HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ZYCLARA safely and effectively. See full prescribing information for ZYCLARA Cream.

ZYCLARA (imiquimod), Cream, 3.75%
For topical use only
Initial U.S. Approval: 1997

----------INDICATIONS AND USAGE----------
ZYCLARA Cream is indicated for the topical treatment of clinically typical, visible or palpable actinic keratoses (AK) of the full face or balding scalp in immunocompetent adults.
(1.1)

----------DOSAGE AND ADMINISTRATION----------
ZYCLARA Cream is not for oral, ophthalmic, or intravaginal use.(2)

- Once daily to the skin of the affected area (either the entire face or balding scalp) for two 2-week treatment cycles separated by a 2-week no-treatment period. (2.1)

----------DOSAGE FORMS AND STRENGTHS----------
Cream, 3.75%, white to faintly yellow cream. (3)

----------CONTRAINDICATIONS----------
- None (4)

----------WARNINGS AND PRECAUTIONS----------
- Intense local inflammatory reactions can occur (e.g., skin weeping, erosion). Dosing interruption may be required (2, 5.1, 6)
- Flu-like systemic signs and symptoms including fatigue, nausea, fever, myalgias, arthralgias, and chills. Dosing interruption may be required (2, 5.2, 6)
- Avoid exposure to sunlight and sunlamps (5.3). Wear sunscreen daily (17.4).
- Avoid concomitant use of Zyclara Cream and any other imiquimod cream.

----------ADVERSE REACTIONS----------
Most common Adverse Reactions (incidence >50%) are local skin reactions erythema, edema weeping/exudate, flaking/scaling/dryness, scabing/crusting and erosin/ulceration (6.2). Other reported reactions (occurring in ≥2% of ZYCLARA-Treated Subjects*)* include headache, fatigue, nausea and fever (see 6.1*)*.

To report SUSPECTED ADVERSE REACTIONS, contact Graceway Pharmaceuticals, LLC at 1-800-328-0255 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

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

Revised: March 2010

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the Full Prescribing Information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Actinic Keratosis

ZYCLARA Cream is indicated for the topical treatment of clinically typical visible or palpable, actinic keratoses (AK), of the full face or balding scalp in immunocompetent adults.

1.2 Unevaluated Populations

Safety and efficacy have not been established for ZYCLARA Cream in the treatment of actinic keratosis, with more than one 2-cycle treatment course in the same area.

The safety and efficacy of ZYCLARA Cream in immunosuppressed patients have not been established.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of patients with xeroderma pigmentosum.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of superficial basal cell carcinoma.

The safety and efficacy have not been established for ZYCLARA Cream in the treatment of external genital warts.

ZYCLARA Cream should be used with caution in patients with pre-existing autoimmune conditions.

2 DOSAGE AND ADMINISTRATION

ZYCLARA Cream is not for oral, ophthalmic, or intravaginal use.

2.1 Actinic Keratosis

ZYCLARA Cream should be applied once daily before bedtime to the skin of the affected area (either entire face or balding scalp) for two 2-week treatment cycles separated by a 2-week no-treatment period. ZYCLARA Cream should be applied as a thin film to the entire treatment area and rubbed in until the cream is no longer visible. Up to 2 packets of ZYCLARA Cream may be applied to the treatment area at each application. **ZYCLARA Cream should be left on the skin for approximately 8 hours, after which time the cream should be removed by washing the area with mild soap and water**. The prescriber should demonstrate the proper application technique to maximize the benefit of ZYCLARA Cream therapy.

Patients should wash their hands before and after applying ZYCLARA cream.

Avoid use in or on the lips and nostrils. Do not use in or near the eyes.

Local skin reactions in the treatment area are common. *[see Adverse Reactions (6.1, 6.2)]* A rest period of several days may be taken if required by the patient's discomfort or severity of the local

skin reaction. **However, neither 2-week treatment cycle should be extended due to missed doses or rest periods.** A transient increase in AK lesion counts may be observed during treatment. Response to treatment cannot be adequately assessed until resolution of local skin reactions. The patient should continue dosing as prescribed. Treatment should continue for the full treatment course even if all actinic keratoses appear to be gone. Lesions that do not respond to treatment should be carefully re-evaluated and management reconsidered.

ZYCLARA Cream is packaged in single-use packets, with 28 packets supplied per box. Patients should be prescribed no more than 56 packets for the total 2-cycle treatment course. Unused packets should be discarded. Partially-used packets should be discarded and not reused.

3 DOSAGE FORMS AND STRENGTHS

Cream, 3.75%, white to faintly yellow cream.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Local Skin Reactions

Intense local skin reactions including skin weeping or erosion can occur after a few applications of ZYCLARA Cream and may require an interruption of dosing. *[see Dosage and Administration (2) and Adverse Reactions (6)]*. ZYCLARA Cream has the potential to exacerbate inflammatory conditions of the skin, including chronic graft versus host disease.

Administration of ZYCLARA Cream is not recommended until the skin is healed from any previous drug or surgical treatment.

Concomitant use of ZYCLARA and any other imiquimod creams, in the same treatment area, should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of local skin reactions.

5.2 Systemic Reactions

Flu-like signs and symptoms may accompany, or even precede, local skin reactions and may include fatigue, nausea, fever, myalgias, arthralgias, and chills. An interruption of dosing and an assessment of the patient should be considered. *[see Adverse Reactions (6)]*

Lymphadenopathy occurred in 2% of subjects treated with ZYCLARA Cream *[see Adverse Reactions (6)]*. This reaction resolved in all subjects by 4 weeks after completion of treatment.

The safety of concomitant use of ZYCLARA Cream and any other imiquimod creams has not been established and should be avoided since they contain the same active ingredient (imiquimod) and may increase the risk for and severity of systemic reactions.

5.3 Ultraviolet Light Exposure

Exposure to sunlight (including sunlamps) should be avoided or minimized during use of ZYCLARA Cream because of concern for heightened sunburn susceptibility. Patients should be warned to use protective clothing (e.g., a hat) when using ZYCLARA Cream. Patients with sunburn should be advised not to use ZYCLARA Cream until fully recovered. Patients who may have considerable sun exposure, e.g. due to their occupation, and those patients with inherent sensitivity to sunlight should exercise caution when using ZYCLARA Cream.

In an animal photo-carcinogenicity study, imiquimod cream shortened the time to skin tumor formation *[see Nonclinical Toxicology (13.1)]*. The enhancement of ultraviolet carcinogenicity is not necessarily dependent on phototoxic mechanisms. Therefore, patients should minimize or avoid natural or artificial sunlight exposure.

6 ADVERSE REACTIONS

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 practice.

6.1 Clinical Trials Experience

The data described below reflect exposure to ZYCLARA Cream or vehicle in 319 subjects enrolled in two double-blind, vehicle-controlled trials. Subjects applied up to two packets of ZYCLARA Cream or vehicle daily to the skin of the affected area (either entire face or balding scalp) for two 2-week treatment cycles separated by a 2-week no treatment period.

Table 1: Selected Adverse Reactions Occurring in ≥ 2% of ZYCLARA-Treated Subjects and at a Greater Frequency than with Vehicle in the Combined Studies

Preferred Term	ZYCLARA Cream 3.75% (N=160)	Vehicle (N=159)
Headache	10 (6%)	5 (3%)
Application site pruritus	7 (4%)	1 (<1%)
Fatigue	7 (4%)	0 (0%)
Nausea	6 (4%)	2 (1%)
Application site irritation	5 (3%)	0 (0%)
Application site pain	5 (3%)	0 (0%)
Pyrexia	5 (3%)	0 (0%)
Anorexia	4 (3%)	0 (0%)
Dizziness	4 (3%)	0 (0%)
Herpes simplex	4 (3%)	1 (<1%)
Pain	4 (3%)	0 (0%)
Chest pain	3 (2%)	0 (0%)
Diarrhea	3 (2%)	0 (0%)
Lymphadenopathy	3 (2%)	0 (0%)

Table 2: Local Skin Reactions in the Treatment Area in ZYCLARA-Treated Subjects as Assessed by the Investigator

	ZYCLARA Cream 3.75% (N=160)		Vehicle (N=159)	
	All Grades*	Severe	All Grades*	Severe
Erythema	154 (96%)	40 (25%)	124 (78%)	0 (0%)
Scabbing/Crusting	149 (93%)	22 (14%)	72 (45%)	0 (0%)
Flaking/Scaling/Dryness	147 (92%)	13 (8%)	123 (77%)	2 (1%)
Edema	120 (75%)	9 (6%)	31 (19%)	0 (0%)
Erosion/Ulceration	99 (62%)	17 (11%)	14 (9%)	0 (0%)
Weeping/Exudate	81 (51%)	9 (6%)	6 (4%)	0 (0%)

* All Grades: mild, moderate or severe

Local skin reactions may extend beyond treatment area.

Overall, in the clinical trials, 11% (17/160) of subjects on ZYCLARA Cream and 0% on vehicle cream required rest periods due to adverse reactions.

Other adverse reactions observed in subjects treated with ZYCLARA Cream include: application site bleeding, application site swelling, arthralgia, cheilitis, chills, dermatitis, herpes

zoster, influenza-like illness, insomnia, lethargy, myalgia, pancytopenia, pruritus, squamous cell carcinoma, and vomiting.

6.2 Postmarketing Experience
There are currently no post-marketing adverse reactions reported for Zyclara Cream.
The following adverse reactions have been identified during post-approval use of Aldara (imiquimod) Cream, 5%. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
Body as a Whole: angioedema.
Cardiovascular: capillary leak syndrome, cardiac failure, cardiomyopathy, pulmonary edema, arrhythmias (tachycardia, supraventricular tachycardia, atrial fibrillation, palpitations), chest pain, ischemia, myocardial infarction, syncope.
Endocrine: thyroiditis.
Gastro-Intestinal System Disorders: abdominal pain.
Hematological: decreases in red cell, white cell and platelet counts (including idiopathic thrombocytopenic purpura)**,** lymphoma
Hepatic: abnormal liver function
Infections and Infestations: herpes simplex.
Neuropsychiatric: agitation, cerebrovascular accident, convulsions (including febrile convulsions), depression, insomnia, multiple sclerosis aggravation, paresis, suicide.
Respiratory: dyspnea.
Urinary System Disorders: proteinuria, urinary retention, dysuria.
Skin and Appendages: exfoliative dermatitis, erythema multiforme**,** hyperpigmentation, hypertrophic scar.
Vascular: Henoch-Schonlein purpura syndrome

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C:

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

Note: The animal multiples of human exposure calculations were based on daily dose comparisons for the reproductive toxicology studies described in this label. The animal multiples of human exposure were based on weekly dose comparisons for the carcinogenicity studies described in this label. For the animal multiple of human exposure ratios presented in this label, the Maximum Recommended Human Dose (MRHD) was set at 2 packets (500 mg cream) per treatment of ZYCLARA Cream (imiquimod 3.75%, 18.75 mg imiquimod).

Systemic embryofetal development studies were conducted in rats and rabbits. Oral doses of 1, 5 and 20 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 15) to pregnant female rats. In the presence of maternal toxicity, fetal effects noted at 20 mg/kg/day (190X MRHD based on AUC comparisons) included increased

resorptions, decreased fetal body weights, delays in skeletal ossification, bent limb bones, and two fetuses in one litter (2 of 1567 fetuses) demonstrated exencephaly, protruding tongues and low-set ears. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 5 mg/kg/day (32X MRHD based on AUC comparisons).

Intravenous doses of 0.5, 1 and 2 mg/kg/day imiquimod were administered during the period of organogenesis (gestational days 6 – 18) to pregnant female rabbits. No treatment related effects on embryofetal toxicity or teratogenicity were noted at 2 mg/kg/day (2.1X MRHD based on BSA comparisons), the highest dose evaluated in this study, or 1 mg/kg/day (134X MRHD based on AUC comparisons).

A combined fertility and peri- and post-natal development study was conducted in rats. Oral doses of 1, 1.5, 3 and 6 mg/kg/day imiquimod were administered to male rats from 70 days prior to mating through the mating period and to female rats from 14 days prior to mating through parturition and lactation. No effects on growth, fertility, reproduction or post-natal development were noted at doses up to 6 mg/kg/day (29X MRHD based on AUC comparisons), the highest dose evaluated in this study. In the absence of maternal toxicity, bent limb bones were noted in the F1 fetuses at a dose of 6 mg/kg/day (29X MRHD based on AUC comparisons). This fetal effect was also noted in the oral rat embryofetal development study conducted with imiquimod. No treatment related effects on teratogenicity were noted at 3 mg/kg/day (14X MRHD based on AUC comparisons).

8.3 Nursing Mothers

It is not known whether imiquimod is excreted in human milk following use of ZYCLARA Cream. Because many drugs are excreted in human milk, caution should be exercised when ZYCLARA Cream is administered to nursing women.

8.4 Pediatric Use

AK is a condition not generally seen within the pediatric population. The safety and efficacy of ZYCLARA Cream for AK in patients less than 18 years of age has not been established.

8.5 Geriatric Use

Of the 160 subjects treated with ZYCLARA Cream in the clinical studies, 78 subjects were 65 years or older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

10 OVERDOSAGE

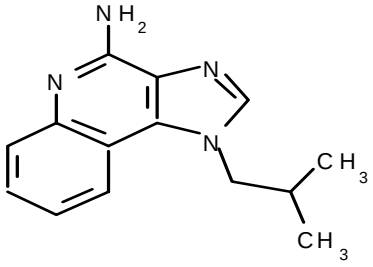
Topical overdosing of ZYCLARA Cream could result in an increased incidence of severe local skin reactions and may increase the risk for systemic reactions.

Hypotension was reported in a clinical trial following multiple oral imiquimod doses of >200 mg (equivalent to the ingestion of imiquimod content of > 21 packets of ZYCLARA). This resolved following oral or intravenous fluid administration.

11 DESCRIPTION

ZYCLARA Cream is intended for topical administration. Each gram contains 37.5 mg of imiquimod in a white to faintly yellow oil-in-water cream base consisting of isostearic acid, cetyl alcohol, stearyl alcohol, white petrolatum, polysorbate 60, sorbitan monostearate, glycerin, xanthan gum, purified water, benzyl alcohol, methylparaben, and propylparaben.

Chemically, imiquimod is 1-(2-methylpropyl)-1*H*-imidazo[4,5-c]quinolin-4-amine. Imiquimod has a molecular formula of $C_{14}H_{16}N_4$ and a molecular weight of 240.3. Its structural formula is:



12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of action of ZYCLARA Cream in treating AK lesions is unknown.

12.2 Pharmacodynamics

The pharmacodynamics of ZYCLARA are unknown.

Imiquimod is a Toll-like receptor 7 agonist that activates immune cells. Topical application to skin is associated with increases in markers for cytokines and immune cells.

In a study of 18 subjects with AK comparing Aldara (imiquimod) Cream, 5% to vehicle, increases from baseline in week 2 biomarker levels were reported for CD3, CD4, CD8, CD11c, and CD68 for Aldara (imiquimod) Cream, 5% treated subjects; however, the clinical relevance of these findings is unknown.

12.3 Pharmacokinetics

Following dosing with 2 packets once daily (18.75 mg imiquimod/day) for up to three weeks, systemic absorption of imiquimod was observed in all subjects when Zyclara Cream was applied to the face and/or scalp in 17 subjects with at least 10 AK lesions. The mean peak serum imiquimod concentration at the end of the trial was approximately 0.323 ng/mL. The median time to maximal concentrations (Tmax) occurred at 9 hours after dosing. Based on the plasma half-life of imiquimod observed at the end of the study, 29.3±17.0 hours, steady-state concentrations can be anticipated to occur by day 7 with once daily dosing.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In an oral (gavage) rat carcinogenicity study, imiquimod was administered to Wistar rats on a 2X/week (up to 6 mg/kg/day) or daily (3 mg/kg/day) dosing schedule for 24 months. No treatment related tumors were noted in the oral rat carcinogenicity study up to the highest doses tested in this study of 6 mg/kg administered 2X/week in female rats (8.2X MRHD based on weekly AUC comparisons), 4 mg/kg administered 2X/week in male rats (7.1X MRHD) based on weekly AUC comparisons) or 3 mg/kg administered 7X/week to male and female rats (14X MRHD based on weekly AUC comparisons).

In a dermal mouse carcinogenicity study, imiquimod cream (up to 5 mg/kg/application imiquimod or 0.3% imiquimod cream) was applied to the backs of mice 3X/week for 24 months. A statistically significant increase in the incidence of liver adenomas and carcinomas was noted in high dose male mice compared to control male mice (24X MRHD based on weekly AUC comparisons). An increased number of skin papillomas was observed in vehicle cream control group animals at the treated site only.

In a 52-week dermal photo-carcinogenicity study, the median time to onset of skin tumor formation was decreased in hairless mice following chronic topical dosing (3X/week; 40 weeks of treatment followed by 12 weeks of observation) with concurrent exposure to UV radiation (5 days per week) with vehicle alone. No additional effect on tumor development beyond the vehicle effect was noted with the addition of the active ingredient, imiquimod, to the vehicle cream.

Imiquimod revealed no evidence of mutagenic or clastogenic potential based on the results of five in vitro genotoxicity tests (Ames assay, mouse lymphoma L5178Y assay, Chinese hamster ovary cell chromosome aberration assay, human lymphocyte chromosome aberration assay and SHE cell transformation assay) and three in vivo genotoxicity tests (rat and hamster bone marrow cytogenetics assay and a mouse dominant lethal test).

Daily oral administration of imiquimod to rats, throughout mating, gestation, parturition and lactation, demonstrated no effects on growth, fertility or reproduction, at doses up to 29X MRHD based on AUC comparisons.

14 CLINICAL STUDIES

In two double-blind, randomized, vehicle-controlled clinical studies, 319 subjects with AK were treated with ZYCLARA Cream, or vehicle cream. Studies enrolled subjects >18 years of age with 5-20 typical visible or palpable AK lesions of the face or scalp. Study cream was applied to either the entire face (excluding ears) or balding scalp once daily for two 2-week treatment cycles separated by a 2-week no-treatment period. Subjects then continued in the study for an 8-week follow-up period during which they returned for clinical observations and safety monitoring. Study subjects ranged from 36 to 90 years of age and 54% had Fitzpatrick skin type I or II. All ZYCLARA Cream-treated subjects were Caucasians.

On a scheduled dosing day, up to two packets of the study cream were applied to the entire treatment area prior to normal sleeping hours and left on for approximately 8 hours. Efficacy was assessed by AK lesion counts at the 8-week post-treatment visit. All AKs in the treatment area were counted, including baseline lesions as well as lesions which appeared during therapy.

Complete clearance required absence of any lesions including those that appeared during therapy in the treatment area. Complete and partial clearance rates are shown in the tables below. Partial clearance rate was defined as the percentage of subjects in whom the number of baseline AKs was reduced by 75% or more. The partial clearance rate was measured relative to the numbers of AK lesions at Baseline.

Table 3: Rate of Subjects with Complete Clearance at 8 Weeks Post Treatment

	ZYCLARA Cream 3.75%	**Vehicle Cream**
Study 1	25.9% (21/81)	2.5% (2/80)
Study 2	45.6% (36/79)	10.1% (8/79)

Table 4: Rate of Subjects with Partial Clearance (≥75%) at 8 Weeks Post Treatment

	ZYCLARA Cream 3.75%	**Vehicle Cream**
Study 1	45.7 (37/81)	18.8 (15/80)
Study 2	73.4 (58/79)	26.6 (21/79)

During the course of treatment, 86% (138/160) of subjects experienced a transient increase in lesions evaluated as actinic keratoses relative to the number present at baseline within the treatment area.

16 HOW SUPPLIED/STORAGE AND HANDLING

ZYCLARA (imiquimod) Cream, 3.75%, is supplied in single-use packets which contain 250 mg of the cream. Available as: Box of 28 packets NDC 29336-710-28. Store at 25^0C (77^0F); excursions permitted to 15^0 to 30^0C (59^0 to 86^0F) [see USP Controlled Room Temperature].

Avoid freezing.

Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling

17.1 Instructions for Administration:

Zyclara Cream should be used as directed by a physician. *[see Dosage and Administration (2)]* Zyclara Cream is for external use only. Contact with the eyes, lips and nostrils should be avoided. *[see Indications and Usage (1)* and *Dosage and Administration (2)*].

The treatment area should not be bandaged or otherwise occluded. Partially-used packets should be discarded and not reused. The prescriber should demonstrate the proper application technique to maximize the benefit of Zyclara Cream therapy.

It is recommended that patients wash their hands before and after applying Zyclara Cream.

17.2 Local Skin Reactions:

Patients may experience local skin reactions during treatment with Zyclara Cream. Potential local skin reactions include erythema, edema, erosions/ulcerations, weeping/exudate, flaking/scaling/dryness, and scabbing/crusting. These reactions can range from mild to severe in intensity and may extend beyond the application site onto the surrounding skin. Patients may also experience application site reactions such as itching, irritation or pain. *[see Adverse Reactions (6)]*

Local skin reactions may be of such an intensity that patients may require rest periods from treatment. Treatment with Zyclara Cream can be resumed after the skin reaction has subsided, as determined by the physician. However, each treatment cycle should not be extended beyond 2 weeks due to missed doses or rest periods. Patients should contact their physician promptly if they experience any sign or symptom at the application site that restricts or prohibits their daily activity or makes continued application of the cream difficult.

Because of local skin reactions, during treatment and until healed, the treatment area is likely to appear noticeably different from normal skin. Localized hypopigmentation and hyperpigmentation have been reported following use of imiquimod cream. These skin color changes may be permanent in some patients.

17.3 Systemic Reactions:

Patients may experience flu-like systemic signs and symptoms during treatment with Zyclara Cream. Systemic signs and symptoms may include fatigue, nausea, fever, myalgia, arthralgia, and chills. *[see Adverse Reactions (6)]* An interruption of dosing or dose adjustment and an assessment of the patient should be considered.

17. 4 Recommended Administration

Dosing is once daily before bedtime to the skin of the affected area (entire face or balding scalp) for two 2-week treatment cycles separated by a 2-week no-treatment period. However, the treatment period should not be extended beyond two 2-week treatment cycles due to missed doses or rest periods. Treatment should continue for the full treatment course even if all actinic keratoses appear to be gone. *[see Dosage and Administration (2.1).*

It is recommended that patients wash their hands before and after applying Zyclara Cream. Before applying the cream, the patient should wash the treatment area with mild soap and water and allow the area to dry thoroughly.

It is recommended that the treatment area be washed with mild soap and water 8 hours following Zyclara Cream application.

Most patients using Zyclara Cream for the treatment of AK experience erythema, flaking/scaling/dryness and scabbing/crusting at the application site with normal dosing. [see Adverse Reactions (6.1)].

Use of sunscreen is encouraged, and patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using Zyclara Cream. *[see Warnings and Precautions (5.3)]*.

Additional lesions may become apparent in the treatment area during treatment. *[see Clinical Studies (14.1)]*.

FDA-Approved Patient Labeling

ZYCLARA **[zi-clar-a]**
(imiquimod)
Cream

IMPORTANT: For use on the skin only (topical). Do not use ZYCLARA cream in or on your eyes, nostrils, mouth or vagina.

Read the Patient Information that comes with ZYCLARA cream 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 with your healthcare provider about your medical condition or treatment. If you do not understand the information, or have any questions about ZYCLARA cream, talk with your healthcare provider or pharmacist.

What is ZYCLARA cream?

ZYCLARA cream is a prescription medicine for use on the face or balding scalp only (a topical medicine) to treat actinic keratosis (AK).

Actinic keratosis is caused by too much sun exposure.

It is not known if ZYCLARA cream is safe and effective:

- in people who do not have a normal immune system.
- in the treatment of patients with xeroderma pigmentosum.
- in the treatment of superficial basal cell carcinoma.
- in the treatment of external genital warts.

It is not known if ZYCLARA cream is safe and effective in children younger than 18 years old.

What should I tell my healthcare provider before using ZYCLARA Cream?

Before you use ZYCLARA cream, tell your healthcare provider if you:

- have problems with your immune system
- are being treated or have been treated for actinic keratosis with other medicines or surgery. You should not use ZYCLARA cream until you have healed from other treatments
- have other skin problems

• have any other medical conditions

• are pregnant or planning to become pregnant. It is not known if ZYCLARA cream can harm your unborn baby. Talk to your healthcare provider if you are pregnant or plan to become pregnant.

• are breast-feeding or plan to breast-feed. It is not known if ZYCLARA cream passes into your breast milk and if it can harm your baby. Talk to your healthcare provider about the best way to feed your baby if you use ZYCLARA cream.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements.

Especially tell your healthcare provider if you have had other treatments for actinic keratosis.

How should I use ZYCLARA Cream?

• **Do not get ZYCLARA cream in or near your eyes**

• **Do not get ZYCLARA cream in or on your nostrils, lips, or vagina.**

• Use ZYCLARA cream exactly as your healthcare provider tells you to use it. Your healthcare provider will tell you where to apply ZYCLARA cream and how often and for how long to apply it for your condition. Do not apply ZYCLARA cream to other areas.

• Using too much ZYCLARA cream, or using it too often, or for too long can increase your chances for having a severe skin reaction or other side effects.

• Talk to your healthcare provider if you think ZYCLARA cream is not working for you.

Applying ZYCLARA cream:

ZYCLARA cream should be applied just before your bedtime.

Do not use more ZYCLARA cream than you need to cover the treatment area.

Do not use more than two packets of ZYCLARA cream on the treatment area.

• Wash the area where the cream will be applied with mild soap and water.

• Allow the area to dry.

• Wash your hands.

• Open a packet of ZYLCARA cream and apply a thin layer to the affected area on

the scalp or face to be treated. You may need to use more than one packet.

• Rub the cream into your skin until you can not see the ZYCLARA cream.

• After you apply ZYCLARA cream, wash your hands with mild soap and water.

• Leave the cream on the treated area for the amount of time your healthcare provider tells you (usually about 8 hours). **Do not** take a bath or get the treated area wet during this time.

• After the right amount of time has passed, wash the treated area with mild soap and water.

• If you forget to apply ZYCLARA cream, just apply the next dose of ZYCLARA cream at your regular time.

• If you get ZYCLARA cream in your mouth or in your eyes rinse well with water right away.

What should I avoid while using ZYCLARA Cream?

• **Do not** cover the treated area with bandages or other closed dressings.

• **Do not** use sunlamps or tanning beds, and avoid sunlight as much as possible during treatment with ZYCLARA cream. Use sunscreen and wear protective clothing if you go outside during daylight.

What are the possible side effects of ZYCLARA Cream?

ZYCLARA Cream may cause serious side effects, including:

• **Local Skin Reactions**: skin redness, scabbing or crusting, flaking, scaling or dryness, swelling, sores or blisters, draining (weeping)

• **Flu-like symptoms**: tiredness, nausea, vomiting, fever, chills, muscle pain, joint pain

The most common side effects of ZYCLARA cream include:

• headache
• itching at application site
• tiredness
• nausea
• skin irritation
• pain at the treatment area

- fever
- loss of appetite
- dizziness
- cold sores
- pain
- chest pain
- diarrhea
- swelling of lymph nodes

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 ZYCLARA cream. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or to Graceway Pharmaceuticals, LLC at 1-800-328-0255.

How do I store ZYCLARA Cream?

- Store ZYCLARA cream at 59° F to 86° F (15° C to 30° C).
- Do not freeze.

Keep ZYCLARA cream and all medicines out of the reach of children.

General Information about ZYCLARA Cream

Medicines are sometimes prescribed for purposes other than those listed in the patient information. Do not use ZYCLARA cream for a condition for which it was not prescribed. Do not give ZYCLARA cream 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 ZYCLARA cream. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about ZYCLARA cream that is written for the health professionals.

What are the ingredients in ZYCLARA Cream?

Active Ingredient: imiquimod

Inactive ingredients: isostearic acid, cetyl alcohol, stearyl alcohol, white petrolatum, polysorbate 60, sorbitan monostearate, glycerin, xanthan gum, purified water, benzyl alcohol, methylparaben, and propylparaben.

Manufactured by
3M Health Care Limited
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Revised March 2010