Summary of Product Characteristics (SmPC)

1. Name of the Medicinal Product

Brand Name:

REGEN-D®60

Generic Name:

Recombinant Human Epidermal Growth Factor Gel, 60µg/g

2. Qualitative and Quantitative Composition

REGEN-D®60 is Human Epidermal Growth Factor produced by recombinant DNA technology. It has been developed by Bharat Biotech International Limited, Hyderabad, India.

Each gram of gel contains:

Purified Bulk of rh- Epidermal Growth Factor	60 µg
Sodium methyl paraben BP	1.8 mg
Sodium propyl paraben BP	0.2 mg
Excipients	q.s

3. Pharmaceutical Form

Gel

4. Clinical Particulars

4.1 Therapeutic indications:

REGEN-D®60 is indicated for first and second degree burn wounds, for healing of door site skin graft area.

4.2 Posology and method of administration:

Posology:

Cleanse the burn wound and surrounding surface with water or saline and pat dry with sterile cotton before the gel is applied. Apply the gel evenly (topical application) on the

affected area of the skin using sterile cotton swab twice a day till the wound area heals. **REGEN-D®60** therapy should be co continued up to a period of 2 to 3 weeks after the wound heals. The continuation of the therapy is at the discretion of the physician.

a) A single tube should be used for individual patient.

b) Avoid direct contact of the tube with the tube with the wound area.

Any unwanted use of the product is not the responsibility of the manufacturer.

4.3 Contraindications:

REGEN-D®60 is generally well tolerated. However, the products should not be applied or repeated to persons known to be hypersensitive to any of the components of the product. Also, it should not be applied to individual who are receiving immunosuppressive or immune - stimulant therapy, or immuno compromised individuals.

4.4 Special warnings and precautions for use:

It is suggested that the medical practitioner ascertain the hypersensitivity status of the subject.

4.5 Interaction with other medicinal products and other forms of interaction:

REGEN-D®60 must not be used with other growth factor containing gel or cream.

4.6 Pregnancy and Lactation:

REGEN-D®60 is contraindicated in pregnant and lactating women.

4.7 Effect on ability to drive and use machines:

Since the product is for topical application, systemic absorption is not expected. However, no studies on the effect of **REGEN-D®60** on the ability to drive and use machines has been performed.

4.8 Undesirable Effects*:*

REGEN-D®60 has proven low reactogenicity and is well tolerated, however skin

irritation /pain, rash at the application site may be seen in very few cases.

4.9 Overdose:

Not applicable.

5. Pharmacological Properties

5.1 Pharmacodynamics properties:

EGF is part of a complex network of growth factors and receptors that together help to modulate the growth of cells. EGF is released by cells, and then is picked up either by the cell itself, stimulating its own growth, or by neighboring cells, stimulating their ability to divide. Receptors on the surface of the cell bind to EGF and relay the signal inside. When the receptor binds to EGF, it is activated by forming a dimer with other receptors.

EGF is essential for mediating the de-differentiation of keratinocytes to an epithelial linage and to reestablish the epithelial barrier. EGF binds to the EGFR, a protein tyrosine kinase receptor, expressed on the majority of cells in the skin. Activation of EGFR leads to a number of biological responses, including migration, proliferation, cytoprotection, cellular differentiation, and apoptosis. In wound healing EGFR plays an important role in re-epithelialization and dermal maturation. Topical use of recombinant human EGF has been shown to increase re-epithelialization and enhance wound healing.

5.2 Pharmacokinetic properties:

Subjects were followed up for various periods of time to evaluate the systemic absorption of **REGEN-D®60** in blood. Sera was analyzed for anti-EGF titers by Indirect ELISA method. The test serum absorbance was less than the seroconversion cut-off value, hence these samples were negative for anti r-human EGF antibody.

Patients with wounds were tested for the presence of rhEGF by collecting the samples from the site of application, the result clearly shows that rhEGF is available at the site of application. Protease enzyme present in the body degrades rhEGF at the site of

applications, however when **REGEN-D®60** was applied, there was sufficient high concentration of rhEGF locally.

5.3 Pre-Clinical & Clinical Trial Experience

Pre-clinical toxicological studies done on rats and rabbits concluded that the rh-EGF is safe and well tolerable with no systemic observations. The study was conducted to evaluate the potential toxicity of repeated doses (75-300 µg/Kg) of recombinant human Epidermal Growth Factor applied topically to rats and New Zealand white rabbits groups. The rh-EGF was not absorbed systematically as revealed in the systemic absorption study conducted in rabbit. There has been significant increase in the DNA and collagen contents in the skin samples treated with rh-EGF. No significant changes were observed control and treated groups with respect to protein contents in the skin.

In another study with rats (Wistarfurth) and rabbits (New Zealand white) to evaluate the potential toxicity of repeated doses (75-300 µg/Kg) of rh-EGF applied topically to rats and rabbits, it was found that there was no observable antibody response in the treated groups with EGF in both rats and rabbits. The DNA content in skin sample of treated group has significantly increased in high dose in both the species on 15th and 31st day. The protein content in the control and treated groups did not differ significantly in both the species studied. The collagen content was significantly increased in medium and high dose groups in males and females both the species on 15th and 31st days.

In another study the application or burns have reduced the healing time to an average of 9 days compared to the usual healing time f 20 days. There were no cases of adverse or serious adverse events observed during the study. Only one case of rash was observed during the study, which after laboratory investigations, confirmed that this was not related to study drug medication. The laboratory investigations showed no difference in the pre- and post - drug administration values.

A multi-centre, double-blind, randomised, parallel, phase 3 study was conducted to evaluate the safety and efficacy of **REGEN-D®60** in comparison with silver sulfadiazine as a treatment for donor site graft and burns. The study showed that

application of **REGEN-D® 60** on donor site grafts have reduced the healing time to an average of 9-10 days compared to the regular healing time of 16-20 days.

Post-Marketing Experience

More than a hundred thousand tubes of various dose strengths have been sold in domestic and international markets since the market authorization. The product is under close surveillance for its safety in the field.

6. Pharmaceutical Particulars

Category: Growth factor

6.1 List of excipients:

Sodium Methylparaben BP

Sodium Propylparaben BP

6.2 Incompatibility:

Recombinant human EGF is combined along with silver sulfadiazine and chlorhexidine, marketed as as **SLVRGEN®** is manufactured by Bharat Biotech and is used for the treatment of first and second - degree burns and ulcers like abrasions, incisions, minor cuts and wounds. No other studies were performed to look for incompatibles with **REGEN-D®60.**

6.3 Shelf life:

The expiry date of the product is indicated on the carton.

6.4 Special precautions for storage:

Store at +2°C to +8°C. Do not freeze.

6.5 Nature and contents of container:

REGEN-D®60 is presented in aluminum tubes with polypropylene screw cap. The pack sizes are 7.5 gms, 15 gms, 30 gms, 50 gms, and 150 gms presentations.

6.6 Special precautions for disposal

Not Applicable

7.0 Marketing Authorization Holder

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