PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

PrTARO-FUSIDIC ACID

Fusidic acid cream

Cream, 2% w/w Fusidic acid
(as hemihydrate), Topical

Taro Standard

Antibiotic

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

For use in the treatment of primary and secondary skin infections caused by sensitive strains of Staphylococcus aureus, Streptococcus spp and Corynebacterium minutissimum. Primary skin infections that may be expected to respond to treatment with Taro-Fusidic Acid (fusidic acid cream) include: impetigo contagiosa, erythrasma and secondary skin infections such as infected wounds and infected burns.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of fusidic acid and other antibacterial drugs, Taro-Fusidic Acid should be used only to treat infections that are proven or strongly suspected to be caused by bacteria.

Appropriate culture and susceptibility studies should be performed. However, while waiting results of these studies and, if antibiotic therapy is considered to be necessary, Taro-Fusidic Acid may be administered to those patients in whom an infection caused by susceptible bacteria is suspected. This antibiotic treatment may subsequently require modification once these results become available.

In addition, local concentrations of fusidic acid are active against other Corynebacteria spp. No cross-resistance has been observed to date between fusidic acid and other antibiotics presently in clinical use.

Resistance to fusidic acid has readily been induced in vitro. The development of resistance has also been shown to occur in the clinical setting.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

2 CONTRAINDICATIONS

Taro-Fusidic Acid (fusidic acid cream 2% w/w) is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including non-medicinal ingredient, or component of the container. For a complete listing, see Dosage Forms, Strengths, Composition and Packaging.

3 DOSAGE AND ADMINISTRATION

3.1 Administration

A small amount of Taro-Fusidic Acid (fusidic acid cream 2% w/w) should be applied to the lesion two to three times daily for 7-14 days. Whenever the lesion is to be covered with a gauze dressing, less frequent applications (1 or 2 daily) may be used. In impetigo contagiosa, it has

been shown to be unnecessary to remove the crusts before application of fusidic acid cream.

When required, incision and drainage of infected skin lesions should be carried out before treatment with Taro-Fusidic Acid.

4 OVERDOSAGE

For topically applied fusidic acid, no information concerning potential symptoms and signs due to overdose administration is available.

Systemic consequences of an overdose of the active substance after accidental oral intake are unlikely to occur. The amount of fusidic acid in one tube of Taro-Fusidic Acid does not exceed the oral daily dose of systemic treatment.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

5 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
topical	Fusidic acid 2% w/w (as hemihydrate) cream: white to off-white cream	Butylhydroxyanisole (E320), cetyl alcohol, glycerin, hydrochloric acid, mineral oil, polysorbate 60, potassium sorbate, purified water and white petrolatum

Packaging

Available in aluminium tubes of 30 g covered with internal epoxy lacquer. The tube has a re-closable white polypropylene screw cap.

6 WARNINGS AND PRECAUTIONS

General

Treatment of severe or refractory skin lesions should be supplemented with the administration of a systemic antibacterial agent. Use of topical antibiotics occasionally allows overgrowth of non-susceptible organisms. If this occurs, or irritation or sensitization develops, treatment with Taro-Fusidic Acid should be discontinued and appropriate therapy instituted.

Susceptibility/Resistance

Development of Drug-Resistant Bacteria

Prescribing Taro-Fusidic Acid in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of resistant

organisms.

Potential for Microbial Overgrowth
Bacterial resistance among *Staphylococcus aureus* has been reported to occur with the use of topical fusidic acid. As with all antibiotics, extended or recurrent use of fusidic acid may increase the risk of developing antibiotic resistance. Limiting therapy with topical fusidic acid to no more than 14 days at a time will minimize the risk of developing resistance.

Fertility
There are no clinical studies with topical fusidic acid regarding fertility. No effects in women of childbearing potential are anticipated, since systemic exposure following topically applied fusidic acid is negligible.

Skin
Taro-Fusidic Acid (Fusidic acid cream 2%) contains butyl hydroxyanisole, cetyl alcohol and potassium sorbate. These excipients may cause local skin reactions (e.g. contact dermatitis). Butyl hydroxyanisole may also cause irritation to the eyes and mucous membranes. Taro-Fusidic Acid should therefore be used with care when applied in the proximity of the eyes.

6.1 Special Populations

6.1.1 Pregnant Women

The safety of fusidic acid in the treatment of infections during pregnancy has not been established. There is evidence to suggest that following systemic administration the drug can penetrate the placental barrier. If the administration of Taro-Fusidic Acid to pregnant patients is considered to be necessary, its use requires that the potential benefits be weighed against the possible hazards to the foetus.

Animal studies have not demonstrated teratogenicity with fusidic acid.

6.1.2 Breast-feeding

The safety of fusidic acid for the treatment of infections in women who are breastfeeding has not been established.

Following systemic administration fusidic acid has been detected in the milk of nursing mothers.

The use of Taro-Fusidic Acid during lactation requires that the potential benefits be weighed against the risks to the nursing infant.

It is recommended to avoid applying Taro-Fusidic Acid on the breast to protect the nursing infant from unintentional oral drug uptake.

7 ADVERSE REACTIONS

7.1 Adverse Reaction Overview

In patients with dermatoses treated with sodium fusidate ointment (Sodium fusidate being the sodium salt of fusidic acid), mild irritation that did not usually require discontinuance of therapy has been occasionally reported. The application of sodium fusidate ointment to deep leg ulcers has been associated with pain. Reports of hypersensitivity reactions have been rare.

7.2 Post-Market Adverse Reactions

The following post-market adverse drug reactions have been reported from world wide experience with fusidic acid and sodium fusidate:

Conjunctivitis, Dermatitis (incl. dermatitis contact, eczema), Rash*, Pruritus, Uriticaria, Blister, Erythema, Angioedema, Hypersensitivity, Application site pain and Application site irritation.

*Various types of rash reactions such as erythematous, pustular, vesicular, maculo-papular and papular have been reported. Rash generalised has also occurred.

8 DRUG INTERACTIONS

No interaction studies have been performed. Interactions with systemically administered medicinal products are considered minimal as the systemic absorption of topical fusidic acid/ sodium fusidate is negligible.

9 ACTION AND CLINICAL PHARMACOLOGY

9.1 Mechanism of Action

The antibacterial action of fusidic acid results from the inhibition of bacterial protein synthesis. The drug interferes with amino acid transfer from aminoacylsRNA to protein on the ribosomes. Fusidic acid may be bacteriostatic or bactericidal depending on inoculum size. Although bacterial cells stop dividing almost within two minutes after contact with the antibiotic *in vitro*, DNA and RNA synthesis continue for 45 minutes and 1-2 hours, respectively.

Fusidic acid is virtually inactive against Gram-negative bacteria. The differences in activity against Gram-negative and Gram-positive organisms are believed to be due to a difference in cell wall permeability.

Mammalian cells are much less susceptible to inhibition of protein synthesis by fusidic acid than sensitive bacterial cells. These differences are believed to be due primarily to a difference in cell wall permeability.

10 STORAGE, STABILITY AND DISPOSAL

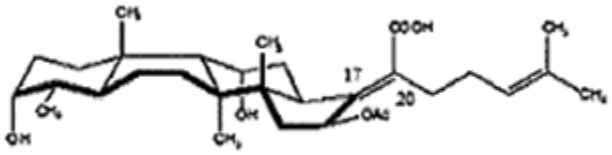
Store between 15°C to 30°C. Use within 28 days of first opening the tube. Dispense and store in original packaging.

PART II: SCIENTIFIC INFORMATION

11 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:	Fusidic Acid Hemihydrate
Chemical name:	*ent*-(17Z)-16α-(Acetyloxy)-3β,11β-dihydroxy-4β,8,14-trimethyl-18-nor-5β,10α-cholesta-17(20),24-dien-21-oic acid hemihydrate
Molecular formula:	$C_{31}H_{48}O_6 \cdot ½H_2O$
Molecular mass:	525.7 g/mol
Structural formula:	



Physicochemical properties: White to almost white crystalline powder, insoluble in water.

12 CLINICAL TRIALS

Comparative Studies

A randomized, double-blind, multiple-center, placebo-controlled, parallel design study comparing Taro-Fusidic Acid 2% (Taro Pharmaceuticals Inc.) to Fucidin® Cream 2% (Leo Pharma Inc., Canada) and both Active Treatments to a Placebo Control in the treatment of impetigo was performed in 335 eligible patients aged 1.5 to 80 years old with a clinical diagnosis of impetigo. A small amount of the cream was applied to the affected areas without a covering dressing 3 times daily for 7 days (21 applications).

The primary efficacy endpoint was the proportion of subjects in each treatment group with clinical cure at follow up visit (Day 14 ± 4 days; 7 days after End of Treatment). Bioequivalence was established if the continuity-corrected 95% Confidence Interval (CI) for the difference in cure proportions was contained within the interval [-2.20, +0.20] for the Per-Protocol (PP) population.

The secondary efficacy endpoints were: The proportion of subjects with clinical cure at the End of Treatment Visit (Day 7 + 3 Days); The proportion of subjects with bacteriological cure at the End of Treatment Visit (Day 7 + 3 Days); The proportion of subjects with bacteriological cure at the Follow-up Visit (Day 14 ± 4 Days; 7 days after the end of treatment)

The test product was determined to be clinically and therapeutically equivalent to the reference product for all efficacy endpoints. The superiority of the active treatments over Vehicle was also demonstrated for all endpoints. Results of the efficacy analyses are summarized in the table below.

Summary of Efficacy Analysis Results

Primary Endpoint: Clinical Cure at Follow-up Visit 7 days Post-treatment			
Parameter	**Test**	**Reference**	**Vehicle**
Per protocol (PP) Population			
n	119	118	
Clinical Cure Percent	90.8	97.5	
Percent Difference	-6.70		
95% CI	(-13.47, 0.07)		
Modified Intent to Treat (mITT) Population			
n	123	118	55
Clinical Cure Percent	90.2	97.5	52.7
Percent Difference	37.52	44.73	
p-value vs Vehicle	<0.0001	<0.0001	
Secondary Endpoint: Clinical Cure at End of Treatment Visit			
Parameter	**Test**	**Reference**	**Vehicle**

Per protocol (PP) Population			
n	119	118	
Clinical Cure Percent	66.4	72.9	
Percent Difference	-6.49		
95% CI	(-19.02, 6.03)		
Modified Intent to Treat (mITT) Population			
n	123	118	55
Clinical Cure Percent	65.9	72.9	36.4
Percent Difference	29.49	36.52	
p-value vs Vehicle	0.0001	<0.0001	
Secondary Endpoint: Bacteriological Cure at Follow-up Visit 7 days Post-treatment			
Parameter	**Test**	**Reference**	**Vehicle**
Per protocol (PP) Population			
n	119	118	
Bacteriological Cure Percent	93.3	99.2	
Percent Difference	-5.88		
95% CI	(-11.51, -0.24)		
Modified Intent to Treat (mITT) Population			
n	123	118	55
Bacteriological Cure Percent	93.5	99.2	58.2
Percent Difference	35.31	40.97	
p-value vs Vehicle	<0.0001	<0.0001	
Secondary Endpoint: Bacteriological Cure at End of Treatment Visit			
Parameter	**Test**	**Reference**	**Vehicle**
Per protocol (PP) Population			
n	119	118	
Bacteriological Cure Percent	93.0	99.1	
Percent Difference	-6.16		
95% CI	(-12.01, -0.32)		
Modified Intent to Treat (mITT) Population			
n	123	118	55
Bacteriological Cure Percent	93.2	99.1	56.6
Percent Difference	36.56	42.54	
p-value vs Vehicle	<0.0001	<0.0001	

CI = confidence interval.

13 PHARMACOLOGY

Fusidic acid/ sodium fusidate shows strong surface activity and is also fat soluble (Stewart, 1964). Using titriated sodium fusidate ointment, Hart (1978) demonstrated the systemic absorption of the ointment applied to the shaved backs of rabbits. Pre-treatment with 1% sodium lauryl sulfate in petroleum jelly increased absorption by from 0.02% to 0.16% to 0.2% to 3.4%. Vickers (1969) using excised human skin demonstrated penetration by fusidic acid and by sodium fusidate comparable to that seen with glucocorticoids. This was later confirmed by Knight (1969). In 1968, Kjelstrup demonstrated the penetration and accumulation of fusidic acid/ sodium fusidate in subcutaneous infected tissue in cases of atheromas. Penetration has also been demonstrated in the skin of an amputated finger, as well as in treated fingers and in bone periosteum.

14 MICROBIOLOGY

In Vitro Studies

Fusidic acid/ sodium fusidate is active in vitro against Gram-positive bacteria and Neisseria species, but has almost no antibacterial activity against Gram-negative organisms. The in vitro susceptibility against a range of clinical isolates is illustrated in Table 1.

In vitro sensitivity to fusidic acid/ sodium fusidate can be determined by the Kirby-Bauer disc diffusion methods using discs containing 10 mcg sodium fusidate.

N.B.: It is important to note that this sensitivity test is invalid if blood is present on the agar medium employed as fusidic acid/ sodium fusidate becomes bound to protein, even in the presence of a very small amount of blood.

The following criteria have been recommended for interpreting the results for Staphylococcus aureus:

Sensitive Organisms
Zone equal to or greater than 20 mm diameter (equivalent to an M.I.C. of 2 mcg/mL or less).

Resistant Organisms
Zone equal to or less than 19 mm diameter. Streptococcal isolates showing inhibition zones of 12-18 mm diameter may be considered as sensitive to fusidic acid/ sodium fusidate.

Table 1. Spectrum of In Vitro Activity of Sodium Fusidate

Species	No. of strains tested	Cumulative percentage of strains inhibited by given concentration of sodium fusidate (in mcg/mL)**										Activity Range in mcg/mL
		0.015	0.03	0.06	0.12	0.25	0.5	1	2*	4	8	
Staph. aureus (penicillin sens.)	149	-	11	50	74	98	100	100	100	100	100	0.03 - 0.3
Staph. aureus (penicillin resist.)												
Strep. pyogenes	10	-	-	-	-	-	-	-	-	40	100	4 - 16
Strep. pneumoniae	13	-	-	-	-	-	-	-	8	46	100	2 - 16
Strep. faecalis	8	-	-	-	-	-	-	13	13	100	100	1 - 8
N. gonorrhoeae	102	-	9	19	30	47	76	92	96	99	100	0.03 - 4
N. meningitidis	108	18	51	81	92	98	100	100	100	100	100	0.015 - 0.5
Clostridium spp.	42	-	-	21	50	74	88	100	100	100	100	0.06 - 1.0
Peptostrep. spp.	15	-	-	13	40	67	73	93	100	100	100	0.06 - 2
Bacteroides fragilis	83	-	-	-	-	1	4	31	80	89	94	0.25 - 16
Bacteroides spp.	72	-	-	7	14	29	47	60	79	90	94	0.06 - 16
Corynebacterium spp.	118	-	-	77	79	-	-	87	-	98	-	0.06 - 12.5

* isolates with MIC's greater than 2 mcg/mL are considered to be insensitive at those serum concentrations achievable with normal doses of fusidic acid/ sodium fusidate.
** Expressed as sodium fusidate

The possibility of synergism between sodium fusidate and other antibiotics has been tested in meat infusion broth inoculated with sensitive strains of Staphylococcus aureus. Synergism has been demonstrated with penicillin V, penicillin G, erythromycin and picromycin.

In another experiment, the M.I.C.'s of combinations of benzyl penicillin or methicillin with fusidic acid were determined by the serial-dilution tube titration method. When the penicillin was added 2 hours before fusidic acid, the combination was synergistic. However when penicillin was added at the same time or later than fusidic acid, the two agents acted antagonistically. It has been suggested that these apparently opposing effects occur because fusidic acid rapidly inhibits protein synthesis, but the action of penicillin requires active cell growth. Fusidic acid and methicillin act antagonistically against staphylococcal strains which are susceptible to methicillin but not in methicillin-resistant strains.

Synergism between the penicillins and fusidic acid has only been observed with strains of Staphylococcus aureus that produce small amounts of penicillinase and not with penicillinase-stable penicillins.

In Vivo Studies

Mice Protection: Sodium fusidate, administered orally at levels of 20 to 2500 mcg per dose was tested in vivo in mice infected with a penicillin-resistant strain of Staphylococcus aureus, Streptococcus pyogenes C 203 or Mycobacterium tuberculosis, var. bovin, strain Ravenel. Sodium fusidate was active against Staphylococcus aureus at all levels, but active against Streptococcus pyogenes C 203 only at levels of 313 mg/dose and above. The drug did not prolong survival times of mice infected with Mycobacterium tuberculosis.

In another study, groups of mice were infected intraperitoneally with Streptococcus pyogenes C 203, Staphylococcus aureus (penicillin-resistant and penicillin-sensitive) or Diplococcus pneumoniae SV.1. When 1 dose of 250 mg/kg sodium fusidate was administered orally 24 or 6 hours prior to the staphylococcal infection, it protected 60% and 80% of the mice treated, respectively. When the single dose of sodium fusidate was administered 4, 2 and 1 hour pre-infection or at the time of infection, 100% of the mice were protected. Sodium fusidate administered subcutaneously failed to protect the mice against Streptococcus pyogenes C 203 and Diplococcus pneumonia infections, regardless of the time of administration. Single subcutaneous and oral doses of sodium fusidate, vernamycin B and erythromycin (4.0, 20.0 and 100 mg/kg) were tested in corticosterone-treated mice which had been infected intradermally with 2 strains of Staphylococcus aureus, all three drugs protected the animals from lesions with the 20 mg/kg s.c. dose when given one hour after infection. When administered subcutaneously one hour pre-infection, erythromycin was 5 times more active.

With the oral route, all three drugs provided complete protection with 100 mg/kg given at the time of infection, but 500 mg/kg or more was required when the drugs were administered 3 to 6 hours post-infection. When the same three drugs were tested against an intraperitoneally-induced staphylococcal infection, erythromycin was the most active drug.

Rabbit Protection: Rabbits were inoculated intradermally for 3 days with two different strains of Staphylococcus. When infection was induced 24 hours before the administration of sodium

fusidate (32.5, 125 or 500 mg/kg), no beneficial effects on the induced lesions were observed; however, when the staphylococcal lesions were produced at the same time or 24 hours following drug administration, erythema was limited and the size of the lesions remained constant throughout the test period (1 week) for all dose levels.

Resistance in vivo

Although resistance to fusidic acid/ sodium fusidate has been rapidly induced in vitro, resistant strains have only occasionally been observed in the clinical setting. In one study, only 3 out of 1025 naturally occurring strains of Staphylococcus aureus were found to be resistant to fusidic acid/ sodium fusidate. In another study, only 10 out of 2700 clinical isolates of Staphylococcus showed resistance to fusidic acid/ sodium fusidate and all 10 strains were coagulase-positive Staphylococci. The degree of resistance exhibited by these strains was comparable to the resistance shown by various mutants in vitro.

Resistant strains of Staph. aureus have emerged following systemic treatment with fusidic acid/ sodium fusidate. In one study resistant strains of Staph. aureus emerged in 6 of 13 burn patients treated with 500 mg fusidic acid/ sodium fusidate two or three times daily for 7 days.

15 TOXICOLOGY

Acute Toxicity
The following Table summarizes the acute toxicity data obtained for mice and rats:

DRUG FORM TESTED	SPECIES	ROUTE OF ADMINISTRATION	NO. OF ANIMALS	LD_{50} (mg/kg)
Sodium fusidate	Mouse	Oral	-	975
	Mouse-M	Oral	50	2150
	Mouse-M	Oral	190	2045
	Mouse-F		115	2100
	Mouse	Subcutaneous	-	313
	Mouse	Intravenous	-	205
	Mouse-M	Intravenous	80	180
	Mouse-F	Intravenous	175	190
	Mouse-M		90	175
	Mouse	Intraperitoneal	-	170
	Rat	Oral	11	2700
Fusidic acid	Mouse	Oral	-	5400
	Mouse	Intraperitoneal	-	355
	Rat Adults Pups	Oral	 10 10	 2263 443
Diethanolamine	Mouse	Intravenous	10	232
Fusidate	Rat	Intravenous	10	192

The signs and symptoms of toxicity of fusidic acid and its salts in mice were decreased activity, ataxia and convulsions; in rats, the only symptoms preceding death were decreased activity and slight salivation.

Dogs: Sodium fusidate was administered as a 10% solution by stomach tube to 2 fasted dogs in single doses of 250 and 500 mg/kg, respectively. Two other fasted dogs received the drug in the form of gelatin capsules in doses of 500 and 1500 mg/kg, respectively.

No effects were noted in the dogs receiving 500 mg/kg by capsules. The remaining 3 dogs vomited within 8 to 60 minutes; the dog given 1500 mg/kg was lethargic for 12 hours, but no other effects were observed during a 7 day observation period. A dose-dependent increase in BSP retention times was observed.

Subacute Toxicity

Rats: Sodium fusidate was administered in the diet of 2 groups composed of 5 male and 5 female rats at doses of 0 or 270 mg/kg/day for 4 weeks. A similar group received 500 mg/kg/day for 1 week and subsequently 1200 mg/kg/day for 3 weeks. None of the animals died during testing and no significant lesions attributable to the drug were found. Except for a slight to moderate weight retardation in males in the high dose group, the average rates of growth of the treated animals were comparable to those of the controls.

Dogs: Sodium fusidate was administered in the diet of 3 groups of 2 dogs each. One group served as the control; another group was dosed at 110 mg/kg/day for 4 weeks and the third group at 250 mg/kg for 1 week followed by 470 mg/kg/day for the next 3 weeks. None of the dogs showed any significant gross or micropathological alterations which were considered to be drug-related.

During the second and third weeks, one of the 2 dogs on the low dose showed reduction in appetite which was apparently due to poor palatability of the drug. One of the 2 dogs showed a slight weight loss. In the high dose group reductions in appetite limited drug intake to an average of 470 mg/kg/day. Both these animals had small weight losses, probably associated with reduced food intake.

Chronic Toxicity

Rats: Sodium fusidate was administered in the diet to 4 groups of 40 rats at doses of 0, 200, 420 or 840 mg/kg daily for 34 weeks. High dose females and to a lesser degree, high dose males showed a small retardation of weight gain. Slight neutrophilia was also noted in both high dose males and females. Ten of the 14 high dose males showed mild fatty metamorphosis of the liver without significant cytopathological change.

In another study, rats received sodium fusidate administration orally at a dose of 200 mg/kg/day for 24 weeks. No influence on growth or hematology and no other toxic effects were observed.

In a third study, fusidic acid was administered orally to a group of 25 male and 25 female rats at a dose of 400 mg/kg/day, 6 days a week for 5 months. No hematological changes or other toxic effects were noted.

Guinea Pigs: No toxic effects were seen when sodium fusidate was administered orally to guinea pigs at doses of 80 mg/kg/day for 50 days.

Dogs: Sodium fusidate was included in the diet of 4 groups of 5 dogs in amounts to result in doses of 0, 90, 190 or 300 mg/kg for 26 weeks. Significant changes observed were: weight loss with significantly reduced appetite in one animal on the high dose; however, all other test animals maintained or gained weight comparable to the control group in spite of slightly reduced food intake ascribed by the investigator to poor palatability; one dog on the high dose showed

definite increases in plasma bilirubin and BSP; one dog on the intermediate dose showed slight to moderate increases in BSP, SGPT and alkaline phosphatase; one dog on the low dose showed a moderate increase in alkaline phosphatase and a slight increase in plasma bilirubin.

In another study, post-mortem examination revealed mild to moderate liver cell damage in one high dose dog (400 mg/kg/day) at 26 weeks, but the other animals showed no morphological changes with this dose attributable to the drug.

Fertility and Reproduction Studies

Two groups, each comprised of 20 male and 20 female rats, received either 0 or 400 mg/kg sodium fusidate per day for 2 weeks before mating to weaning. Caesarian sections were performed on half the dams on the 20th day; the remainder were allowed to deliver naturally.

There were no significant differences between the treated and control dams with respect to per cent resorptions, the condition of the uteri or the number and weights of the pups. No soft tissue abnormalities were found in the pups of either group but skeletal anomalies (control group 2 pups missing ribs and dosed group 1 pup occipital bone formation incomplete and 1 pub rib deformities) appeared in 4% of the pups in both groups. The viability and lactation indices, reflecting neonatal development, were higher in the treated group than the control group, but all values were within normal limits.

Teratology Studies

Mice: Pregnant mice were divided into 3 groups of 16-19 animals each and given daily doses of 20, 100 and 200 mg/kg sodium fusidate by gavage from the 6th to 15th day of gestation. Another group of 23 pregnant mice, serving as controls, received just water by gavage. On the 18th day of pregnancy, half the dams were sacrificed. The remainder was allowed to go to term.

Sex distribution of fetuses and young, fetal weight, birth weight and weight increase were normal and similar for all groups. The mean incidence of resorption was 1.2, 1, 0.5 and 0.6 per dam for the 20, 100 and 200 mg/kg groups and control group, respectively. Average litter size in the treated group did not differ significantly from that of the controls in any of the groups.

Rats: Pregnant rats were divided into 3 groups of 29-31 animals each and given daily doses of 20, 100 or 200 mg/kg sodium fusidate by gavage from the 3rd to the 15th day of gestation. Another group of 59 pregnant rats, serving as controls, received just water by gavage. On the 21st day of pregnancy, half the dams were sacrificed. The remaining dams were allowed to go to term.

The average rate of resorption was 1.2, 1.8, 1.7 and 1.3 per dam for the 20, 100 and 200 mg/kg and control groups, respectively. Litter size and sex distribution of the fetuses and young of the dosed animals were comparable to the controls with no dose-related differences. Birth weights and weight gain over a 4 month period were comparable for all groups. No fetal deformities were observed in any group.

Rabbits: Eighteen pregnant rabbits were treated orally with 125 mg sodium fusidate in tablet form once per day from the 6th to the 18th day of pregnancy. Eleven pregnant animals, serving as controls, received a placebo tablet each day. On the 30th day of pregnancy 9 treated animals

and 3 controls were sacrificed. The remaining animals were allowed to go to term.

Sex distribution of fetuses and young, fetal and birth weights and weight gain were normal and similar for both groups. Three dead foetuses were found in each of 2 treated animals and in 1 control animal. Average litter size was lower in the treated group (4.8 young per litter) than in the control group (7.6 young per litter). Macroscopic examinations of the young failed to reveal any teratogenic or other abnormalities.

Skin Tolerance Studies
Daily application of sodium fusidate to the ears of rabbits for a period of one month evolved neither general intolerance, local irritation to the eye, change in capillary permeability of the treated region, nor sensitization to the irritant effects of locally applied chloroform.

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PATIENT MEDICATION INFORMATION
READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

TARO-FUSIDIC ACID
Fusidic acid cream, Taro Standard
2% w/w

Read this carefully before you start taking **Taro-Fusidic Acid** 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-Fusidic Acid**.

What is Taro-Fusidic Acid used for?
Taro-Fusidic Acid is used to treat conditions where the skin is infected by germs (bacteria), such as:

- Impetigo (a weeping, crusty and swollen patch of skin)
- Erythrasma (brown, scaly patches of skin, usually in skin fold areas, such as armpits or under breasts)
- Infected cuts and burns

Antibacterial drugs like Taro-Fusidic Acid treat only bacterial infections. They do not treat viral infections. Although you may feel better early in your treatment, Taro-Fusidic Acid should be used exactly as directed. Misuse or overuse of Taro-Fusidic Acid could lead to the growth of bacteria that will not be killed by Taro-Fusidic Acid (resistance). This means that Taro-Fusidic Acid may not work for you in the future. Do not share your medicine.

How does Taro-Fucidic Acid work?

Taro-Fusidic Acid contains fusidic acid. It is an antibiotic which is used to kill bacteria that cause infections.

What are the ingredients in Taro-Fusidic Acid?

Medicinal ingredients:	2% w/w fusidic acid (as hemihydrate)
Non-medicinal ingredients:	Butylhydroxyanisole (E320), cetyl alcohol, glycerin, hydrochloric acid, mineral oil, polysorbate 60, potassium sorbate, purified water, white petrolatum.

Taro Fusidic Acid comes in the following dosage form:
Taro-Fusidic Acid is a white to off-white cream.

Do not use Taro-Fusidic Acid if:

- you are allergic to any ingredient in Taro-Fusidic Acid or to any component of the container.

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

- are pregnant or if you become pregnant during treatment with Taro-Fusidic Acid
- are breastfeeding or intend to breastfeed

Other warnings you should know about:

- Do not use Taro-Fusidic Acid more than 14 days.
- If you use Taro-Fusidic Acid more than 14 days the bacteria may become resistant to antibiotics.
- Taro-Fusidic Acid contains butylhydroxyanisole, cetyl alcohol and potassium sorbate as non-medicinal ingredients. These ingredients may cause a red, itchy rash (contact dermatitis) on your skin where Taro-Fusidic Acid is applied. Butylhydroxyanisole may also cause irritation to the eyes and mucous membranes (such as lips or genital area).
- Do not let Taro-Fusidic Acid get into your eyes. If the cream gets into the eye, this may lead to eye irritation.

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

The following may interact with Taro-Fusidic Acid:
The use of fusidic acid with other medicines has not been studied. However, since medicines can interact with each other, tell your healthcare professional if you are using other medicines to treat your skin infection.

How to take Taro-Fusidic Acid:
Usual dose:

- Without a covering dressing apply a small amount of Taro-Fusidic Acid to the affected area two to three times daily for 7-14 days.
- With a covering dressing: one or two applications daily may be enough.

It is not necessary to remove any crusts caused by impetigo before applying Taro-Fusidic Acid. Use Taro-Fusidic Acid exactly as directed. Do not apply more or less of it or apply it more often than prescribed by your healthcare professional.

Overdose:

If you think you, or a person you are caring for, have used too much or accidentally swallowed Taro-Fusidic Acid, contact a healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
If you forget to use Taro-Fusidic Acid, use it as soon as you remember. Next time, follow your regular application routine.

What are possible side effects from using Taro-Fusidic Acid?
These are not all the possible side effects you may feel when taking Taro-Fusidic Acid. If you

experience any side effects not listed here, contact your healthcare professional. Please also see Warnings and Precautions.

Side effects from using Taro-Fusidic Acid may include:

- Itching, burning sensation, irritation or pain in the area where the medication is used
- Various types of skin rashes (dermatitis)
- Skin redness
- Blistering of the skin
- Hives — also known as urticaria (a skin reaction that causes itchy welts)

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	
RARE **Allergic reactions (angioedema):** dizziness, itching, severe rash, swelling (mouth, throat, lips, hands), trouble breathing			□
Conjunctivitis: pink or red colour in the white of the eye(s), watery eyes, itchy or scratchy eyes, discharge from the eye(s), crusts on the eyelids or lashes		□	

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 at 15°C to 30°C. Use within 28 days of first opening the tube. Dispense and store in original packaging to ensure product stability.
Keep out of reach and sight of children and pets.

If you want more information about Taro-Fusidic Acid:

- 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://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.taro.ca or by calling 1-800-268-1975.

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