210 mm

140 mm

Sonoin E Gel
(Isotretinoin + Erythromycin)

سنوئن ای جیل
(آئسوٹریٹینائن + ایریتھرومائیسین)

COMPOSITION:

Each gram contains:

Isotretinoin ……0.5mg
Erythromycin……....20mg

(Innovator's Specifications)

DESCRIPTION:

Sonoin E Gel (Isotretinoin + Erythromycin) is a topical gel with two active ingredients erythromycin 2% w/w and isotretinoin 0.05% w/w with a primary indication for the treatment of moderate acne vulgaris.

INDICATIONS:

Sonoin E Gel (Isotretinoin + Erythromycin) is indicated for the topical treatment of mild to moderate acne vulgaris in adults and children over 12 years of age.

MECHANISM OF ACTION:

Isotretinoin

Isotretinoin is the 13-cis-isomer of all-trans-retinoic acid. It is structurally and pharmacologically related to vitamin A, which regulates epithelial cell growth and differentiation. It is thought that topically applied isotretinoin acts in a comparable way to its stereoisomer, tretinoin, by:

Stimulating mitosis in the epidermis.

Reducing intercellular cohesion in the stratum corneum and eliminating mature comedones (closed and open).

Contesting the hyperkeratosis characteristic of acne vulgaris by suppressing the formation of micromedo.

Preventing the formation of lesions through inflammatory process inhibition .

Mediating an increased production of less cohesive sebaceous cells, which appears to promote the initial expulsion of comedones and their subsequent prevention.

Facilitating percutaneous absorption when co-administered with other topical drugs.

Isotretinoin has topical anti-inflammatory actions, which are mediated by the inhibition of leukotriene-B_4-induced migration of polymorphonuclear leukocytes. The migration of LTB4 into human skin is significantly inhibited by topically applied isotretinoin.

Erythromycin:

Erythromycin is a macrolide antibiotic with a broad and essentially bacteriostatic action against many Gram-positive and to a lesser extent Gram-negative bacteria. Erythromycin binds reversibly to the 50S subunit of the bacterial ribosome, blocking the formation of peptide bonds between amino acids thus inhibiting protein synthesis and cell growth in susceptible organisms. Depending on the organism and dose administered, erythromycin exhibits either bacteriostatic or bactericidal activity. Applied topically, erythromycin suppresses *Propionibacterium acnes*, resident bacteria of sebaceous follicles, thus reducing the *P. acnes* mediated hydrolysis of triglycerides to fatty acids and therefore decreasing fatty acid formation. Erythromycin has also demonstrated inhibitory effects on the production of *P. acnes*-associated inflammatory mediators. Therefore, it also works to control acne lesion counts by direct antibacterial effects and indirect anti-inflammatory effects.

DOSAGE & ADMINISTRATION:

Isotretinoin + Erythromycin Gel is for topical use only.

Adults & children over 12 years

Wash the skin gently with a mild cleanser and dry fully. Apply Isotretinoin + Erythromycin Gel in a thin film over the entire affected area once or twice daily. Avoid close proximity to eyes, lips, and other mucous membranes. Hands should be washed after application.

Eight weeks of treatment may be required before a therapeutic effect is observed. The efficacy and safety of Isotretinoin + Erythromycin Gel has not been studied beyond 12 weeks in acne vulgaris clinical trials.

The prescriber should evaluate the benefit of continuing treatment beyond 12 weeks of uninterrupted use, taking account of an increased risk of antimicrobial resistance. Patients should be advised that excessive application will not improve efficacy, but may increase the risk of skin irritation.

If undue irritation (redness, peeling, or discomfort) occurs, patients may use a moisturizer as needed and should reduce frequency of application or temporarily interrupt treatment. The normal frequency of application should be resumed once the irritation subsides. Treatment should be discontinued if the irritation persists.

Efficacy has not been established for less than once daily dosing frequencies. Due to the flammable nature of Isotretinoin + Erythromycin Gel patients should avoid smoking or being near an open flame during application and immediately after use.

Pediatric population

The safety and efficacy of Isotretinoin + Erythromycin Gel has not been established in children less than 12 years of age, therefore Isotretinoin + Erythromycin Gel is not recommended for use in this population.

Use in the Elderly

There are no specific recommendations for use in the elderly.

Renal impairment

No dosage adjustment is necessary. As there is low systemic absorption of isotretinoin and erythromycin following topical application, renal impairment is not expected to result in systemic exposure of clinical significance.

Hepatic impairment

No dosage adjustment is necessary. As there is low systemic absorption of isotretinoin and erythromycin following topical application, hepatic impairment is not expected to result in systemic exposure of clinical significance.

PHARMACOKINETICS:

Absorption

Studies support the conclusion that systemic absorption of erythromycin and isotretinoin from topical application of Isotretinoin + Erythromycin Gel is low and is not different from that of drug products containing the individual drug substances.

Distribution:

Distribution of erythromycin or isotretinoin throughout the body after topical application has not been considered, as there is no evidence that the compounds are absorbed to any measurable extent after being applied to the skin. Erythromycin is about 65% bound to plasma proteins, primarily to alpha 1 acid glycoprotein (approximately 55%). Isotretinoin is more than 99.9% bound to plasma proteins, primarily albumin.

Metabolism:

No data exist relating to the metabolism, if any, of erythromycin on the skin. After systemic administration, erythromycin is inactivated in the liver by demethylation of the d-desosamine group, a reaction catalyzed by cytochrome P450 IIA.

Very little data exist describing the metabolism of isotretinoin after topical applications to human skin. Isotretinoin may be metabolized by Cytochrome P450 enzymes or other endogenous oxidative agents and radicals in the skin.

Elimination:

Topically applied (Isotretinoin + Erythromycin) is unlikely to reach systemic circulation in measurable quantities. If very small quantities of Isotretinoin or Erythromycin are absorbed, they will be oxidised and excreted in bile or in urine, respectively.

WARNINGS & PRECAUTIONS:

Local tolerability and photoallergy reactions

Isotretinoin + Erythromycin Gel should be used with caution in patients with a history of local tolerability reactions or photoallergy.

Irritancy

Contact with the mouth, eyes, lips, other mucous membranes or areas of broken skin should be avoided. In case of accidental contact, rinse well with water. Care should be taken not to let the medicine accumulate in skin folds. Due to the irritant nature of isotretinoin, caution should be used when applying to sensitive areas of the skin, such as the neck, abraded or eczematous skin, or when treating patients with inflammatory skin conditions that may coexist with acne, e.g. rosacea or perioral dermatitis. Concomitant topical acne therapy should be used with caution because a cumulative irritant effect may occur. If irritancy or dermatitis occurs, reduce frequency of application or temporarily interrupt treatment and

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resume once the irritation subsides. Treatment should be discontinued if the irritation persists. In patients whose skin has been subjected to procedures such as depilation, chemical hair treatments, chemical peels, dermabrasion or laser resurfacing, the skin should be allowed to recover before application is considered. Cosmetics that have a strong drying effect, including products with high concentrations of alcohol and/or astringents, or that have a potential irritating effect should be used with caution as a cumulative irritant effect may occur.

Resistance to erythromycin:

The treatment of acne with topical antibiotics is associated with the development of antimicrobial resistance in *Propionibacterium acnes* as well as other bacteria *(e.g. Staphylococcus aureus, Streptococcus pyogenes)*. The use of erythromycin may result in resistance developing in these organisms. If there is evidence of the development of clinical resistance during treatment (e.g. poor response or worsening of the condition), treatment with Isotretinoin + Erythromycin Gel should be discontinued.

Cross-resistance

Cross-resistance with other antibiotics of the macrolide group and with clindamycin may occur. The use of antibiotic agents may be associated with the overgrowth of antibiotic-resistant organisms. If this occurs, discontinue use.

Pseudomembranous colitis

Isotretinoin + Erythromycin Gel should be used with caution in patients with or with a history of regional enteritis, ulcerative colitis, or antibiotic-associated colitis (including pseudomembranous colitis). Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. Although this is less likely to occur with topically applied Isotretinoin + Erythromycin Gel, if prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

Sensitivity to sunlight and environmental exposure:

As isotretinoin may cause increased sensitivity to sunlight, sunlamps should not be used and deliberate or prolonged exposure to sunlight should be avoided or minimised. When exposure to strong sunlight cannot be avoided, patients should be advised to use a broad-spectrum sunscreen product (protects against UVA and UVB rays) and wear protective clothing. Due to the potential for photosensitivity, resulting in greater risk for sunburn, Isotretinoin + Erythromycin Gel should be used with caution in patients with a personal or family history of skin cancer. If a patient has sunburn, this should be resolved before using Isotretinoin + Erythromycin Gel. Weather extremes, such as wind or cold, may be more irritating to patients using isotretinoin-containing products. Isotretinoin + Erythromycin Gel contains butylated hydroxytoluene which may cause local skin reactions (e.g. contact dermatitis) or irritation to the eyes and mucous membranes.

Pregnancy:

Isotretinoin + Erythromycin Gel is contraindicated in pregnancy, or in women planning a pregnancy. If the product is used during pregnancy, or if the patient becomes pregnant while taking this drug, treatment should be discontinued. There are limited data on the use of Isotretinoin + Erythromycin Gel in pregnant women.

Erythromycin:

There are limited data on the use of topical erythromycin in pregnant women. No effects during pregnancy are anticipated since systemic exposure to erythromycin is very low.

Isotretinoin:

Orally administered retinoids have been associated with congenital abnormalities. When used in accordance with the prescribing information, topically administered retinoids are generally assumed to result into low systemic exposure due to minimal dermal absorption. However, there could be individual factors (e.g. damaged skin barrier, excessive use) that contribute to an increased systemic exposure.

Breast-feeding

Isotretinoin + Erythromycin Gel has not been studied during breast-feeding. Percutaneous absorption of erythromycin is low; however, it is not known whether erythromycin is excreted in human milk after topical application. Erythromycin is excreted in human milk following oral and parenteral administration. There is insufficient information on the excretion of topically applied isotretinoin in human milk. A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Isotretinoin + Erythromycin Gel therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

SIDE EFFECTS:

Common side effects include are:

Rash, dryness, erythema, scaling, burning, pruritus, skin irritation, pain, application site reactions including eczema, exfoliative dermatitis.

Rare side effects include are:

Allergic reaction, photosensitivity reaction, skin discolouration, skin Hyperpig-mentation, skin hypopigmentation, urticaria, facial edema.

DRUG INTERACTIONS:

No formal drug-drug interaction studies have been conducted with Isotretinoin + Erythromycin Gel.

Isotretinoin + Erythromycin Gel should not be used in combination with clindamycin-containing products due to possible antagonism to the clindamycin component.

Concomitant application of oxidising agents, such as benzoyl peroxide, should be avoided since they may reduce the efficacy topical isotretinoin. If combination therapy is required, they should be applied at different times of the day (e.g. one in the morning and the other in the evening).

CONTRAINDICATIONS:

Hypersensitivity to the active substances or to any of the excipients.

Isotretinoin + Erythromycin Gel is contraindicated in pregnancy and in women planning a pregnancy.

OVER DOSAGE:

Symptoms

In the event of accidental ingestion, gastrointestinal adverse reactions similar to those following orally administered erythromycin may be seen (e.g. nausea, vomiting, diarrhoea).

Oral ingestion of a 50g tube of Isotretinoin + Erythromycin Gel would result in less exposure than achieved with the recommended dosage of oral isotretinoin. Consequently, the theoretical occurrence of symptoms of overdosage (e.g. hypervitaminosis A) is highly unlikely. The formulation contains a significant quantity of ethanol. Systemic absorption of this should be considered a possibility in the event of overdosage.

Treatment

Appropriate symptomatic measures should be taken to provide relief from skin irritation due to excessive application. Accidental ingestion should be managed as clinically indicated.

STORAGE & INSTRUCTIONS:

Store below 25°C. Do not freeze or refrigerate.
Protect from heat, sunlight and moisture.
Keep away from the reach of the children.
Replace cap firmly after use.
This product should be used within 2 months after opening the tube and discard any unused portion.

To be sold on the prescription of a registered medical practitioner only.

خوراک وہدایات:

متاثرہ حصے پر دن میں ایک سے دو بار لگائیں یا ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔ دوا کو ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ ریفریجریٹر میں نہ رکھیں۔ دھوپ، گرمی، نمی اور منجمد ہونے سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔ صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔

HOW SUPPLIED:

Sonoin E Gel
10g Tube

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549,Sundar Industrial Estate,
Lahore, Pakistan.