PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrTARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE

Clotrimazole and Betamethasone Dipropionate Cream, USP
1% w/w clotrimazole / 0.05% w/w betamethasone (as betamethasone dipropionate)

Topical Antifungal and Corticosteroid Agent

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE (clotrimazole and betamethasone dipropionate) is indicated for:

- the topical treatment of the following fungal dermal infections complicated by inflammatory pruritus: tinea pedis, tinea cruris, and tinea corporis due to *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum*, and *Microsporum canis*.

1.1 Pediatrics

Pediatrics: Based on the available data, the safety and effectiveness in children below the age of 12 have not been established with betamethasone dipropionate and clotrimazole.

1.2 Geriatrics

Geriatrics: There is insufficient data to suggest that use in the geriatric population is associated with differences in safety or effectiveness.

2 CONTRAINDICATIONS

TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE 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.
- patients who are sensitive to other corticosteroids or imidazoles.
- untreated bacterial and tubercular infections involving the skin and in certain viral diseases such as herpes simplex, chicken pox and vaccinia.

3 DOSAGE AND ADMINISTRATION

3.1 Dosing Considerations

TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE should not be used with occlusive dressings.

3.2 Recommended Dose and Dosage Adjustment

Based on the available data, Health Canada has not authorized the use of betamethasone dipropionate and clotrimazole in children below 12 years of age (See INDICATIONS).

3.3 Administration

A thin film of TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE should be applied to cover completely the affected and surrounding skin areas twice daily, in the morning and at night, for two weeks in tinea cruris and tinea corporis, and for four weeks in tinea pedis. The use of TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE for longer than four weeks is not recommended.

Clinical improvement, with relief of erythema and pruritus, usually occurs within three to five days of treatment. If a patient with tinea cruris and tinea corporis shows no clinical improvement after one week of treatment with TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE, the diagnosis should be reviewed. In tinea pedis, the treatment should be applied for two weeks prior to making that decision. Treatment with TARO-CLOTRIMAZOLE/ BETAMETHASONE DIPROPIONATE should be discontinued if the condition persists after two weeks in tinea cruris and tinea corporis and after four weeks in tinea pedis. Alternate therapy may then be instituted, if indicated, with an appropriate antifungal preparation.

4 MISSED DOSE

If a dose is missed, the patient can resume treatment with the next scheduled application.

5 OVERDOSAGE

No specific antidote is available, and treatment should be symptomatic.

Betamethasone dipropionate:
Excessive or prolonged use of topical corticosteroids can suppress pituitary-adrenal function, resulting in secondary adrenal insufficiency, and produce manifestations of hypercorticism, including Cushing's disease.

Clotrimazole:
Overdosage by topical clotrimazole administration is highly improbable, since application of C_{14} labelled clotrimazole to intact or diseased skin under occlusive dressing for 6 hours did not yield measurable quantities (lower detection limit 0.001 µg/mL) of radioactive material in the sera of human subjects.

Treatment:
Appropriate symptomatic treatment of corticosteroid overdosage is indicated. Acute hypercorticoid symptoms are usually reversible. Treat electrolyte imbalance, if necessary. In cases of chronic toxicity, slow withdrawal of corticosteroids is advised.

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
Topical	

TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE is a smooth white cream free of foreign matter.

Each gram of TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE contains 10.0 mg clotrimazole, USP, and 0.64 mg betamethasone dipropionate, USP, (equivalent to 0.5 mg (0.05%) betamethasone) in a hydrophilic emollient cream. Tubes of 15 and 50 g.

7 WARNINGS AND PRECAUTIONS

General
Patients should be advised to inform subsequent physicians of the prior use of corticosteroids.

Occlusive dressings should not be used, as this may result in an increase in the systemic absorption of topical corticosteroids or clotrimazole.

If irritation or hypersensitivity develops with the use of TARO-CLOTRIMAZOLE/ BETAMETHASONE DIPROPIONATE (clotrimazole and betamethasone dipropionate), treatment should be discontinued, and appropriate therapy instituted.

Endocrine and Metabolism
Systemic absorption of topical corticosteroids has produced reversible hypothalamic- pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

Systemic absorption of topical corticosteroid agents will be increased with the use of more potent corticosteroid agents, with prolonged usage or if extensive body surface areas are treated. Therefore, patients receiving large doses of potent topical corticosteroids, applied to a large surface area should be evaluated periodically for evidence of HPA axis suppression. If HPA axis suppression occurs, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute with a less potent corticosteroid agent.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticotherapy.

Monitoring and Laboratory Tests
If there is a lack of response to TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE, appropriate microbiological studies should be repeated to confirm the diagnosis and rule out other pathogens before instituting another course of antimycotic therapy.

The following tests may be helpful in evaluating HPA axis suppression due to the corticosteroid component:

Urinary free cortisol test
ACTH stimulation test

Ophthalmologic
TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE should not be used in or near the eyes since this preparation is not formulated for ophthalmic use.

Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes of visual disturbances which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Skin
Suitable precautions should be taken in using topical corticosteroids in patients with stasis dermatitis and other skin diseases with impaired circulation.

Prolonged use of corticosteroid preparations may produce striae or atrophy of the skin or subcutaneous tissue. If this occurs, treatment should be discontinued.

7.1 Special Populations

7.1.1 Pregnant Women

There are no adequate and well-controlled studies in pregnant women on teratogenic effects of a topically applied combination of clotrimazole and betamethasone dipropionate. Therefore, TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Drugs containing corticosteroids should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

7.1.2 Breast-feeding

Since it is not known whether the components of TARO-CLOTRIMAZOLE/ BETAMETHASONE DIPROPIONATE are excreted in human milk, caution should be exercised when this product is administered to a nursing woman.

7.1.3 Pediatrics

Safety and effectiveness in children below the age of 12 have not been established with clotrimazome and betamethasone dipropionate.

The use of TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE in diaper dermatitis is not recommended.

Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than mature patients because of greater absorption due to a larger skin surface area to body weight ratio.

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical dermatologics containing a corticosteroid to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The following adverse reactions have been reported in connection with the use of clotrimazole and betamethasone dipropionate: paresthesia in 5 of 270 patients (1.85%), maculopapular rash, edema, and secondary infection, each in 1 of 270 (0.37%) patients.

Adverse reactions reported with the use of clotrimazole are as follows: erythema, stinging, blistering, peeling, edema, pruritis, urticaria, and general irritation of the skin.

The following local adverse reactions are reported infrequently when topical corticosteroids are used as recommended. These reactions are listed in an approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria.

Systemic adverse reactions, such as vision blurred, have also been reported with the use of topical corticosteroids.

9 DRUG INTERACTIONS

9.1 Drug-Drug Interactions

Interactions of clotrimazole and betamethasone dipropionate with other drugs have not been established.

9.2 Drug-Herb Interactions

Interactions of clotrimazole and betamethasone dipropionate with herbal products have not been established.

9.3 Drug-Laboratory Test Interactions

Interactions of clotrimazole and betamethasone dipropionate with laboratory tests have not been established.

10 ACTION AND CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Betamethasone dipropionate with clotrimazole combines the anti-inflammatory, antipruritic and vasoconstrictive activity of betamethasone dipropionate with the antifungal activity of clotrimazole. The primary action of clotrimazole is against dividing and growing organisms, possibly through reaction with the cell membrane.

10.2 Pharmacodynamics

Betamethasone dipropionate was compared with other fluorinated topical corticosteroids in the McKenzie/Stoughton vasoconstrictor test. In this test, betamethasone dipropionate was significantly more active ($p < 0.05$) than fluocinolone acetonide, fluocortolone caproate plus fluocortolone, flumethasone pivalate and betamethasone valerate. The results showed betamethasone dipropionate to be active in a concentration of 0.000016%, the lowest concentration tested which showed activity.

10.3 Pharmacokinetics

Betamethasone Dipropionate
Betamethasone dipropionate, as is characteristic of a corticosteroid, is absorbed through the skin, becomes highly but reversibly bound to plasma proteins, is metabolized at both hepatic and extrahepatic sites to yield mostly inactive substances and is almost completely excreted within 72 hours.

In rats and mice with intact skin, only about 10% of the applied dose of betamethasone dipropionate is absorbed. In skin with the stratum corneum removed, betamethasone is about 90% absorbed when applied cutaneously. The absorbed portion of the steroids is distributed rapidly and found in all organs within 24 hours of administration. By 48 hours, nearly 90% of the initial dose was excreted with the remaining portion found in organs of the digestive tract and kidneys. In rodents, betamethasone dipropionate or its metabolites were excreted

predominantly in the feces. The high levels found in the feces indicates that betamethasone dipropionate is metabolized by the liver and excreted in the bile. The two major metabolites of betamethasone dipropionate were shown to be betamethasone 17- propionate and 6 beta 17-propionate and 6 beta-hydroxybetamethasone17-propionate.

Clotrimazole

The percutaneous absorption of clotrimazole was examined in humans with radiolabelled clotrimazole (1% cream). The results demonstrated that the highest concentration of clotrimazole remained in the epidermis, particularly the stratum corneum. Very low subcutaneous levels of the drug were detected, and 48 hours after application, serum concentrations were below the detection level of the assay (0.001 mg/L). Urine concentration of the drug was consistently below 0.5% of the radioactivity applied to the skin. Negligible systemic absorption of the drug after intravaginal insertion of one (1) 100 mg tablet was found. The average serum level 24 hours after insertion was approximately 0.03 mg/L. When given orally, however, clotrimazole is rapidly and nearly completely absorbed and distributed throughout the body within hours. The highest concentrations of the drug were found in the liver, adipose tissue and skin. In the rat, the clotrimazole absorbed is eliminated predominantly (more than 90%) in the feces within 48 hours. In man, nearly 25% of the drug is excreted in the urine with the rest excreted in the feces by six (6) days.

11 STORAGE, STABILITY AND DISPOSAL

Store between 15°C and 30°C.

PART II: SCIENTIFIC INFORMATION

12 PHARMACEUTICAL INFORMATION

Drug Substance

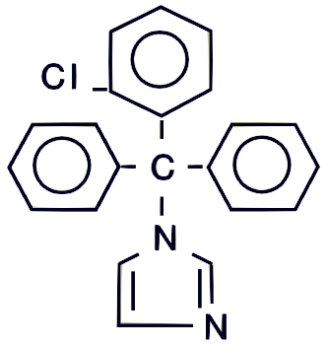
Drug Substance: Clotrimazole

Proper Name: Clotrimazole

Chemical Name(s): I. 1-[(2-Chlorophenyl)diphenylmethyl]-1*H*-imidazole

II. 1-(*o*-Chloro-α,α-diphenylbenzyl)imidazole

Structural formula:



Empirical formula: $C_{22}H_{17}ClN_2$

Molecular weight: 344.8 g/mol

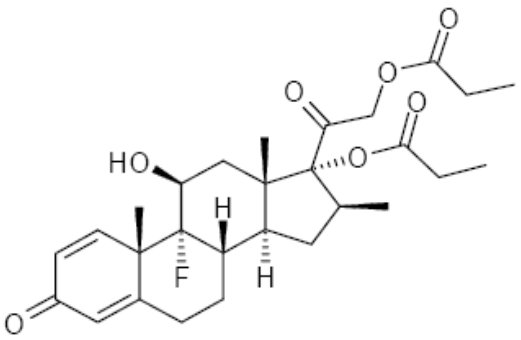
Description: White to off-white crystalline powder.

Drug Substance: Betamethasone dipropionate

Proper Name: Betamethasone dipropionate

Chemical name: 9-Fluoro-11β, 17,21-trihydroxy-16β-methylpregna-1, 4-diene-3,20-dione 17,21-dipropionate

Structural formula:



Empirical formula: $C_{28}H_{37}FO_7$

Molecular weight: 504.6 g/mol

Description: Betamethasone dipropionate is a white to off white powder.

13 MICROBIOLOGY

In vitro, clotrimazole exhibits fungistatic and fungicidal activity against isolates of *Trichophyton rubrum*, *Trichophyton mentagrophytes*, *Epidermophyton floccosum* and *Microsporum canis*. In general the *in vitro* activity of clotrimazole corresponds to that of tolnaftate and griseofulvin against the mycelia of dermatophytes (*Trichophyton*, *Microsporum*, and *Epidermophyton*).

At concentrations of <2 μg/mL clotrimazole was fungicidal for many isolates of *Candida albicans*, *Trichophyton sp.*, *Microsporum sp*. *and Epidermophyton sp*. At concentrations <5 μg/mL clotrimazole was fungistatic for other isolates of these species. Addition of bovine serum to the culture media at a final concentration of 30% resulted in somewhat higher MIC's of clotrimazole.

In vivo studies in guinea pigs infected with *Trichophyton mentagrophytes* have shown no measurable loss of clotrimazole activity due to combination with betamethasone dipropionate.

Strains of fungi having a natural resistance to clotrimazole have not been reported.

No single-step or multiple-step resistance to clotrimazole has developed during successive passages of *Trichophyton mentagrophytes*.

In studies of the mechanism of action in fungal cultures, the minimum fungicidal concentration

of clotrimazole caused leakage of intracellular phosphorous compounds into the ambient medium with concomitant breakdown of cellular nucleic acids, and accelerated potassium efflux. Both of these events began rapidly and extensively after addition of the drug to the cultures.

14 NON-CLINICAL TOXICOLOGY

Acute Toxicity:
Oral LD_{50} of clotrimazole and betamethasone dipropionate in male and female rats and mice was greater than 40 mL/kg, equivalent to 35.2 grams of clotrimazole and betamethasone dipropionate cream/kg when animals were given a single oral dose. Compound-related findings within 48 hours of dosing included rough hair coat, diarrhea, hypoactivity and hypothermia in several rats. Hypoactivity and ptosis occurred within 4 hours in the majority of mice dosed.

Subacute Dermal Toxicity Studies (Rabbits):
In two (2) simultaneous studies, New Zealand White rabbits with intact or abraded skin were used. In each study, 15 male and 15 female rabbits were assigned to five (5) groups (3/sex/group). Two (2) of these groups were dosed by applying clotrimazole and bethamethasone dipropionate over approximately 1.5% and 10% of the body surface at total daily doses of 0.15 and 0.5 g/kg (0.75 and 0.25 g/kg b.i.d.) respectively for 21-25 consecutive days. Two (2) additional groups were dosed in a similar manner over approximately 10% of the body surface with either 10% clotrimazole or vehicle cream at 0.5 g/kg and served as a comparative or vehicle control group. A fifth group remained untreated. Doses were approximately 9 and 31 times the proposed human daily dose.

Signs of corticosteroid activity in clotrimazole and betamethasone dipropionate -dosed rabbits included:1) progressive skeletal muscle wasting (slight to moderate in low-dose and slight to severe in high-dose rabbits); 2) distended abdomen; 3) marginal decreases in hematocrit, hemoglobin and erythrocytes; 4) moderate to marked decreases in lymphocytes; 5) moderate to marked decreases in serum glucose, alkaline phosphatase, SGOT and SGPT; and 6) marginal increases in blood urea nitrogen. Signs of minimal dermal irritation were observed in all dosed rabbits which included wrinkling and drying of the skin and transient, sporadic episodes of very slight to moderate erythema at the application site. In addition, papules progressing to scabs were observed intermittently on most vehicle and clotrimazole control rabbits. In contrast, papules occurred in only four (4) clotrimazole and betamethasone dipropionate-dosed rabbits (high- dose, intact). Thickening of the skin at the application site was observed in all clotrimazole- dosed rabbits and was not observed in any of the other rabbits.

The principal compound-related changes observed at necropsy for clotrimazole and betamethasone dipropionate-dosed animals (low and high dose groups) were: muscle wasting, enlarged, friable, pale or discoloured livers, reduced size of the spleen, lymph nodes, testes, thymus, adrenals, prostate and thyroids, pale kidneys and reduced thickness of the skin at the application site.

Thickening of the skin at the application site was observed for several vehicle control and the majority of the clotrimazole control rabbits. Decreased absolute and/or relative weights were recorded for the following organs/tissues of clotrimazole and betamethasone dipropionate low and high-dose rabbits: adrenals, prostate, testes and skeletal muscle. Increased kidney and liver

weights also occurred in these groups. Organ weight changes for clotrimazole-dosed rabbits included increased weights of the adrenals (abraded only), kidneys, liver (abraded only), and prostate, and decreased weights of the testes (intact only).

Histopathological examination revealed the following changes in the clotrimazole and betamethasone dipropionate low and high dose rabbits: 1) atrophy of the adrenal cortex; 2) bone resorption; 3) hypocellularity of bone marrow 4) atrophy of the thymus, spleen, lymph nodes, testes and thyroid; 5) myodegeneration of the muscle (primarily in high dose rabbits); 6) thinning of the untreated epidermis; 7) vacuolization of renal cortical tubular epithelium. Such observations are not unexpected following treatment with a corticosteroid and are consistent with the observations made throughout the study.

These data indicate that under the conditions of this study, clotrimazole and betamethasone dipropionate were relatively well tolerated locally when applied topically to rabbits with intact or abraded skin. In fact, dermal irritation was shown to be less severe for clotrimazole and betamethasone dipropionate than that observed for rabbits treated with clotrimazole alone. The systemic changes observed with clotrimazole and betamethasone dipropionate were expected and are typical of those observed after topical administration of corticosteroids.

Reproduction and Teratology:
Betamethasone Dipropionate
In animals, betamethasone dipropionate has been shown to interfere with fetal development in a manner typical of corticosteroids when administered to mice, rats and rabbits at doses in excess of those recommended for man.

Animals were treated intramuscularly with dose levels between 0.324 - 32.5 mg/kg for mice, 1-2 mg/kg for rats and 0.002 - 0.8 mg/kg for rabbits.

In rats, there were no indications of adverse effects on either the dams or the pups, but in both the mouse and rabbit, teratogenic effects typical of corticosteroids were observed.

Clotrimazole
Studies in pregnant rats with intravaginal doses up to 100 mg/kg have revealed no evidence of harm to the fetus due to clotrimazole.

High oral doses of clotrimazole in rats and mice ranging from 80 to 120 mg/kg resulted in embryotoxicity (possibly secondary to maternal toxicity), impairment of mating, decreased litter size and number of viable young and decreased pup survival to weaning. However, clotrimazole was not teratogenic in mice, rabbits and rats at oral doses up to 200, 180 and 100 mg/kg, respectively. Oral absorption in the rat amounts to approximately 90% of the administered dose.

Mutagenicity:
In tests for mutagenesis, chromosomes of the spermatophores of Chinese hamsters which have been exposed to clotrimazole were examined for structural changes during the metaphase. Prior to testing, the hamsters had received five oral clotrimazole doses of 100 mg/kg body weight. The results of this study showed that clotrimazole had no mutagenic effect.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

PrTARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE
Clotrimazole and Betamethasone Dipropionate Cream

Read this carefully before you start taking TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE 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 TARO-CLOTRIMAZOLE/ BETAMETHASONE DIPROPIONATE.

What is TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE used for?
TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE is used to treat the following skin infections caused by a fungus:

- athlete's foot (tinea pedis)
- jock itch (tinea cruris)
- ringworm (tinea corporis)

How does TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE work?
TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE contains two medicines, betamethasone dipropionate and clotrimazole.
Clotrimazole interferes with the growth of the fungus that is causing your skin problem.
Betamethasone dipropionate reduces the swelling, redness and itching of your skin.

What are the ingredients in TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE?
Medicinal ingredients: betamethasone dipropionate and clotrimazole
Non-medicinal ingredients: purified water, cetostearyl alcohol, white petrolatum, mineral oil, cetomacrogol 1000, phosphoric acid, monobasic sodium phosphate, propylene glycol, benzyl alcohol as preservative and sodium hydroxide to adjust the pH.

TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE comes in the following dosage forms:
As a cream containing 0.05 % betamethasone dipropionate and 1.0 % clotrimazole.

Do not use TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE if you:

- are allergic to betamethasone dipropionate or clotrimazole
- are allergic to any of the other ingredients in TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE or to a component of the container
- are allergic to a medicine similar to that in TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE called a corticosteroid or an imidazole
- have any untreated skin infection
- have certain viral diseases such as herpes simplex, chicken pox or vaccinia

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

- are pregnant or planning on becoming pregnant. It is not known if TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE can harm your unborn baby. Your health care professional will decide whether giving you TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE outweighs the potential risk to the unborn baby.
- are breastfeeding or planning to breastfeed. It is not known whether TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE can pass into your breastmilk. Your healthcare professional will decide whether you should stop breastfeeding or stop the use of TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE.
- have diseases of your skin that are caused by poor blood flow. An example is a disease called stasis dermatitis.

Other warnings you should know about:

Use in children:

It is not known if TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE is safe and effective in children less than 12 years of age. Use of TARO-CLOTRIMAZOLE/ BETAMETHASONE DIPROPIONATE in children should be limited. Long-term use of this medicine may affect your child's hormones. This may affect your child's growth and development. TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE cream should not be used to treat diaper rash or redness. You should avoid applying TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE cream in the diaper area of a child.

Eyes:

Do not use TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE in or near your eyes. Talk to your healthcare professional if you develop blurred vision or other eye problems while using TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE.

Skin:

Do not use too much TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE on large areas of your body. Talk to your healthcare professional if you develop sensitive skin or irritation, extremely dry skin, scaling or flaking of your skin or stretch marks (striae). These symptoms may happen if you use TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE for a long time. Your healthcare professional may need to stop your treatment.

Use of too much TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE on large areas of the skin or for too long may lead to serious problems. These include changes in your hormone levels, Cushing's disease, a condition where your body produces too much cortisol and changes in your sugar levels. You should not use too much TARO-CLOTRIMAZOLE/ BETAMETHASONE DIPROPIONATE on large areas of your skin. Talk to your healthcare professional if you are not sure how to safely apply TARO-CLOTRIMAZOLE/ BETAMETHASONE DIPROPIONATE.

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

How to take TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE:

- Follow all instructions given to you by your healthcare professional.
- Apply a thin layer to the affected and surrounding skin area.
- Make sure the cream covers the entire affected area.
- Do not cover the treated areas with a bandage, plaster or wrap of any kind. This can lead to serious side effects.
- The use of TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE for longer than four weeks is not recommended.

Usual dose:
TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE should be applied twice a day, in the morning and at night. It is usually applied for two weeks for jock itch (tinea cruris) and ring worm (tinea corporis). It is usually applied for four weeks for athlete's foot (tinea pedis). Your healthcare professional will tell you exactly for how long you should use TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE. It is not recommended that TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE be used for longer than four weeks.

Overdose:

If you think you have applied too much TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed dose
If you miss a dose, apply it as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. Do not apply a double dose to make up for a missed dose.

What are possible side effects from using TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE?
These are not all the possible side effects you may feel when using TARO-CLOTRIMAZOLE/ BETAMETHASONE DIPROPIONATE. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include the following:

- Burning, itching, irritation, dryness, blistering, stinging, redness or swelling of the skin
- New skin infection
- Thinning of the skin
- Swelling of the hair follicles
- Excessive hair growth
- Acne outbreaks that result in redness and blushing
- Patches of lighter skin tone
- Skin redness around the mouth

- Rash
- Stretch marks (striae)
- Peeling of the skin
- Hives
- General skin irritation
- A feeling of tingling or of pins and needles on your skin (paresthesia)
- Blurred vision

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 between 15°C and 30°C.

Keep out of reach and sight of children.

If you want more information about TARO-CLOTRIMAZOLE/BETAMETHASONE DIPROPIONATE:

- 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 www.taro.ca, or by calling 1-800-268-1975.

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