AUSTRALIAN PRODUCT INFORMATION – RESOLVE PLUS 1.0 (MICONAZOLE NITRATE, HYDROCORTISONE) CREAM

1 NAME OF THE MEDICINE

Miconazole nitrate, Hydrocortisone.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Miconazole nitrate 2%w/w; Hydrocortisone 1% w/w.

Contains phenethyl alcohol as preservative. For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

White, glossy cream.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Inflamed or itchy skin conditions such as: tinea; thrush; seborrheic dermatitis; thrush infected napkin rash; intertriginous eruptions; inflamed fungal infections where bacterial infection may be present.

For conditions without a significant inflammatory component an antifungal agent without hydrocortisone, such as Resolve Cream, should be used.

4.2 DOSE AND METHOD OF ADMINISTRATION

A small amount should be gently rubbed into the infected skin and surrounding area 2 times daily. Resolve Plus 1.0 cream should be used until the inflammation has subsided. Once inflammation has subsided continue with an antifungal agent without hydrocortisone, such as Resolve Cream, until symptoms disappear. Continue treatment with the antifungal agent without hydrocortisone for 14 days after symptoms disappear.

4.3 CONTRAINDICATIONS

- Do not use in the eyes
- Acne
- Hypersensitivity to miconazole nitrate, hydrocortisone, phenethyl alcohol or any other ingredient.
- Herpes and other viral diseases of the skin (such as chicken pox), perioral dermatitis and ulcerative skin conditions.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

For external use only. Avoid contact with eyes.

If hypersensitivity develops, discontinue use.

Long term corticosteroid use may increase the risk of hypothalamic-pituitary axis suppression, especially under occlusion. Use for longer than 4 weeks can cause atrophic striae, prolonged use on flexures and intertriginous areas is undesirable.

If an associated infection develops during the use of Resolve Plus 1.0 and does not respond to therapy, its use should be discontinued until the infection is adequately controlled.

Use in the elderly

No data available.

Paediatric use

This preparation is not recommended for use in children under 2 years of age.

The risk of systemic absorption, and hence systemic toxicity, is greater in children due to the higher permeation properties of the skin and a larger skin surface to body weight ration than adults.

Effects on laboratory tests

No data available.

Visual disturbance

Visual disturbance may be reported with systemic and topical 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 which may include cataract, glaucoma or rare diseases such as central nervous system chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No data available.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy – Pregnancy Category A

Hydrocortisone and miconazole nitrate are Category A drugs as defined in the Prescribing Medicines in Pregnancy Database, approved by the Australian Drug Evaluation Committee. Category A drugs are those which have been taken by a large number of pregnant women and women of child bearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Use in lactation

It is not known whether corticosteroids and miconazole are distributed into breast milk following topical application. However, Resolve Plus 1.0 cream should be used with

caution in breastfeeding mothers. If application to the breasts is required, then the product should be applied immediately after breastfeeding.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

After the application of Resolve Plus 1.0 cream a slightly stinging sensation may occasionally be noticed. This transient symptom is most likely to disappear after several applications. Other side effects (especially under occlusion) may include itching, redness, allergy, acneform eruptions and skin atropy (thinning of the skin).

Table 1: Adverse drug reactions in patients treated with miconazole and hydrocortisone cream

System organ class	Adverse drug reactions	
	Frequency category	
	Uncommon (≥ 1/1,000 to < 1/100)	Not known.
Immune system disorders		Anaphylactic reaction, hypersensitivity
Eye disorders		Vision, blurred
Skin and subcutaneous tissue disorders	Skin irritation, urticarial, pruritus	Angioedema, rash, contact dermatitis, erythema, skin inflammation, application site reaction
General disorders and administration site conditions	Irritability	

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

Resolve Plus 1.0 cream is a broad-spectrum anti-fungal and anti-inflammatory cream containing hydrocortisone 1% w/w and miconazole nitrate 2% w/w as the active ingredients. Hydrocortisone has anti-inflammatory, anti-eczematous, anti-allergic and anti-pruritic properties. Miconazole is particularly active against species of medical interest such as *Candida*, *Trichophyton*, *Epidermophyton*, *Microsporum*, *Pityrosporum*, other yeast-like fungi and dermatophytes as well as Gram positive bacteria such as *Streptococcus pyogenes* and *Staphylococcus aureus*.

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Miconazole nitrate is an antifungal agent that acts by altering the permeability of the cell membrane in sensitive fungi.

Hydrocortisone is an anti-inflammatory agent, the topical application of which often produces dramatic suppression of skin diseases in which inflammation or pruritis are prominent features.

Clinical trials

This information is not available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

The absorption of miconazole is not significant when applied topically.

Hydrocortisone is absorbed through the skin allowing penetration to the deeper layers. The extent of the absorption is greater for inflamed skin and other skin conditions such as eczema and psoriasis. Absorption is also greater in areas such as the ear, scrotum, axillae, face and scalp. Absorption is aided by occlusive dressing due to the resulting hydration of the skin. However, occlusive dressings may not be appropriate as the resulting warm and moist conditions provide a favourable environment for favourable growth. Once absorbed, the pharmacokinetics are similar to systemic steroids.

Metabolism

Hydrocortisone is metabolised in the liver, most likely by reduction of the 5,6 double bond and the C3 and C20 keto groups. The resultant hydroxyl derivatives are then conjugated with glucuronic acid.

Cortisone, an 11-keto-steroid is formed from hydrocortisone; the 11-keto-steroids are then reduced and conjugated to yield glucuronide metabolites. A small percentage of hydrocortisone is converted to the 17-keto-steroid. The C21 hydroxyl group is conjugated with sulphate.

Excretion

When radioactive-carbon, ring-labelled steroids are injected intravenously in man, most of the radioisotope is recovered in the urine within 72 hours. Neither bilary nor faecal excretion is of any quantitative importance in man. It has been estimated that the liver metabolises at least 70% of the hydrocortisone secreted.

Preclinical safety data

No data available.

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Refer to section 2 – Qualitative and quantitative composition.

1,3-Butylene glycol, cetostearyl alcohol, citric acid, dibasic sodium phosphate, dimeticone 350, disodium edetate, light liquid paraffin, PEG-40 stearate, phenethyl alcohol, povidone, purified water, self-emulsifying glyceryl monostearate, xanthan gum.

6.2 INCOMPATIBILITIES

Incompatibilities were not assessed as part of the registration of this product.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods. The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

10g, 15g and 30g laminate tubes.

Not all pack sizes may be marketed.

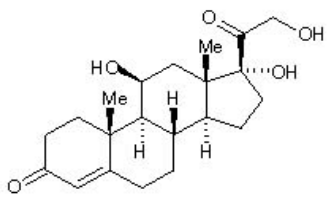
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

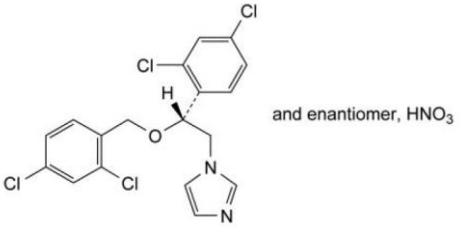
6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Hydrocortisone



Miconazole nitrate



CAS number

Hydrocortisone *CAS no. 50-23-7*

Miconazole nitrate *CAS no. 22832-87-7*

7 MEDICINE SCHEDULE (POISONS STANDARD)

S3

8 SPONSOR

Ego Pharmaceuticals Pty Ltd
21-31 Malcolm Rd
Braeside, Victoria 3195.

9 DATE OF FIRST APPROVAL

30/8/2000.

10 DATE OF REVISION

26/10/2018.

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.4	Addition of Visual disturbances to Special Warnings and Precautions for Use.
4.8	Addition of Visual disturbances to Adverse drug reactions Table 1.