PRODUCT LITERATURE

ARISONE CREAM 1%

Each 100 g contains
Hydrocortisone Acetate 1 g

Preservative
Methyl Paraben 0.1% w/w

Description
Odourless, soft white cream.

Pharmacodynamics / Pharmacokinetics
Hydrocortisone is an anti-inflammatory steroid. Its anti-inflammatory action is due to reduction in the vascular component of the inflammatory response and reduction in the formation of inflammatory fluid and cellular exudates. The granulation reaction is also decreased due to the inhibition effect of Hydrocortisone on connective tissue. Stabilisation of most cell granules and lysomal membranes decreases the mediators involved in inflammatory response and reduces release of enzymes in prostaglandin synthesis. The vasoconstrictor action of Hydrocortisone may also contribute to its anti-inflammatory activity.

Mechanism of action / Effect:
Corticosteroids diffuse across cell membranes and complex with specific cytoplasmic receptors. These complexes then enter the cell nucleus, bind to DNA (chromatin), and stimulate transcription of messenger RNA (mRNA) and subsequent protein synthesis of various inhibitory enzymes responsible for the anti-inflammatory effects of topical corticosteroids. These anti-inflammatory effects include inhibition of early processes such as edema, fibrin deposition, capillary dilatation, movement of phagocytes into the area, and phagocytic activities. Later processes, such as capillary production, collagen deposition, and keloid formation also are inhibited by corticosteroids. The overall actions of topical corticosteroids are catabolic. Factors that increase the clinical efficacy and potential for adverse effects of topical corticosteroids include enhancement of pharmacologic activity of the compound by altering molecular structure, increasing stratum corneum penetration of the compound, and increasing bioavailability of the compound from the vehicle.
The pharmacologic activity of topical corticosteroids is increased by several changes in molecular structure. Addition of a 9-alpha-fluorine atom increases the anti-inflammatory glucocorticoid activity, but simultaneously increases undesired mineralocorticoid activity. Mineralocorticoid activity is diminished by addition of a 16-hydroxy or 16-methyl group. Substitution or masking of 16- or 17-hydroxy groups with longer side chains such as acetonide, propionate, or valerate increases lipophilicity and subsequently stratum corneum penetration.

Absorption:
Absorbed systemically across the stratum corneum.
Stratum corneum penetration is primarily enhanced by increasing skin hydration and/or temperature, or by changes in molecular structure of the compound.
Hydrating the skin with occlusive dressings such as plastic wrap, a tight-fitting diaper or one covered with plastic pants, plastic tape, or dermatological patches can increase corticosteroid penetration by up to tenfold. Ointment bases inhibit evaporation of moisture from skin. Intertriginous areas (axillae and groin) are self-occluding. Intertriginous areas and the face also have inherently thinner skin, are more macerated and therefore, allow for increased absorption.
Absorption of topical corticosteroids has been greatly increased by altering the product vehicle or the drug substance itself. Vehicles containing substances that solubilize the corticosteroid enhance absorption. Increasing the concentration of the drug increases skin penetration but also may increase wastage of the drug. Decreasing drug particle size has been shown to increase topical bioavailability.
Increased percutaneous absorption of corticosteroids also occurs when the skin or mucosa is abraded or inflamed, when body temperature is elevated, with prolonged use, or with extensive use.
There is some systemic absorption of topical corticosteroids through the oral mucosa; absorption increases with increased potency and prolonged use.

Biotransformation:
Primarily in skin; once absorbed systemically, in the liver. Corticosteroids that contain substituted 17-hydroxyl groups or that are fluorinated are resistant to local metabolism in the skin. Repeated application results in a cumulative depot effect in the skin, which may lead to a prolonged duration of action, increased side effects, and increased systemic absorption.

Indication
For inflammatory condition responding to steroid therapy.

Application
Apply a thin layer on the affected area 2 - 3 times a day until complete resolution of lesion.

Route of Administration
Topical

Contraindications
Bacterial (e.g. impetigo), viral (e.g. Herpes simplex) or fungal (e.g. candidal or dermatophyte) infections of the skin.
Hypersensitivity to the active substance or to any of the excipients.
Use on the eyes and face, Ano-genital region, Broken or infected skin including cold sores, acne and athlete's foot.

Warnings and Precautions
1. There is no good evidence that topical corticosteroids are efficacious against immediate (Type 1) allergic skin reactions or short-lived weal and flare reactions from other causes.
2. Topical corticosteroids are ineffective in granulomatous conditions and other inflammatory reactions involving the deeper regions of the dermis.
3. Topical corticosteroids are not generally indicated in psoriasis excluding widespread plaque psoriasis provided that warnings are given.
Topical corticosteroids may be hazardous in psoriasis for a number of reasons including rebound relapses following development of tolerance, risk of generalised pustular psoriasis, and local and systematic toxicity due

to impaired barrier function of the skin. Careful patient supervision is important.
Although generally regarded as safe, even for long-term administration in adults, there is potential for overdosage in infants and children. Extreme caution is required in dermatoses of infancy especially napkin eruption where the napkin can act as an occlusive dressing and increase absorption . In infants and children, courses of treatment should therefore not normally exceed 7 days.
Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions, which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy, and a systemic administration of antimicrobial agents.

As with all corticosteroids, prolonged application to the face is undesirable.
Do not use under an occlusive dressing.
This medicinal product contains chlorocresol, which may cause allergic reactions.
This medicinal product also contains cetostearyl alcohol in the excipient cetomacrogol emulsifying wax, and may cause local skin reactions (e.g., contact dermatitis).

Topical steroid withdrawal syndrome:
Long term use of topical steroids can result in the development of rebound flares after stopping treatment (topical steroid withdrawal syndrome). A severe form of rebound flare can develop which takes the form of a dermatitis with intense redness, stinging and burning that can spread beyond the initial treatment area. It is more likely to occur when delicate skin sites such as the face and flexures are treated. Should there be a reoccurrence of the condition within days to weeks after successful treatment a withdrawal reaction should be suspected. Reapplication should be with caution and specialist advise is recommended in these cases or other treatment options should be considered.

The label will state mild steroid.

Interactions with Other Medicaments
None known

Pregnancy and Lactation:
Pregnancy
There is inadequate evidence of safety in human pregnancy. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intra-uterine growth retardation. There may therefore be a very small risk of such effects in the human foetus.

Breastfeeding
There is no evidence against use in lactating women. However, caution should be exercised when Hydrocortisone Cream is administered to nursing mothers. In this event, the product should not be applied to the chest area.

Side Effects / Adverse Reactions
Hydrocortisone preparations are usually well tolerated, but if any signs of hypersensitivity appear, application should stop immediately.

Striae may occur especially in intertriginous areas.

Skin and Subcutaneous Tissue Disorders: Not known (cannot be estimated from available data)

Withdrawal reactions - redness of the skin which may extend to areas beyond the initial affected area, burning or stinging sensation, itch, skin peeling, oozing pustules.

Overdose and Treatment
Not applicable

Storage
Store below 30°C in a dry place, protected from direct light.
Jauhkan daripada kanak-kanak
Keep away from reach of children.

CONTROLLED MEDICINE / UBAT TERKAWAL

Shelf Life
Expiry date: 2 years from date of manufacture

Packing
Packed in plastic container of 15g,30g,50 g and 450g.

Name and Address of Product Distributor:
ZONTRON PHARMACEUTICALS SDN. BHD. (445695-T)
Lot 10 & 11, PERDA Industrial Park,
Lorong IKS Simpang Ampat B,
14100 Simpang Ampat, S.P.S.,
Pulau Pinang, Malaysia.

Name and Address of Product Registration Holder / Manufacturer :
TERAPUTICS SDN. BHD. (590500-W)
Lot 10 & 11, PERDA Industrial Park,
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