Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Stiemycin 2% w/v Cutaneous Solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Contains erythromycin 20 mg/ml (2% w/v)

Excipients with known effect:
Contains propylene glycol 372.8 mg/ml (37.28% w/v)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cutaneous solution.
A clear, colourless liquid with an odour of ethanol.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Stiemycin is indicated in adults and adolescents for the topical treatment of acne vulgaris.

4.2 Posology and method of administration

Apply Stiemycin over the whole affected area twice daily, after washing with soap and water.

Patients should be advised that a therapeutic effect may not be seen until after 6-8 weeks of treatment. Treatment duration should be kept to a minimum to avoid antimicrobial resistance

If there has been no improvement after 6-8 weeks, or if the condition becomes worse, treatment should be discontinued.

Due to the flammable nature of Stiemycin Cutaneous Solution, patients should avoid smoking or being near an open flame during application and immediately after use.

Paediatric population
The safety and efficacy of Stiemycin in children under the age of 12 years have not been established.

Elderly patients
There are no specific recommendations.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.

4.4 Special warnings and precautions for use

Concomitant topical acne therapy should be used with caution because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating or abrasive agents. If irritancy or dermatitis occurs, erythromycin should be discontinued.

Avoid contact with the eyes, mouth, lips, other mucous membranes and areas of broken skin.

Cross-resistance and cross-sensitivity with other antibiotics of the macrolide group and clindamycin may occur.

The use of antibiotic agents may be associated with the overgrowth of antibiotic-resistance organisms. If this occurs, discontinue use.

Use with caution in patients with or with a history of regional enteritis, ulcerative colitis or antibiotic-associated colitis (including pseudomembranous colitis).

As with other broad spectrum antibiotics, pseudomembranous colitis has been reported with erythromycin, and may range in severity from mild to life-threatening. Although this is unlikely to occur with topically applied erythromycin, if prolonged or significant diarrhoea occurs or the patient suffers from abdominal cramps, treatment should be discontinued immediately and the patient investigated further, as the symptoms may indicate antibiotic-associated colitis.

Stiemycin contains propylene glycol which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

Clindamycin and erythromycin have been shown to be antagonistic *in vitro*.

4.6 Fertility, pregnancy and lactation

Fertility
There are no data on the effect of topical erythromycin on fertility in humans.

Pregnancy
There is limited data on the use of topical erythromycin in pregnant women. No effects during pregnancy are anticipated since systemic exposure to erythromycin is very limited. However, topical erythromycin should be used during pregnancy only if the expected benefit justifies the potential risk to the foetus.

Breast-feeding
As percutaneous absorption of erythromycin is negligible, it is not known whether erythromycin is excreted in human milk after topical application. Topical erythromycin should be used during lactation only if the expected benefit justifies the potential risk to the infant.

If used during lactation, it should not be applied to the breast area to avoid accidental ingestion by the infant.

4.7 Effects on ability to drive and use machines

Stiemycin has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

The following convention has been used for the classification of adverse reactions:

Very common ≥1/10
Common ≥1/100 to <1/10
Uncommon ≥1/1000 to <1/100
Rare ≥1/10000 to <1/1000
Very rare <1/10000
Not known* (cannot be estimated from the available data).

Clinical trial data

Skin and subcutaneous tissue disorders
Very common: Skin burning sensation, skin irritation, dry skin, especially on initiation of treatment, application site stinging, application site erythema, especially on initiation of treatment

Post-marketing data

Immune system disorders
Rare: Allergic reactions

Gastrointestinal disorders
Rare: Diarrhoea, abdominal discomfort, upper abdominal pain

Skin and subcutaneous disorders
Rare: Rash, urticaria, pruritus

General disorders and administration site conditions
Rare: Facial oedema

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 preferably through the online reporting option accessible from the IMB homepage. A downloadable report form is also accessible from the IMB website, which may be completed manually and submitted to the IMB via 'freepost'. Alternatively, the traditional post-paid 'yellow card' option may also continue to be used.

FREEPOST
Pharmacovigilance Section
Irish Medicines Board
Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.imb.ie
e-mail: imbpharmacovigilance@imb.ie

4.9 Overdose

Symptoms
In the event of accidental ingestion, the same gastrointestinal adverse reactions as those seen with orally administered erythromycin may be seen.

The formulation contains a significant quantity of ethanol. Systemic absorption of this should be considered a possibility in the event of overdosage.

Management
Further management should be as clinically indicated or as recommended by the National Poisons Information Centre of Ireland.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group**:** Anti-infectives for treatment of acne, erythromycin
ATC code: D10AF02

Mechanism of action
Erythromycin is a macrolide antibiotic with a narrow spectrum of microbiological activity which acts by interfering with bacterial protein synthesis. Erythromycin suppresses *Propionibacterium acnes,* a resident bacteria of sebaceous follicles, and as a result of this organism's role in the hydrolysis of triglycerides to free fatty acids, administration decreases fatty acid formation. This is thought to be responsible for its effectiveness in reducing acne lesion counts.

Resistance and cross resistance
Propionibacterium acnes typically reside within follicles as a symbiotic microbe and it is also implicated in acne pathogenesis. Topical use of antibiotics as erythromycin in the treatment of acne vulgaris is dependent on their activity against *P. acnes,* these agents reduce the numbers of propionibacteria on the skin.

Acquired resistance to erythromycin, clindamycin and tetracyclines used for the treatment of acne vulgaris has been reported.

Mutations in the genes encoding the 23S and 16S subunit of ribosomal RNA are the known mechanisms involved in *P. acnes* resistance relative to the use of erythromycin. Nevertheless, recent studies suggest that there are yet unidentified resistance mechanism evolved in the process.

Continuous use of erythromycin for more than 8-12 weeks can increase the risk of development of erythromycin-resistant *P. acnes*.

The widespread use of topical and oral antibiotics to treat acne results in dissemination of cross-resistant strains of propionibacteria.
Most of erythromycin–resistant strains showed cross-resistance with clindamycin.
Studies show less common cross-resistance phenotype against macrolide, lincosamide and type B streptogramin.

Commonly susceptible species to Erythromycin *
Gram-positive cocci *Corynebacterium* *Hemophilus influenza* *Legionella pneumophila* *Chlamydia organism* *Treponema pallidum* *Mycoplasma pneumoniae* *Ureaplasma urealyticum*
Species for which acquired resistance may be a problem*
Gram-positive cocci

* The frequencies of bacterial resistance may vary geographically. The range could be between 25-50%.
The inclusion of benzoyl peroxide in association with topical erythromycin for the treatment of acne vulgaris may reduce erythromycin-resistant *P. acnes.*

5.2 Pharmacokinetic properties

Percutaneous absorption of erythromycin from Stiemycin solution is negligible.

5.3 Preclinical safety data

The clinical and pre-clinical safety of erythromycin is well established. Erythromycin has been in wide-spread use for many years.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polyoxyethylene 4 lauryl ether
Ethanol
Propylene glycol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

Keep container tightly closed when not in use. Contents are flammable. Keep away from fire, flame or heat. Do not leave in direct sunlight.

6.5 Nature and contents of container

Amber glass bottle (Class 3 glass) of 25ml or 50ml capacity, fitted with a Dab-o-matic applicator neck plug and polypropylene cap.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Ltd
Stonemasons Way
Rathfarnham
Dublin 16
Ireland
Trading as Stiefel

8 MARKETING AUTHORISATION NUMBER

PA 1077/129/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17 April 1989

Date of last renewal: 17 April 2004

10 DATE OF REVISION OF THE TEXT

January 2014