BRINERDIN®
For the treatment of hypertension

Composition

Each sugar-coated tablet contains:

Reserpine	0.1 mg
Clopamide	5.0 mg
Dihydroergocristine (as mesylate)	0.5 mg

Properties

BRINERDIN is an effective and well-tolerated antihypertensive agent. Reserpine exerts its effect through a central action; clopamide is a diuretic of the thiazide type promoting water and sodium excretion; dihydroergocristine inhibits the hypertensive response to stress.

Controlled clinical studies have demonstrated the superiority of BRINERDIN over its single components and over any combination of any two of these.

The additive effect of the three components in relatively low doses leads to an easily-controlled lowering of blood pressure with a minimum of side effects. BRINERDIN usually reduces blood pressure after 4 to 7 days. The optimum effect is reached after 1 to 4 weeks.

Pharmacokinetics

Reserpine is about 40% absorbed after oral administration. Peak plasma concentrations are reached 1 to 3 hours after ingestion. Elimination takes place with half-lives of 4.5 hours (α-phase) and about 50 hours (β-phase) respectively. Less than 1% of the dose is excreted unchanged in the urine, the greater part being extensively metabolized by the liver and the metabolites excreted mainly with the urine.

Clopamide is rapidly and almost completely (> 90%) absorbed from the gastrointestinal tract. Peak plasma concentrations are reached 1 to 2 hours after ingestion. The elimination half-life is 6 hours. Excretion is mainly via the kidney, about 30% as unchanged drug. Protein binding is 46% and the distribution volume 1.5 L/kg.

Dihydroergocristine is about 25% absorbed after oral administration. Peak plasma concentrations are reached 0.6 hours after administration. Its elimination half-lives are 2 hours (α-phase) and 14 hours (ß-phase) respectively. Protein binding is 68% and the distribution volume 16 l/kg. Total clearance is 1800 mL/minute. Less than 1% is excreted as unchanged drug in the urine, the principal route of excretion being via the bile into the faeces.

Indications

Essential hypertension of all grades of severity

Dosage

Initial treatment
1 tablet per day. In severe hypertension 2 or 3 tablets daily may be required. Since the effect of BRINERDIN is relatively slow in onset, the dosage should not be increased more frequently than once per week.

Maintenance treatment
1 tablet per day or every other day is sufficient in most cases.

Caution is required in the elderly, who may be more sensitive to the effect on blood pressure and electrolytes.

BRINERDIN may be combined with other antihypertensive drugs, such as β-blockers or vasodilators.

Contraindications

Hypersensitivity to any of the components and to sulphonamides (clopamide belongs to this group); therapy-resistant hypokalaemia; severe liver or renal disorders; severe coronary insufficiency, recent myocardial infarction, advanced arteriosclerosis; history of mental depression, electroconvulsive therapy; active peptic ulcer, ulcerative colitis; pregnancy and breast-feeding

Precautions

In diabetic patients, the dosage of antidiabetic agents may have to be adjusted.

BRINERDIN should be given with caution in patients with gout, as a further increase in serum uric acid may be caused. If this occurs, appropriate treatment should be given and BRINERDIN replaced by a non-diuretic antihypertensive drug.

The serum potassium level should be checked regularly during therapy with BRINERDIN. In the majority of patients, potassium supplements are not required, provided a diet containing adequate potassium-rich food (fruit, vegetable, fish, low-fat cheese etc.) is taken.

In patients with impaired renal function, thiazide diuretics may be less effective in lowering blood pressure. Renal function should be closely monitored, as it may be further impaired by the use of antihypertensive drugs.

Because fatigue or orthostatic hypotension may occur during the initial phase of treatment with antihypertensive drugs, patients driving a vehicle or operating machinery should exercise caution until they have determined their individual reaction to treatment.

BRINERDIN should be kept out of the reach of children.

Interactions

With thiazides
Since thiazide diuretics lower renal lithium clearance, lithium dosage should be reduced when BRINERDIN is given concomitantly.
As corticosteroids and non-steroidal anti-inflammatory drugs may diminish the excretion of sodium and water, the dosage of BRINERDIN may have to be increased when such drugs are used concurrently.
The effect of oral anticoagulants may be reduced by thiazide diuretics.

With reserpine
Concurrent use of reserpine with an MAO inhibitor may cause serious potentiation of its CNS depressant effect; if an MAO inhibitor is added to a regimen including reserpine, moderate to severe hypertension and hyperpyrexia may occur.
Concurrent use of alcohol or CNS depressants may enhance the CNS depressant effect of reserpine.
Reserpine may decrease the therapeutic effect of levodopa; dosage adjustments of either or both medications may be necessary.

Side effects

Gastrointestinal disturbances (nausea and vomiting), electrolyte disturbances (especially hypokalaemia); orthostatic hypotension; fatigue; muscle weakness; nasal congestion; mental depression or thrombocytopenia may rarely occur.

Overdosage

Symptoms: nausea, vomiting, diarrhoea; flushing, headache, dizziness; thirst, hypokalaemia, muscle weakness; hypotension, bradycardia, cardiac arrhythmias, depression, confusion and coma
Treatment: elimination of the drug by gastric lavage, followed by administration of charcoal. If indicated, supportive symptomatic treatment including monitoring of the cardiovascular system and of fluid; restoration of the electrolyte balance