1.3 PRODUCT INFORMATION

1.3.1 Summary of Product Characteristics (SmPC)

1. Name of the Medicinal Product

Beclomethasone Diproionate, Phenylepherine, Lignocaine Cream

2. Qualitative and Quantitative Composition

Composition:

Beclomethasone Diproionate ……. 0.025 % w/w

Phenylephrine Hydrochloride ……. 0.10 % w/w

Lignocaine Hydrochloride …….……. 2.50 % w/w

Chlorocresol ……. 0.1 % w/w

(As Preservative)

Cream Base……..……. Q.S.

3. Pharmaceutical Form

Cream.

4. Clinical Particulars

4.1 Therapeutic Indications

Proctosedyl bd is indicated for pain and bleeding associated with anal fissures and internal or external haemorrhoids; post haemorrhoidectomy pain; minor degrees of proctitis.

4.2 Posology and Method of Administration

Apply a small amount of cream two or three times a day initially, using the applicator if internal administration is required. When inflammation is subsiding, once-daily application is sufficient in most cases. One tube should provide treatment for at least a week.

4.3 Contraindications

Corticosteroids should not be used in the presence of infection unless effective chemotherapy is also employed. Hypersensitivity to any component of the preparation.

4.4 Special Warnings and Precautions for Use

Beclomethasone Dipropionate - Visual disturbance may be associated 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 serous chorioretinopathy (CSCR). In case of systemic absorption : Pheochromocytoma crisis. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

Precautions: Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established; however topical steroids should not be used extensively in pregnancy, i.e. in large amounts or for prolonged periods.

Beclomethasone Dipropionate **-** In case of systemic absorption: Hypertrophic cardiomyopathy has been reported after systemic administration of glucocorticosteroids in preterm infants. In infants receiving administration of systemic glucocorticosteroids, echocardiograms should be performed to monitor myocardial structure and function.

Phenylepherine- Many people using this medication do not have serious side effects. Stop using this medication and tell your doctor right away if you have any serious side effects, including: fast/irregular heartbeat, pounding headache, nervousness, shakiness (tremor), trouble sleeping.

Lignocaine- A very serious allergic reaction to this drug is rare. However, get medical help right away if you notice any symptoms of a serious allergic reaction, including: new/worsening rash, new or worsening itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Prolonged and intensive treatment with active, corticosteroid preparations may cause local atrophic changes in the skin.

Betamethasone is not usually recommended for use when pregnant. A dermatologist (skin care specialist) may prescribe it if they feel the benefits outweigh the risks. Small amounts of betamethasone used on small areas of skin are unlikely to cause any problems in pregnancy.

Eye disorders: Chorioretinopathy (frequency - not known) ; Blurred vision (frequency – not known). Endocrine disorders: Pheochromocytoma crisis (corticosteroids class effect) (Frequency - not known) (systemic), Cardiac Disorders: Hypertrophic cardiomyopathy in preterm infants (systemic).

Do not take phenylephrine if you are taking a monoamine oxidase (MAO) inhibitor, such as isocarboxazid (Marplan), phenelzine (Nardil), selegiline (Eldepryl, Emsam, Zelapar), and tranylcypromine (Parnate), or if you have stopped taking one of these medications within the past 2 weeks.

Phenylephrine: Cardiac Disorders - Frequency Not Known: Reflex bradycardia, Renal and Urinary disorders - Frequency not known: Urinary retention

This medicine may cause a rare, but serious blood problem called methemoglobinemia. The risk may be increased in children younger than 6 months of age, elderly patients, or patients with certain inborn defects.

4.6 Pregnancy and Lactation

Use with caution in pregnant or lactating women. Should not be used extensively in pregnant women i.e., in large amounts or for prolonged periods.

4.7 Effects on Ability to Drive and Use Machines

Not applicable.

4.8 Undesirable Effects

Check with your doctor right away if you have a skin rash, blistering, burning, crusting,

dryness, flaking of the skin, itching, scaling, severe redness, stinging, swelling, or irritation on the skin.

The lidocaine and phenylephrine topical may interfere with swallowing, and numbness of the tongue or buccal mucosa may increase the danger of biting trauma.

Local anaesthetics, (e.g. lidocaine) and sympathomimetics, (e.g. phenylephrine) may produce systemic adverse effects as a result of the raised plasma concentrations which ensue when the rate of absorption into the circulation exceeds the rate of breakdown, for example, by absorption of large amounts through mucous membranes or damaged skin or from highly vascular areas.

Possible Systemic Effects due to Lidocaine

The systemic toxicity of local anaesthetics mainly involves the central nervous system and the cardiovascular system. Excitation of the CNS may be manifested by restlessness, excitement, nervousness, dizziness, tinnitus, blurred vision, nausea and vomiting, muscle twitching and tremors, and convulsions. Numbness of the tongue and perioral region may appear as an early sign of systemic toxicity. Excitation may be transient and followed by depression with drowsiness, respiratory failure and coma. There may be simultaneous effects on the cardiovascular system with myocardial depression and peripheral vasodilatation resulting in hypotension and bradycardia; arrhythmias and cardiac arrest may occur.

Some local anaesthetics cause methaemoglobinaemia.

Possible Systemic Effects due to Phenylephrine.

Sympathomimetics may produce a wide range of adverse effects, most of which mimic the results of excessive stimulation of the sympathetic nervous system. These effects are mediated via the various types of adrenergic receptor, and the adverse effects of an individual drug depend to some extent upon its relative agonist activity on these different types of receptor at a given dose.

Central effects of sympathomimetic agents include fear, anxiety, nervousness, restlessness, tremors, insomnia, confusion, irritability, psychotic states and epileptiform convulsions. Appetite may be reduced and nausea and vomiting may occur.

Effects on the cardiovascular system are complex. Stimulation of alpha-adrenergic receptors produced vasoconstriction with resultant hypertension. This vasoconstriction

is sometimes sufficiently severe to produce gangrene when sympathomimetics are infiltrated into the digits. The rise of blood pressure may produce cerebral haemorrhage and pulmonary oedema. There may also be a reflex bradycardia, but stimulation of β_1-adrenergic receptors of the heart may produce tachycardia and cardiac arrhythmias, anginal pain, palpitations, and cardiac arrest: hypotension with dizziness and fainting, and flushing, may occur. An increased incidence of sudden death, sometimes attributed to the induction of ventricular arrhythmias, has been associated with the excessive use of sympathomimetic agents in aerosol form; although the association has been questioned by some authorities, it is important to avoid excessive doses.

Other effects that may occur with sympathomimetic agents include difficulty in micturition, particularly in the case of prostatic hypertrophy, and urinary retention, dyspnoea, weakness, altered metabolism, sweating, hyperpyrexia and hypersalivation. Headache is also common.

4.9 Overdose

Symptoms

Because a severe toxic reaction to phenylephrine is of rapid onset and short duration, treatment is primarily supportive. Prompt injection of a rapidly acting alpha-adrenergic blocking agent such as phentolamine (dose 5 to 10mg i.v.) has been recommended.

Treatment

Treatment of a patient with toxic manifestations consists of ensuring adequate ventilation and arresting convulsions. Ventilation should be maintained with oxygen by assisted or controlled respiration as required. If convulsions occur they must be treated rapidly by intravenous administration of succinylcholine 50-100mg and/or 5-15mg diazepam. As succinylcholine will arrest respiration, it should only be used if the clinician has the ability to perform endotracheal intubation and to manage a totally paralysed patient. Thiopentone may also be used to abort convulsions in dosage 100-200mg. Adrenaline in repeated doses and sodium bicarbonate should be given as rapidly as possible.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic groups:

Beclomethasone Diproionate: Antifungal, Antibiotic; ATC Code: D07AC01

Lidocaine: Anaesthetics for topical use, lidocaine, ATC Code: D04A B 01

Phenylephrine: Sympathomimetics excluding antiglaucoma preparations,

ATC code: S01FB01

Betamethasone is a glucocorticosteroids receptor agonist. This leads to changes in genetic expression once this complex binds to the GRE. The anti-inflammatory actions of corticosteroids are thought to involve lipocortins phospholipase A2 inhibitory proteins which, through inhibits Arachidonic acid, control the biosynthesis of prostaglandins and leukotrienes.

Lidocaine is primarily used for its local anaesthetic properties. Like other anaesthetics lidocaine impairs the generation and conduction of the nerve impulses by slowing depolarization. This results from blocking of the large transient increase in permeability of the cell membrane to sodium ions that follows initial depolarization of the membrane. Lidocaine also reduces the permeability of the resting axon to potassium and to sodium ions. The site of action of lidocaine is on a specific receptor site in the sodium channel.

Lidocaine is more effective as a local anaesthetic on small non-myelinated nerve fibres, while myelinated A fibres are blocked before C fibres. The actions of lidocaine are prolonged by the use of a vasoconstrictor such as adrenaline.

Lidocaine has effects on the central nervous system to produce restlessness and tremor, and frank convulsions may occur. Central stimulation may be followed by depression and death due to respiratory failure. Lidocaine has weak neuromuscular blocking activity.

In the heart lidocaine's main activity is to reduce automaticity by decreasing the rate of diastolic depolarization. Lidocaine has little or no effect on conduction in the His-Purkinje system. The duration of the action potential is decreased due to blockade of the sodium channel and the effective refractory period is shortened.

Phenylephrine

Phenylephrine is a relatively selective α_1-adrenoceptor agonist. It has weak α_2-adrenoceptor agonist activity and some activity as a β-adrenoceptor agonist. It is also termed a sympathomimetic vasoconstrictor. Most of the α_1-stimulant activity is due to a direct action on the receptors and relatively little is due to an indirect effect via release of noradrenaline.

Phenylephrine causes a rise in blood pressure which is accompanied by a profound reflex bradycardia which can be antagonised by atropine. Cardiac output is slightly decreased but there is a marked fall in blood flow to the renal, cutaneous, splanchnic and skeletal muscle vascular beds. Coronary blood flow is however, increased by phenylephrine and pulmonary arterial pressure is increased.

5.2 Pharmacokinetic Properties

Absorption

Lidocaine is readily absorbed from the gastrointestinal tract, from mucous membranes and through damaged skin. Absorption through intact skin is poor. Local anaesthetics are weak bases and at tissue pH can diffuse through connective tissue and cellular membranes to reach the nerve fibre where ionisation can occur.

Biotransformation

Systemic bioavailability is only about 40% following administration, peak plasma concentrations are achieved in 1-2 hours. The mean plasma half-life is in the range 2-3 hours. Penetration into the brain appears to be minimal.

Distribution

The volume of distribution is between 200 and 500L.

Elimination

Both phenylephrine and its metabolites are excreted in urine with <20% as unchanged drug. There is no evidence that any of the metabolites are pharmacologically active.

5.3 Preclinical Safety Data

Not known.

6. Pharmaceutical Particulars

6.1 List of Excipients

Cetostearyl Alcohol, Self-Emulsifying Glyceryl Monostearate, Cetomacrogol Emulsifying Wax, White Soft Paraffin, Light Liquid Paraffin, Methyl Paraben, Propyl Paraben, Propylene Glycol, Sodium Acid Phosphate, Sodium Phosphate and Purified Water.

6.2 Incompatibilities

Phenylephrine

No known incompatibilities.

Lidocaine

Lidocaine hydrochloride has been reported to be incompatible in solution with amphotericin, sulphadiazine sodium, methohexitone sodium, cephazolin sodium, or phenytoin sodium.

The lidocaine content of buffered cardioplegic solutions has been reported to decrease when stored in polyvinyl chloride containers at ambient temperatures but not when stored at 4°C. This loss appeared to result from pH-dependent sorption of lidocaine onto the plastic and did not occur when lidocaine solutions were stored in glass bottles.

6.3 Shelf Life

36 months

6.4 Special Precautions for Storage

Do not store above 25°C. Keep the container tightly closed.

6.5 Nature and Contents of Container

1 ANUHEAL (30 gm Lamitube) packed in inner carton with a packaging insert.

6.6 Special Precautions for Disposal and Other Handling

Not applicable.

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