatrics

Geriatrics (≥ 65 years of age):
Evidence from clinical studies of EUCRISA did not include sufficient numbers of patients aged 65 years and over to determine whether they respond differently from younger patients.

2 CONTRAINDICATIONS

EUCRISA is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container.

For a complete listing, see Dosage Forms, Strengths, Composition and Packaging.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Not applicable

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Not applicable

4.2 Recommended Dose and Dosage Adjustment

Apply a thin layer of EUCRISA twice daily to affected areas.

4.3 Administration

EUCRISA should be applied topically twice daily to all affected areas of skin.

EUCRISA is for topical use only and not for ophthalmic, oral, or intravaginal use.

4.4 Missed Dose

Advise patients if they forget to use EUCRISA as directed, to apply it as soon as possible, then go back to their regular schedule.

5 OVERDOSAGE

EUCRISA is not for oral use.

There are no data from clinical trials regarding signs and symptoms of overdose of EUCRISA. Overdosage with EUCRISA is not anticipated with dermal application. If surplus EUCRISA has been applied, the excess should be thoroughly wiped off.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging.

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Topical	Ointment: 30g, 60g and 100g 20 mg of crisaborole per gram (2%) of white to off-white ointment	butylated hydroxytoluene, edetate calcium disodium, mono- and di-glycerides, paraffin, white petrolatum, propylene glycol.

EUCRISA contains 2% crisaborole (w/w) in a petrolatum-based, white to off-white ointment and is for topical use. Each gram of EUCRISA contains 20 mg of crisaborole in an ointment containing white petrolatum, propylene glycol, mono- and di-glycerides, paraffin, butylated hydroxytoluene, and edetate calcium disodium.

EUCRISA is supplied in 30g, 60g, and 100g multilaminate tubes.

7 WARNINGS AND PRECAUTIONS

Hypersensitivity
Hypersensitivity reactions, including contact urticaria, have occurred in patients treated with EUCRISA. Hypersensitivity should be suspected in the event of severe pruritus, swelling and erythema at the application site or at a distant site. If signs and symptoms of hypersensitivity occur, discontinue EUCRISA immediately and initiate appropriate therapy.

7.1 Special Populations

7.1.1 Pregnant Women

There is no available data with EUCRISA in pregnant women to inform the drug-associated risk for major birth defects and miscarriage. In animal reproduction studies, there were no adverse developmental effects observed with oral administration of crisaborole in pregnant rats and rabbits during organogenesis at doses up to 3 and 2 times, respectively, the maximum recommended human dose (MRHD).

7.1.2 Breast-feeding

It is unknown if EUCRISA is excreted in human milk. There is no information available on the effects of the drug on the breastfed infant or the effects on milk production after topical application of EUCRISA to women who are breastfeeding. EUCRISA is systemically absorbed. The lack of clinical data during lactation precludes a clear determination of the risk of EUCRISA to a breastfed infant. Therefore, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EUCRISA and any potential adverse effects on the breastfed infant from EUCRISA or from the underlying maternal condition. Because many drugs are excreted in human milk, precaution should be exercised.

7.1.3 Pediatrics

Pediatrics (2 to <18 years): Based on the data submitted and reviewed by Health Canada, the safety and effectiveness of EUCRISA for topical treatment of mild to moderate atopic dermatitis have been established in pediatric patients age 2 years and older. Use of EUCRISA in this age group is supported by evidence from two multicenter, randomized, double-blind, parallel-group, vehicle-controlled 28-day trials which included 1,313 pediatric patients 2 to <18 years old (see ADVERSE REACTIONS and CLINICAL TRIALS).

The safety and effectiveness of EUCRISA in pediatric patients below the age of 2 years have not been established.

7.1.4 Geriatrics

Evidence from clinical studies of EUCRISA did not include sufficient numbers of patients aged 65 years and over to determine whether they respond differently from younger patients.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most common drug-related adverse events reported in clinical trials among patients with mild to moderate atopic dermatitis 2 years of age and older have been application site reactions.

8.2 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

In two randomized, double-blind, parallel-group, vehicle-controlled Phase 3 clinical trials (Studies AN2728-AD-301 and AN2728-AD-302), 1012 patients 2 to 79 years of age with mild to moderate atopic dermatitis were treated with EUCRISA twice daily for 4 weeks. The adverse reaction reported by ≥1% of EUCRISA-treated patients is listed in Table 2.

Table 2: Adverse Reaction Occurring in ≥1% of Patients in Atopic Dermatitis Trials through Week 4

Adverse Reaction	EUCRISA N=1012 n (%)	Vehicle N=499 n (%)
Application site pain[a]	45 (4.45%)	6 (1.20%)

[a] Refers to skin sensations such as burning or stinging.

8.3 Less Common Clinical Trial Adverse Reactions

Less common (<1%) adverse reactions in patients treated with EUCRISA included application site reactions (including contact dermatitis and pruritus) and flare of atopic dermatitis.

In an open-label, single arm, long-term safety study, 517 patients 2 to 72 years of age (including 454 patients 2 to 17 years of age), who had completed one of the Phase 3 studies without safety issues that precluded further treatment, were treated with EUCRISA twice daily intermittently for up to 48 weeks in 28 day on-treatment or off-treatment cycles. A total of 9 (2%) patients discontinued the therapy due to adverse events. The most frequently reported adverse events included atopic dermatitis, application site pain, and application site infection.

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Results for clinical laboratory testing have not identified clinically important changes from baseline to the end of study in mean or median values for any hematology or biochemistry parameters in any of the clinical studies in patients with atopic dermatitis.

8.5 Clinical Trial Adverse Reactions (Pediatrics)

See Clinical Trial Adverse Reactions.

8.6 Post-Market Adverse Reactions

Not applicable

9 DRUG INTERACTIONS

9.1 Serious Drug Interactions Box

Not applicable

9.2 Overview

In vitro studies using human liver microsomes indicated that under the conditions of clinical use, crisaborole and metabolite 1 are not expected to inhibit cytochrome P450 (CYP) 1A2, 2B6, 2C8, 2C9, 2C19, 2D6, and 3A4.

In vitro studies using human liver microsome for metabolite 2 showed that it did not inhibit activities of CYP2C19, 2D6, and 3A4; was a weak inhibitor of CYP1A2 and 2B6; and a moderate inhibitor of CYP2C8 and 2C9.

In vitro studies in human hepatocytes showed that under the conditions of clinical use, crisaborole and metabolites 1 and 2 are not expected to induce CYP enzymes.

9.3 Drug-Drug Interactions

The most sensitive enzyme, CYP2C9, was further investigated in a clinical trial with coadministration of EUCRISA with warfarin, a CYP2C9 substrate. The results of this study showed no drug interaction potential.

9.4 Drug-Food Interactions

Interactions with food have not been evaluated, as not applicable for topical products.

9.5 Drug-Herb Interactions

Interactions with herbal products have not been evaluated.

9.6 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been evaluated.

9.7 Drug-Lifestyle Interactions

Interactions with lifestyle have not been evaluated.

10 ACTION AND CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Crisaborole is a phosphodiesterase 4 (PDE-4) inhibitor. PDE-4 inhibition results in increased intracellular cyclic adenosine monophosphate (cAMP) levels. While the specific mechanism(s) by which crisaborole exerts its therapeutic action is not well defined, crisaborole reduces the production of some inflammatory cytokines implicated in the pathophysiology of atopic dermatitis.

10.2 Pharmacodynamics

At therapeutic doses, EUCRISA ointment is not expected to prolong QTc to any clinically relevant extent. In a thorough QT/QTc study of healthy volunteers, there was no clinically important prolongation of QT/QTc interval induced by either crisaborole or its metabolites and there were no clinically significant effects on heart rate or PR or QRS intervals.

A randomized clinical study was carried out to determine the potential of EUCRISA ointment, 2%, to induce sensitization and to cause irritation by repeated topical application to normal skin of healthy volunteers (18 years of age or older) under controlled conditions. In this study, EUCRISA showed no evidence of skin sensitization potential. Some skin irritations (e.g. erythema, edema and papules) were reported.

10.3 Pharmacokinetics

Table 3 - Summary of EUCRISA Pharmacokinetic Parameters in 2 – 17 year old patients with mild to moderate atopic dermatitis and treated BSA range from 27% - 92%

	C_{max} ng/ml	**T_{max} (hrs, median (range))**	**AUC_{0-12}(ng.hr/ml)**
Steady State Mean (SD)	127 (196)	3.00 (3.00 – 24.0)	949 (1240)

Absorption:
The pharmacokinetics (pK) of EUCRISA were investigated in 33 pediatric patients 2 to 17 years of age with mild to moderate atopic dermatitis and a mean ± SD body surface area involvement of 49 ± 20% (range 27% to 92%). In this study, patients applied approximately 3 mg/cm^2 of EUCRISA ointment (dose range was approximately 6 g to 30 g per application) twice daily for 8 days. The lower limit of quantification for the pK assay used to detect presence of crisaborole in plasma was 0.2 ng/mL.

Plasma concentrations were quantifiable in all the patients. The mean ± SD maximum plasma concentration (C_{max}) and area under the concentration time curve from 0 to 12 hours post dose

(AUC_{0-12}) for crisaborole on Day 8 were 127 ± 196 ng/mL and 949 ± 1240 ng*h/mL, respectively (Table 3). Systemic concentrations of crisaborole were at steady state by Day 8. Based on the ratios of AUC_{0-12} between Day 8 and Day 1, the mean accumulation factor for crisaborole was 1.9.

Distribution:
Based on an in vitro study, crisaborole is 97% bound to human plasma proteins.

Metabolism:
Crisaborole is substantially metabolized into inactive metabolites. The major metabolite 5-(4-cyanophenoxy)-2-hydroxyl benzylalcohol (metabolite 1), is formed via hydrolysis; this metabolite is further metabolized into downstream metabolites, among which 5-(4-cyanophenoxy)-2-hydroxyl benzoic acid (metabolite 2), formed via oxidation, is also a major metabolite.

Pharmacokinetics of metabolites 1 and 2 were assessed in the PK study described above and the systemic concentrations were at or near steady state by Day 8. Based on the ratios of AUC_{0-12} between Day 8 and Day 1, the mean accumulation factors for metabolites 1 and 2 were 1.7 and 6.3, respectively.

Elimination:
Renal excretion of metabolites is the major route of elimination.

Special Populations and Conditions

Pediatrics:
A multicenter, open-label maximal use, systemic exposure study with a pK Phase and a non-pK Safety Phase was conducted in children and adolescents with mild to moderate AD. Based on the pK exposures, no difference was seen in pK exposures in patients between the various age cohorts (2 to <18 years old).

Geriatrics
PK profiles of crisaborole and its two metabolites have not been assessed in geriatric subjects.

Renal Impairment
PK profiles of crisaborole and its two metabolites have not been assessed in patients with renal impairment.

Hepatic Impairment
PK profiles of crisaborole and its two metabolites have not been assessed in patients with hepatic impairment.

11 STORAGE, STABILITY AND DISPOSAL

Store below 25°C.

12 SPECIAL HANDLING INSTRUCTIONS

Advise the patient or caregivers to read the Patient Medication Information.

Hypersensitivity:
Advise patients to discontinue EUCRISA and seek medical attention immediately if signs or symptoms of hypersensitivity occur (see WARNING and PRECAUTIONS).

Administration Instructions:
Advise patients or caregivers that EUCRISA is for external use only and is not for ophthalmic, oral, or intravaginal use.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Crisaborole

Chemical name:

4(1-hydroxy-1,3,-dihydrobenzo[c][1,2]oxaborol-5-yloxy)benzonitrile

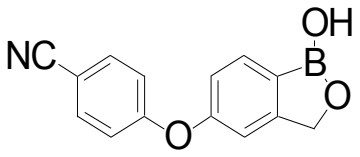
4-[(1,3-dihydro-1-hydroxy-2,1- benzoxaborol-5-yl)oxy]benzonitrile

5-(4-cyanophenoxy)-1,3-dihydro-1-hydroxy- [2,1]-benzoxaborole

Molecular formula: $C_{14}H_{10}BNO_3$

Molecular mass: 251.1 daltons

Structural formula:



Physicochemical properties: EUCRISA contains 2% crisaborole (w/w) in a petrolatum-based, white to off-white ointment and is for topical use. The active ingredient, crisaborole, is a phosphodiesterase-4 (PDE-4) inhibitor. Crisaborole drug substance is freely soluble in common organic solvents such as isopropyl alcohol and propylene glycol, and insoluble in water.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

The efficacy and safety of EUCRISA (crisaborole ointment, 2 %) was evaluated in two pivotal Phase 3, multicenter, randomized, double-blind, parallel-group, vehicle-controlled trials (Studies AN2728-AD-301 and AN2728-AD-302) that were identical in study design (Table 4). Patients with mild to moderate atopic dermatitis were randomized 2:1 to receive EUCRISA or vehicle applied twice daily for 28 days. Based on the amount of drug used in 28 days, the mean drug (EUCRISA Ointment, 2%) used per patient per application was approximately 3 grams in these clinical trials.

A total of 1,522 patients 2 to 79 years of age were enrolled in these studies. Overall, demographic characteristics and baseline disease characteristics were balanced between two treatment groups. The mean age was 12.3 years in the EUCRISA group and 12.1 years in the

vehicle group. About 62% of patients in both treatment groups were 2 to 11 years of age, and 31-37% of patients were 2 to 6 years of age. At baseline, 38.5% of the patients had an Investigator's Static Global Assessment (ISGA) score of 2 (mild), and 61.5% had an ISGA score of 3 (moderate), in the overall assessment of atopic dermatitis (erythema, induration/papulation, and oozing/crusting) on a severity scale of 0 to 4. The mean treatable percent body surface area at baseline was 18% (range from 5% to 95%). Moderate or severe baseline pruritus was reported in approximately 70% of patients.

Table 4 - Summary of Trial Design and Patient Demographics for Pivotal Phase 3 Clinical Trials in Atopic Dermatitis

Study #	Trial design	Dosage, route of administration and duration	Study patients (n)	Mean age (Range) (years) And Gender	Efficacy Endpoints
AN2728-AD-301	Multi-center, randomized, double-blind, vehicle-controlled	Crisaborole ointment 2%, topical application twice daily for 28 days	503	12.0 (2-65) Male: 43.5% Female: 56.5%	The primary efficacy endpoint was the proportion of patients at Day 29 who achieved success, defined as an ISGA grade of Clear (score of 0) or Almost Clear (score of 1) with a 2-grade or greater improvement from baseline. The secondary efficacy endpoints were the proportion of patients at Day 29 with ISGA grade of Clear (score of 0) or Almost Clear (score of 1) and the time to success in ISGA.
		Vehicle ointment topical application twice daily for 28 days	256	12.4 (2-63) Male: 44.1% Female: 55.9%	
AN2728-AD-302	Multi-center, randomized, double-blind, vehicle-controlled	Crisaborole ointment 2%, topical application twice daily for 28 days	513	12.6 (2-79) Male: 45.0% Female: 55.0%	
		Vehicle ointment topical application twice daily for 28 days	250	11.8 (2-79) Male: 44.8% Female: 55.2%	

14.2 Study Results

In these Phase 3 trials, the primary efficacy endpoint was the proportion of patients at Day 29 who achieved success, defined as an ISGA grade of Clear (score of 0) or Almost Clear (score of 1) with a 2-grade or greater improvement from baseline, comparing EUCRISA-treated patients to vehicle-treated patients. The secondary efficacy endpoints included the proportion of patients at Day 29 with ISGA grade of Clear (score of 0) or Almost Clear (score of 1), and the time to success in ISGA.

The results of the primary efficacy endpoint from two pivotal trials are summarized in Table 5.

Table 5: Results of the Primary and Secondary Efficacy Endpoints in Patients with Mild to Moderate Atopic Dermatitis at Day 29

	AN2728-AD-301		AN2728-AD-302	
	EUCRISA (N=503)	Vehicle (N=256)	EUCRISA (N=513)	Vehicle (N=250)
Primary Efficacy Endpoint --- Success in ISGA[a]	32.8%	25.4%	31.4%	18.0%
p-value	0.038		<0.001	
Secondary Efficacy Endpoint --- ISGA Clear (0) or Almost Clear (1)[b]	51.7%	40.6%	48.5%	29.7%
p-value	0.005		<0.001	

[a] Defined as an ISGA score of Clear (0) or Almost Clear (1) with a 2-grade or greater improvement from baseline.
[b] A 2-grade or greater improvement from baseline was not required.

The results of the primary efficacy endpoint showed that patients treated with EUCRISA (crisaborole ointment, 2 %) had a statistically significant higher rate (32.8% and 31.4%) of success in ISGA at Day 29 when compared with those treated with Vehicle (25.4% and 18.0%) in both pivotal trials, respectively.

Similarly, the results of the secondary efficacy endpoint showed that patients treated with EUCRISA (crisaborole ointment, 2 %) had a statistically significant higher rate (51.7% and 48.5%) of Clear or Almost Clear ISGA scores ratings at Day 29 when compared with those treated with Vehicle (40.6% and 29.7%) in both pivotal trials, respectively. The time to success in ISGA was also statistically significantly earlier in the EUCRISA group than in the vehicle group in both trials.

14.3 Comparative Bioavailability Studies

Not applicable

15 NON-CLINICAL TOXICOLOGY

Carcinogenicity
In an oral carcinogenicity study in Sprague-Dawley rats, oral doses of 30, 100, and 300 mg/kg/day crisaborole were administered to rats once daily for 104 weeks. A drug-related higher incidence of benign granular cell tumors in the uterus with cervix and vagina (combined) was noted in 300 mg/kg/day crisaborole treated female rats (1.5 times the MRHD on an AUC comparison basis). The clinical relevance of this finding is unknown.

In a dermal carcinogenicity study in CD-1 mice, topical doses of 2%, 5% and 7% crisaborole ointment were administered once daily for at least 99 (females) or 104 (males) weeks. No drug-

related neoplastic findings were noted at topical doses up to 7% crisaborole ointment (1 times the MRHD on an AUC comparison basis).

Genotoxicity
Crisaborole revealed no evidence of mutagenic or clastogenic potential based on the results of two in vitro genotoxicity tests (Ames assay and human lymphocyte chromosomal aberration assay) and one in vivo genotoxicity test (rat micronucleus assay).

Reproductive and Developmental Toxicology
Rat and rabbit embryo-fetal development was assessed after oral administration of crisaborole. Crisaborole did not cause adverse effects to the fetus at oral doses up to 300 mg/kg/day in pregnant rats during the period of organogenesis (3 times the MRHD on an AUC comparison basis). No treatment-related fetal malformations were noted after oral treatment with crisaborole in pregnant rats at doses up to 600 mg/kg/day (13 times the MRHD on an AUC comparison basis) during the period of organogenesis. Maternal toxicity was produced at the high dose of 600 mg/kg/day in pregnant rats and was associated with findings of decreased fetal body weight and delayed skeletal ossification. Crisaborole did not cause adverse effects to the fetus at oral doses up to the highest dose tested of 100 mg/kg/day in pregnant rabbits during the period of organogenesis (2 times the MRHD on an AUC comparison basis).

In a prenatal/postnatal development study, pregnant rats were treated with crisaborole at doses of 150, 300, and 600 mg/kg/day by oral gavage during gestation and lactation (from gestation day 7 through day 20 of lactation). Crisaborole did not have any adverse effects on fetal development at doses up to 300 mg/kg/day (3 times the MRHD on an AUC comparison basis). Maternal toxicity was produced at the high dose of 600 mg/kg/day in pregnant rats and was associated with findings of stillbirths, pup mortality, and reduced pup weights.

No effects on fertility were observed in male or female rats that were administered oral doses up to 600 mg/kg/day crisaborole (13 times the MRHD on an AUC comparison basis) prior to and during early pregnancy.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PR EUCRISA ™
Crisaborole ointment 2%

Read this carefully before you start taking **EUCRISA** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **EUCRISA**.

What is EUCRISA used for?

- EUCRISA is a non-steroid prescription medicine used on the skin to treat mild to moderate eczema (atopic dermatitis).
- EUCRISA is for topical use only. Do not use EUCRISA in your eyes, mouth, or vagina.
- EUCRISA is for adults and children 2 years of age and older.
- It is not known if EUCRISA is safe and effective in children under 2 years of age.

How does EUCRISA work?

The exact way EUCRISA works is not known. It is thought that it reduces the amount of substances in the body that trigger the rash and itchiness caused by eczema.

What are the ingredients in EUCRISA?

Medicinal ingredients: Crisaborole.

Non-medicinal ingredients: Butylated hydroxytoluene, edetate calcium disodium, mono- and di-glycerides, paraffin, propylene glycol, white petrolatum.

EUCRISA comes in the following dosage forms:

White to off-white ointment containing 20 mg of crisaborole per gram (2%).

Do not use EUCRISA if:

- you or your child are allergic to crisaborole or any of the other ingredients in EUCRISA.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take EUCRISA. Talk about any health conditions or problems you may have, including if you:

- are pregnant or planning to become pregnant. It is not known if EUCRISA may harm your unborn baby.
- are breast-feeding or plan to breast-feed. It is not known if EUCRISA passes into breast milk. Talk with your doctor about the best way to feed your baby if you take EUCRISA.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

There are currently no known drugs that interact with EUCRISA.

How to take EUCRISA:

- EUCRISA is usually applied twice daily. Use EUCRISA exactly as your healthcare provider tells you to use it.
- Do not use in your eyes, mouth, or vagina. Topical medicine is for use only on the skin.
- Rinse with water if this medicine gets in you or your child's eyes, mouth, or vagina.
- Wash your hands after applying EUCRISA, unless you are using it to treat eczema on your hands. All caregivers who apply EUCRISA for someone else should wash their hands after applying it.

Usual dose:

- Apply a thin layer of EUCRISA to affected areas twice daily.
- Your doctor will tell you how to use EUCRISA based on you or your child's medical condition and response to the drug. Do not use any more or any less of the drug than your doctor says.

Overdose:

Because EUCRISA is for topical use only, it is unlikely that you or your child will overdose on EUCRISA. If you or your child applies too much EUCRISA, thoroughly wipe it off.

If you think you or your child have taken too much EUCRISA, seek emergency medical attention, or call your regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you or your child forget to use EUCRISA as directed, apply it as soon you remember. Then go back to the regular dosing schedule. Do not apply twice as much the next time you use it.

What are possible side effects from using EUCRISA?

These are not all the possible side effects you may feel when taking EUCRISA. If you experience any side effects not listed here, contact your healthcare professional.

The most common side effect of EUCRISA is pain on the area where you applied it, such as burning or stinging.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON **Application site pain**: such as burning or stinging.	**X**		
RARE **Allergic reactions:** EUCRISA may cause allergic reactions at or near the application site. These can be serious and may include hives, itching, swelling, and redness.			**X**

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store below 25°C.

Keep out of reach and sight of children.

If you want more information about EUCRISA:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp); the manufacturer's website http://www.Pfizer.ca, or by calling 1-800-463-6001.

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