PACKAGE INSERT

SCHEDULING STATUS:

Schedule 3

PROPRIETARY NAME (and dosage form):

CIPLA-INDAPAMIDE Tablets

COMPOSITION:

Each tablet contains 2,5 mg indapamide.

PHARMACOLOGICAL CLASSIFICATION:

A 7.1 Hypotensive medicines.

PHARMACOLOGICAL ACTION:

Indapamide is an antihypertensive diuretic. Its antihypertensive mechanism of action is not clearly understood but possibly involves both renal and extra-renal effects. The diuretic effect (reduction of extracellular fluid and blood volume) probably contributes only minimally since blood pressure is decreased at doses well below the effective diuretic dose. The antihypertensive effect possibly results from reduction of peripheral vascular resistance.

A reduction in left ventricular mass in hypertensive patients has been shown to be associated with prolonged use of indapamide.

Pharmacokinetics

Indapamide is rapidly absorbed after oral administration. Peak blood levels are reached within 2 hours and peak antihypertensive effect after a single dose is reached after approximately 24 hours. The onset of antihypertensive action after multiple doses occurs within 1 to 2 weeks and time to peak effect is 8 to 12 weeks. Indapamide undergoes extensive hepatic biotransformation and only 7% remains unchanged in the urine. The elimination half-life in whole blood is approximately 14 hours. Indapamide binds to plasma proteins (71-79%) and elastin in vascular smooth muscle.

INDICATIONS:

CIPLA-INDAPAMIDE tablets are indicated in the management of mild to moderate hypertension.

CONTRA-INDICATIONS:

Severe hepatic function impairment.

Hypersensitivity to indapamide.

Safety in pregnancy and lactating mothers has not been established.

WARNINGS:

Elderly patients may be more sensitive to the hypotensive and electrolyte effects of **CIPLA-INDAPAMIDE** tablets and are more likely to have age-related renal function impairment. The risk-benefit should be considered in patients presenting the following medical problems: anuria or severe renal function impairment, diabetes mellitus, a history of gout, hyperuricaemia, hepatic function impairment and sympathectomy.

DOSAGE AND DIRECTIONS FOR USE:

Adults: One tablet containing 2,5 mg indapamide to be taken in the morning. **CIPLA-INDAPAMIDE** tablets may be used in conjunction with other agents for the management of hypertension.

Children: Appropriate studies on the age effects relationship of indapamide in children have not been performed and hence a dosage has not been established.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Side Effects

Incidence less frequent requiring medical attention: allergic reaction (skin rash, itching, hives), electrolyte imbalance, specifically hyponaturaemia (dryness of mouth, increased thirst, unusual tiredness or weakness), hypochloraemic alkalosis, or hypokalaemia (irregular heartbeat, mood or mental changes, muscle cramps or pain, nausea or vomiting, weak pulse). Electrolyte imbalance is dose related, with hypokalaemia occurring fairly frequently, but is usually not symptomatic.

Incidence less frequent requiring medical attention only if they continue or are bothersome: diarrhoea, headache, loss of appetite, orthostatic hypotension as a result of volume depletion (dizziness or light-headedness, especially when getting up from a lying or sitting position); trouble sleeping; upset stomach.

Special precautions

Patients sensitive to other sulphonamide-type medications may be sensitive to **CIPLA-INDAPAMIDE tablets.**

The following medications may interact with **CIPLA-INDAPAMIDE tablets**: amiodarone, coumarin or indandione-derivative anticoagulants, digitalis glycosides, other antihypertensives, non-depolarising neuromuscular blocking agents and sympathomimetics. Concurrent use with lithium is not recommended.

Laboratory test values may change in patients taking **CIPLA-INDAPAMIDE** tablets, specifically decreased serum concentrations of calcium and protein-bound iodine (slightly), and potassium and sodium (but usually within normal limits); increased serum concentrations of uric acid (but usually within

normal limits); and increased plasma renin activity.
Recommended patient monitoring includes determination of the concentrations of blood glucose and urea nitrogen, and serum uric acid and electrolytes.

Treatment with **CIPLA-INDAPAMIDE** tablets may require concurrent administration of potassium supplements or potassium-sparing diuretics in patients considered at higher risk of developing hypokalaemia. However, caution should be exercised as the loss of potassium is usually not clinically significant and supplementation may lead to the development of hyperkalaemia.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Symptoms of overdosage: Refer to side-effects and special precautions.

Treatment: Immediate evacuation of the stomach followed by supportive, symptomatic treatment and monitoring of serum electrolyte concentrations and renal function.

IDENTIFICATION:

White round tablets with sharp edges.

PRESENTATION:

Cartons containing 30 or 600 blister-packed tablets.

STORAGE INSTRUCTIONS:

Store below 25°C. Protect from light and moisture.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

31/7.1/0097

NAME AND BUSINESS ADDRESS OF THE APPLICANT:

Cipla Medpro (Pty) Ltd
Rosen Heights
Pasita Street
Rosen Park
7530

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

28 June 1997

VOUBILJET

SKEDULERING STATUS:

Skedule 3.

EIENDOMSNAAM (EN DOSEERVORM):

CIPLA-INDAPAMIDE Tablette.

SAMESTELLING

Elke tablet bevat 2,5mg indapamied.

FARMAKOLOGIESE KLASSIFIKASIE

A 7.1 Hipotensiewe middels.

FARMAKOLOGIESE WERKING

Indapamied is 'n diuretikum met antihipertensiewe aktiwiteit. Sy antihipertensiewe werkingsmeganisme is nie ten volle opgeklaar nie dog hou waarskynlik verband met beide renale en ekstra-renale effekte. Die diuretiese effek (vermindering van ekstrasellulêre vog en bloedvolume) dra waarskynlik slegs in 'n geringe mate by tot bloeddrukverlaging aangesien dit plaasvind by dosisse aansienlik laer as wat nodig is vir effektiewe diurese. Die antihipertensiewe effek kan verskynlik toegeskryf word aan verlaagde perifere vaskulêre weerstand.

Dit is aangetoon dat 'n verlaging in linker ventrikulêre masse by hipertensiewe pasïente verband hou met die langdurige gebruik van indapamied.

Farmakokinetika

Indapamied word vinnig opgeneem na orale toediening. Piek bloedvlakke word binne 2 ure verkry en die grootste antihipertensiewe effek met 'n enkele dosis kom voor na ongeveer 24 uur. Die begin van bloeddrukverlagende werking met meervoudige doseering vind na 1 tot 2 weke plaas en die volle effek is binne 8 tot 12 weke waarneembaar. Indapamied ondergaan uitgebreide biotransformasie in die lewer en slegs 7% kom onveranderd in die urien voor. Die eliminasiehalfleeftyd in die bloed is ongeveer 14 uur. Indapamied bind vir 71-79% aan plasma proteïene en bind ook aan elastien in vaskulêre gladdespier.

INDIKASIES

CIPLA-INDAPAMIDE tablette is aangedui vir die behandeling van ligte tot matige hipertensie.

KONTRA-INDIKASIES

Erge inkorting van lewerfunksie.

Hipersensitiwiteit teenoor indapamied.

Veiligheid tydens swangerskap en borsvoeding is nog nie vasgestel nie.

WAARSKUWINGS

Bejaarde pasïente mag meer gevoelig wees vir die hipotensiewe effek en elektrolietverlies met **CIPLA-INDAPAMIDE** tablette en nieraantasting kom meer dikwels by dié ouderdomsgroep voor. Die moontlike voordele moet deeglik opgeweeg word teenoor potensiële nadelige effekte vir pasïente met die volgende toestande: anurie of erge inkorting van nierfunksie, diabetes mellitus, 'n geskiedenis van jig, hiperuriesemie, inkorting van lewerfunksie se simpatektomie.

DOSIS EN GEBRUIKSAANWYSINGS

Volwassenes: Een tablet bevattende 2,5mg indapamied soggens. **CIPLA-INDAPAMIDE** tablette kan in kombinasie met ander antihipertensiewe middels gebruik word.

Kinders: Toepaslike studies oor die verwantskap tussen ouderdom en effek van indapamied by kinders is nog nie uitgevoer nie en derhalwe is kinderdosis nog nie vasgestel nie.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREëLS

Newe effekte

Voorkoms seldsaam (benodig mediese aandag): allergiese reaksie (veluitslag, jeuk, galbulte); elektroliedversteuring, naamlik hiponatremie (droë mond, dorsigheid, ongewone moegheid of swakheid), hipochloremiese alkalose, of hipokalemie (onreëlmatige hartklop, gemoeds of verstandelike veranderinge, spierkrampe of spierpyn, naarheid of braking, swak pols). Elektroliet versteuning is dosisafhanklik met hipokalemie wat redelik dikwels voorkom alhoewel dit gewoonlik asimptomaties is.

Voorkoms minder algemeen of seldsaam (benodig mediese aandag indien dit voortduur of lastig raak): diarree, hoofpyn, verlies aan eetlus, ortostatiese hipotensie as gevolg van volumeverlies (duiseligheid of lighoofdigheid, veral as die persoon regop kom uit 'n lêende of sittende posisie); slaapsteurnisse; omgekrapte maag.

Spesiale voorsorgmaatreëls

Pasïente sensitief vir ander sulfoonamiedverwante medikasie, mag ook gevoelig wees vir **CIPLA-INDAPAMIDE** tablette.

Die volgende medikasie mag interreageer met **CIPLA-INDAPAMIDE** tablette: amiodaroon, kumarien of teenstolsmiddels wat derivate is van indandioon, digitalis glikosiede, ander antihipertensiewe middels, nie-depolariserende neuromuskulêre blokkeermiddels en simpatomimetika. Gelyktydige gebruik met litium word nie aanbeveel nie.

Vlakke van laboratoriumtoetse kan verander by pasïente wat **CIPLA-INDAPAMIDE** tablette neem, veral verlaagde serumkonsentrasies van kalsium en proteïengebonde jodium (geringe), en kalium en natrium (alhoewel gewoonlik binne normale grense); verhoogde serumkonsentrasies van uriensuur (alhoewel gewoonlik binne normale grense); en verhoogde plasma-renien aktiwiteit.

Aanbevole pasïentmonitering sluit in die bepaling van bloedglukose en ureastikstofkonsentrasies asook serum uriensuur en elektroliete.

Behandeling met **CIPLA-INDAPAMIDE** tablette mag gelyktydige kaliumaanvulling benodig of die gebruik van kaliumsparende diuretika by daardie pasïente wat 'n verhoogde risiko vertoon om hipokalemie te ontwikkel. Sorg moet egter aan die dag gelê word aangesien kaliumverlies gewoonlik nie klinies beduidend is nie en aanvulling geredelik tot die ontstaan van hiperkalemie kan lei.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN

Simptome van oordosering: Verwys na newe-effekte en spesiale voorsorgmaatreëls.

Behandeling: Onmiddelike maaglediging gevolg deur ondersteunende, simptomatiese behandeling en monitering van serum elektroliedkonsentrasies en nierfunksie.

IDENTIFIKASIE

Wit, ronde tablette met skerp kante.

AANBIEDING

Kartonne met 30 of 600 stulpverpakte tablette.

BERGINGSAANWYSINGS

Bewaar onder 25°C. Beskerm teen lig en vogtigheid.

HOU BUITE BEREIK VAN KINDERS.

REGISTRASIE NOMMER

31/7.1/0097

NAAM EN BESIGHEIDSADRES VAN DIE APPLIKANT

Cipla Medpro ((Edms) Bpk
Rosen Heights
Pasita Straat
Rosen Park
7530

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET

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