PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

ADCO ZILDEM 180 SR Sustained Release Capsule

ADCO ZILDEM 240 SR Sustained Release Capsule

COMPOSITION

Each **ADCO ZILDEM 180 SR** sustained release capsule contains diltiazem 180 mg as diltiazem hydrochloride.

List of excipients: erythrosine (E127), ethylcellulose, gelatine, indigo carmine (E132), povidone K 30, shellac, sugar spheres, talc, titanium dioxide (E171).

Contains sugar: sucrose 87,75 mg.

Each **ADCO ZILDEM 240 SR** sustained release capsule contains diltiazem 240 mg as diltiazem hydrochloride.

List of excipients: erythrosine (E127), ethylcellulose, gelatine, indigo carmine (E132), povidone K 30, shellac, sugar spheres, talc, titanium dioxide (E171).

Contains sugar: sucrose 117 mg.

CATEGORY AND CLASS

A 7.1 Vasodilators, hypotensive, antihypertensive medicines include other antihypertensive medicines e.g. ACE-inhibitors, ARB's, RAAS, etc.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Diltiazem is a calcium antagonist (calcium-channel blocker) that blocks the slow inward influx of calcium ions across membranes of cardiac muscle, and of smooth muscle in coronary and peripheral arteries. By this means, diltiazem reduces myocardial oxygen demand, increases myocardial oxygen supply, and reduces blood pressure.

Pharmacokinetic properties

Diltiazem is subject to an extensive first-pass effect, giving an absolute bioavailability (compared to intravenous dosing) of about 40 %. Diltiazem undergoes extensive hepatic metabolism; therefore, only 2 % to 4 % of the unchanged drug appears in the urine. In cases of serious liver damage, delayed biotransformation may be anticipated. *In vitro* studies show that 70 % to 80 % of diltiazem is bound to plasma proteins. Single oral doses of 30 to 120 mg result in detectable

plasma levels within 30 to 60 minutes and peak plasma levels two to three hours after drug administration. The plasma elimination half-life following single or multiple drug administration is approximately 3,5 hours. Desacetyldiltiazem is also present in the plasma at levels of 10 % to 20 % of the parent drug and has 25 % to 50 % coronary vasodilatation activity of diltiazem. There is a departure from dose-linearity when single doses of diltiazem above 60 mg are given; a 120 mg dose gave plasma levels three times that of the 60 mg dose.

INDICATIONS

Prophylaxis of angina pectoris, including Prinzmetal's angina.
For the treatment of mild to moderate hypertension.

CONTRAINDICATIONS

- Hypersensitivity to diltiazem or any of the excipients of **ADCO ZILDEM SR** (see **COMPOSITION**).
- Since teratogenic effects were noted in animals, **ADCO ZILDEM SR** should not be administered to pregnant women or to women of child-bearing age.
- **ADCO ZILDEM SR** is excreted in human milk, and therefore should not be administered to lactating women.
- **ADCO ZILDEM SR** should not be administered to patients with decompensated cardiac insufficiency, sick sinus syndrome, conduction disturbances (sino-atrial or atrio-ventricular block) and bradycardia (pulse rate less than 55 beats / min).
- **ADCO ZILDEM SR** should not be administered to patients with severe impairment of liver and kidney function.
- It is not safe to administer **ADCO ZILDEM SR** to patients suffering from porphyria.
- Safety in children has not been established.

WARNINGS AND SPECIAL PRECAUTIONS

ADCO ZILDEM SR should be administered with caution to elderly patients and patients with impairment of liver and kidney function. In these patients, treatment should commence with reduced doses.
If bradycardia is noted, dosage should be decreased, and then discontinued if bradycardia persists.
Administer with caution to patients with pre-existing hypotension and also to those with impaired left ventricular function due to potential negative inotropic properties of diltiazem. Diltiazem (as in **ADCO ZILDEM SR)** has been associated with the development of congestive heart failure.

Contains sugar

Contains sucrose which may have an effect on the glycaemic control of patients with diabetes

mellitus. Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose mal-absorption or sucrase-isomaltase insufficiency should not take **ADCO ZILDEM SR**.

INTERACTIONS

Patients receiving **ADCO ZILDEM SR** in combination with diuretics, ACE-inhibitors and other antihypertensive agents should be regularly monitored. Concomitant use with alpha-blockers such as prazosin should be strictly monitored because of the possible marked synergistic hypotensive effect of this combination.

ADCO ZILDEM SR should be administered with caution to patients taking beta-blocker agents or digitalis glycosides as these may have an additive effect on depression of AV conduction.
The combination of **ADCO ZILDEM SR** with the beta-blocker propranolol may enhance the bioavailability of the propranolol significantly, and thus produce elevated levels of propranolol in the serum. Adjustment in the propranolol dosage may be warranted.

The combination of **ADCO ZILDEM SR** with digitalis glycosides can inhibit digitalis glycoside metabolism and elevate serum levels, which may cause digitalis glycoside toxicity.

Case reports have suggested that blood levels of carbamazepine, cyclosporin, and theophylline may be increased when given concurrently with diltiazem (as in **ADCO ZILDEM SR**). Care should be exercised in patients taking these medicines.

Cimetidine's inhibition of the hepatic cytochrome P450 system causes an increase in plasma diltiazem concentrations. An adjustment in the diltiazem dose may be warranted.

Patients who are taking **ADCO ZILDEM SR** should inform the anaesthetist accordingly before receiving anaesthesia.

HUMAN REPRODUCTION

Pregnancy

Since teratogenic effects were noted in animals, **ADCO ZILDEM SR** should not be administered to pregnant women or to women of child-bearing age (see **CONTRAINDICATIONS**).

Lactation

ADCO ZILDEM SR is excreted in human milk, and therefore should not be administered to lactating women, (see **CONTRAINDICATIONS**).

DOSAGE AND DIRECTIONS FOR USE

PROFESSIONAL INFORMATION

Adults

For the treatment of angina and hypertension:

The dosage of **ADCO ZILDEM SR** should be titrated with an immediate release preparation to meet the needs of the individual patient. The usual maximum dosage is 360 mg/day.

Once the daily dosage has been optimised, **ADCO ZILDEM SR** may be substituted where appropriate.

One 180 mg capsule once or twice daily or one 240 mg capsule once daily.

The **ADCO ZILDEM SR** capsules should be swallowed intact with some liquid.

Elderly and patients with impaired hepatic or renal function:

Treatment should commence with reduced doses.

SIDE EFFECTS

Psychiatric disorders

There have been reports of hyperactivity, sometimes with associated psychiatric symptoms

Nervous system disorders

Nausea, dizziness, confusion, headache

Cardiac disorders

Bradycardia, first-degree atrio-ventricular block

Vascular disorders

Ankle oedema, hypotension, flushing. The effects of vasodilation, particularly ankle oedema, are dose dependent and are more frequent in the elderly

Gastrointestinal disorders

Heartburn, gastric discomfort

Hepato-biliary disorders

Isolated cases of clinical hepatitis have been reported which resolved on cessation of therapy.

Skin and subcutaneous tissue disorders

Rash has been reported in association with diltiazem (as in **ADCO ZILDEM SR)**. These reactions are generally mild and resolve on cessation of therapy; however, erythema multiforme or exfoliative dermatitis has been reported less frequently.

Reproductive system and breast disorders

PROFESSIONAL INFORMATION

Gynaecomastia

General disorders and administration site conditions

Malaise

Investigations

Transient increases in alkaline phosphatase, lactic dehydrogenase (LDH), SGOT and SGPT have been observed.

ADCO ZILDEM SR administration should be stopped if signs of hypersensitivity are observed.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

(see **SIDE EFFECTS**).

Treatment is symptomatic and supportive.

ADCO ZILDEM SR is an extended release capsule and effects may be slow in onset and prolonged.

IDENTIFICATION

ADCO ZILDEM 180 SR: Size 1 hard gelatin capsules, natural transparent cap and opaque pink body filled with white-grey to light yellow granules.

ADCO ZILDEM 240 SR: Size 0 hard gelatin capsules, natural transparent cap and scarlet opaque body filled with white-grey to light yellow granules.

PRESENTATION

PVC/PVDC blisters on aluminium foil packed into individual cartons in strips of 10 capsules.

Pack sizes of 30 and 100 capsules.

STORAGE INSTRUCTIONS

Store in a cool (at or below 25 ºC) dry place.

Keep blister in carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

ADCO ZILDEM 180 SR: 30/7.1/0183

ADCO ZILDEM 240 SR: 30/7.1/0184

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PROFESSIONAL INFORMATION

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