For the Use of a Registered Medical Practitioner only

1. Generic Name and Brand Name

Diltiazem Hydrochloride Gel 2% w/w

CremaGel®

2. Qualitative and Quantitative Composition

Diltiazem Hydrochloride I.P……. 2% w/w

Gel base ……..q.s.

3. Dosage Form and Strength

Refer section 1 & 2

4. Clinical Particulars

4.1 Therapeutic Indications

For the treatment of anal fissure.

4.2 Posology and Method of Administration

Insert 1.5 – 2 cm of CremaGel (measuring strip provided with every tube) into the anal canal. Either with clean index finger OR by taking the gel on a clean piece of gauge / cotton and gently pushing it in to the anus and apply gel once before & after the morning defecation and then subsequently before & after each defecation. Application of CremaGel at bedtime is a must. A sitz bath is advised, before the application of CremaGel, for better results. Close the tube tightly, immediately after each use.

4.3 Contraindications

Diltiazem is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker (2) patients with second - or third - degree AV block except in the presence of a functioning ventricular pacemaker (3) patients with severe hypotension (systolic BP < 90 mm/Hg) (4) patients who have demonstrated hypersensitivity to the drug and (5) patients with acute myocardial infarction and pulmonary congestion admission.

4.4 Special Warnings and Precaution for Use

Cardiac Conduction: Diltiazem hydrochloride prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second/third degree AV block. Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction.

Congestive Heart Failure: Worsening of congestive heart failure has been reported in patients with pre-existing impairment of ventricular function. Experience with the use of diltiazem hydrochloride in combination with beta-blockers in patients with impaired ventricular function is limited. Caution should be exercised when using this combination.

Hypotension: Decreases in blood pressure associated with diltiazem hydrochloride therapy may occasionally result in symptomatic hypotension. Enhanced antihypertensive effect may occur if used with other antihypertensive drugs or drugs that cause hypotension.
Acute Hepatic Injury: Mild elevations of transaminases with and without concomitant elevation in alkaline phosphatase and bilirubin have been observed in clinical studies.
As patients may experience faintness and/or dizziness, particularly the elderly, reaction time when driving or operating machinery may be impaired especially at the start of treatment.

4.5 Drug Interactions
Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction.
Caution should be exercised when using Cremagel with Beta Blockers in patients with impaired ventricular function.
Increased depression of cardiac conduction with risk of bradycardia and AV block may occur when diltiazem is given with drugs such as amiodarone, digoxin, and mefloquine. Diltiazem is extensively metabolised in the liver by the cytochrome P450 isoenzyme CYP3A4 and may also inhibit the metabolism of drugs sharing the same pathway. Interactions may also be expected with enzyme inducers, such as carbamazepine, phenobarbital, phenytoin, and rifampicin, and with enzyme inhibitors, such as cimetidine and HIV-protease inhibitors.

4.6 Use in Special Population
Pregnancy and lactation: There are no well-controlled studies in pregnant women; therefore, use Diltiazem, hydrochloride in pregnant women only if the potential benefit justifies the potential risk to the fetus.
There are no well-controlled studies in lactating women. However, Diltiazem is excreted in human milk. Therefore, use Diltiazem hydrochloride in lactating mother only if the potential benefit justifies the potential risk to the fetus.

Pediatric Population: Safety and effectiveness in children have not been established.

Renal and Hepatic impairment: The drug should be used with caution in patients with impaired renal or hepatic function.

4.7 Effects on Ability to Drive and Use Machines
Do not use the ointment while driving or working around machinery if you are drowsy, dizzy, have lightheadedness, or blurred vision.

4.8 Undesirable Effects
Most common adverse events are headache, peripheral edema, dizziness, asthenia, dyspepsia, diarrhea, dyspnoea, bronchitis, A-V block, infection, flu like syndrome, extra systoles.

4.9 Overdose

There is no specific antidote to Diltiazem. Over dosage is unlikely to occur with the topical formulation. Headache, fainting or dizziness are the most common indications of overdosage. When these symptoms are observed, treatment should cease for a minimum period of 8 hours and then symptoms are observed, treatment should cease for a minimum period of 8 hours and then the dosage halved. Simple analgesics such as paracetamol may be helpful for headache. If headache is severe and persistent, cease administration.

5. Pharmacological Effects

Clinical Pharmacology

Anal fissure is an ischemic ulcer of the anal mucosa, cause by hyper tonicity of the internal anal sphincter (IAS). The most common site is the posterior midline of the anal canal.

The initiating factor is thought to be trauma from the passage of a particularly hard or painful bowel movement. Low-fiber diets, such as those lacking in raw fruits and vegetables, are associated with the development of anal fissures.

Calcium channel blockers like diltiazem if applied to the anal mucosa cause a fall in maximum anal resting pressure due to relaxation of the internal anal sphincter muscle, amounting to a reversible 'chemical Sphincterotomy'.

Initial therapy for an anal fissure is medical in nature and more than 75% of acute anal fissures resolve without further therapy. The goal of treatment is to relieve the constipation and to break the cycle of hard bowel movement, associated pain and worsening constipation. Softer bowel movements are easier and less painful for the patient to pass.

5.1 Mechanism of Action

For the treatment of anal fissure and relief of the symptoms associated with anal fissure. Diltiazem hydrochloride is a calcium channel blocker and vasodilator. It increases blood flow to smooth muscles and relaxes muscle tone.

5.2 Pharmacodynamic Properties

Diltiazem is a calcium channel blocker. They act by blocking calcium channels, reducing sphincter spasming and thereby resulting in a greater blood flow in the internal anal sphincter.

5.3 Pharmacokinetic Properties

Comparison of diltiazem and its major metabolite systemic exposure levels following administration of a 120 mg oral dose or thrice daily topical doses (8.5 mg; 2% w/w cream) of the commercial cream diltiazem formulation, demonstrated substantially lower levels of diltiazem and its major metabolites with the proposed new dose regimen and administration route. Systemic diltiazem exposure was lower by more than 30-fold and 80-fold based on AUC and Cmax respectively (refer to “Plasma kinetics in human subjects”), for the topical compared to oral route at the lowest dose generally employed clinically for cardiovascular indications (120-360 mg/day). Similar observations were

made for diltiazem metabolites. Thus, with markedly reduced systemic exposure to diltiazem and its metabolites, no novel safety concerns are anticipated.

6. Nonclinical Properties

6.1 Animal Toxicology or Pharmacology

In a repeat dose toxicity/local tolerance dog study, thrice daily (with the general exception of the first and last days) intrarectal, intraanal or perianal diltiazem administration of the proposed formulation at identical or greater strengths (2-8% w/w), for 1, 8 or 2 weeks, respectively, did not raise any new safety concerns. In all studies, diltiazem was well tolerated with no remarkable systemic effects.

This is not unexpected given the relatively low systemic exposure from the topical administration routes.

Diltiazem hydrochloride is well tolerated when administered thrice daily (with exception of the first and last treatment days) intrarectally, perinanally or intraanally to dogs for 1, 2 or 8 weeks respectively using 2%, 4% and/or 8% cream strengths of the intended commercial formulation. The presence of the primary metabolite desacetyl diltiazem at a 5% concentration in a 4% commercial cream formulation did not alter perianal tolerance of diltiazem hydrochloride in dogs.

Diltiazem hydrochloride cream was also well-tolerated when administered perianally/intraanally twice daily to rabbits for up to 90 days using the intended commercial 2% or a simplified 2% cream formulation. No dermal or rectal irritancy above that of the vehicle control was observed.

Guinea pig sensitisation studies demonstrated that both the intended commercial 2% and a simplified 2% cream diltiazem hydrochloride formulation did not cause any dermal or contact sensitisation and therefore it is classified as a non-sensitiser.

7. Description

CremaGel is supplied for tropical administration, as a gel form of Diltiazem Hydrochloride Gel. Each g of CremaGel contains Diltiazem Hydrochloride 2% w/w.

8. Pharmaceutical Properties

8.1 Incompatibilities

Not applicable

8.2 Shelf Life

Refer Pack

8.3 Packaging Information

Refer Pack

8.4 Storage and Handling Instructions

Refer Pack

9. Patient Counseling Information

Appropriate treatment

Cremagel is indicated for the treatment of anal fissure.
Apply Cremagel once before & after the morning defecation and then subsequently before & after each defecation.
Application of CremaGel at bedtime is a must.
A sitz bath is advised, before the application of CremaGel, for better results.

Drug Interaction
Do not use Cremagel if you are allergic to Diltiazem or any of the other ingredients of this medicine. Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicine such as amiodarone, beta blockers, digoxin, and mefloquine.

10. Details of Manufacturer
Refer pack for manufacturer details.

Marketed By:
Abbott India Limited
Angel Space, Lifestyle Bldg. No. D-4,
Gala No. 4 to 10, 14 to 20, Ground Floor,
107 to 110 & 117 to 120 1st Floor,
207 to 210 & 217 to 220 2nd Floor,
Pimplas Village, Dist. Thane,
Bhiwandi - 421 302, Maharashtra, India.

® - Regd. Trademark of Abbott GMBH & CO. KG.

11. Details of Permission or License Number
Refer pack for license details.

12. Date of Revision
Version: 7.0, dated 12-Jan-26

For Product Complaints/Adverse events or Queries please write to **webmasterindia@abbott.com**

Referencehttps://www.tga.gov.au/sites/default/files/auspar-diltiazem-hydrochloride-170510.pdf
https://hemorrhoidcentersamerica.com/wp-content/uploads/diltiazemointment.pdf