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Ketorite™
(Alpha Keto Analogue)
Tablet

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COMPOSITION:
Each film coated tablet contains:

alpha-Ketophenylalanine, Calcium salt	68 mg.
alpha-Hydroxymethionine, Calcium salt	59 mg.
alpha-Ketoisoleucine. Calcium salt	67 mg.
alpha-Ketoleucine. Calcium salt	101 mg.
alpha-Ketovaline, Calcium salt	86 mg.
L-Tryptophan	23 mg.
L-Threonine	53 mg.
L-Tyrosine	30 mg.
L-Histidine	38 mg.
L-Lysine acetate	105 mg.
Total nitrogen content per tablet	36 mg.
Calcium content per tablet	50 mg.

Product Specs.: Innovator

DESCRIPTION:
Ketosteril tablets are administered for nutrition therapy in chronic kidney disease. Ketorite allows the intake of essential amino acids while minimising the amino-nitrogen intake.

CLINICAL PHARMACOLOGY:
Mechanism of Action:
Following absorption, the keto- and hydroxy-analogues are transaminated to the corresponding essential amino acids by taking nitrogen from non-essential amino acids, thereby decreasing the formation of urea by re-using the amino group. Hence, the accumulation of uraemic toxins is reduced. Keto and hydroxy acids do not induce hyperfiltration of the residual nephrons. Ketoacid containing supplements exert a positive effect on renal hyperphosphataemia and secondary hyperparathyroidism.
Moreover, renal osteodystrophy may be improved. The use in combination with a very low protein diet allows to reduce nitrogen intake while preventing the deleterious consequences of inadequate dietary protein intake and malnutrition.
Pharmacokinetics:
The plasma kinetics of amino acids and their integration in the metabolic pathways are well established. It should nevertheless be noted that in uraemic patients, the cause of the changed plasma levels, which occur frequently in these patients, does not seem to be the absorption of the supplied amino acids, i. e. the absorption itself is not disturbed.
The changed plasma levels seem to be due to impaired post-absorptive kinetics, which can be detected in a very early stage of the disease. In healthy individuals, the plasma levels of ketoacids increase within 10 min after oral administration. Increases of up to the 5-fold the baseline levels are achieved. Peak levels occur within 20-60 min, and after 90 min levels stabilise in the range of the base levels.
Gastrointestinal absorption is thus very rapid. The simultaneous increases in the levels of the ketoacids and the corresponding amino acids show that the ketoacids are transaminated very rapidly. Due to the physiological utilisation pathways of ketoacids in the body it is likely that exogenously supplied ketoacids are very rapidly integrated into the metabolic cycles. Ketoacids follow the same catabolic pathways as classical amino acids. No specific study on ketoacid excretion has been performed to date.

DRUG INTERACTION STUDIES:
Concomitant administration of calcium-containing drugs may cause or aggravate elevated serum calcium levels. Drugs that form hardly soluble compounds with calcium (e.g. tetracyclines, quinolines such as ciprofloxacin and norfloxacin as well as drugs containing iron, fluoride or estramustine) should not be taken at the same time to avoid disturbed absorption of the active substances. An interval of at least two hours should elapse between the ingestion of these drugs. The susceptibility to cardioactive glycosides, and hence the risk for arrhythmia will increase, if produces elevated serum calcium levels.
Uraemic symptoms improve under therapy, Thus, in case of aluminium hydroxide administration, the dose of this drug has to be reduced if necessary. Serum phosphate levels should be monitored for a decrease.

INDICATION AND USAGE:
Prevention and treatment of damages due to faulty or deficient protein metabolism in chronic kidney disease in connection with a limited dietary protein intake of 40 g/day or less (adult). Usually this applies to patients whose glomerular filtration rate (GFR) is less than 25 mL/min.

DOSAGE AND ADMINISTRATION:
If not otherwise prescribed the dose for adults (70 kg body weight) is 4 to 8 tablets three times daily during meals. The tablets must not be chewed. Ingestion during meals facilitates proper absorption and the metabolisation into the corresponding amino acids. There is no experience in children.

METHOD OF ADMINISTRATION:
For oral use:
Tablets are administered as long as the glomerular filtration rate (GFR) is below 25 mL/min, and concomitantly, dietary protein is restricted to 40 g/day or less (adult

CONTRAINDICATIONS:
- Hypersensitivity to the active substances or to any of the excipients.
- Hypercalcaemia.
- Disturbed amino acid metabolism.

WARNINGS & PRECAUTIONS:
The serum calcium level should be monitored regularly. Ensure sufficient calorie intake. No experience has been gained so far with the administration in paediatric patients. In the presence of hereditary phenylketonuria, attention should be given to the fact that contains phenylalanine. Monitoring of the serum phosphate levels is needed in case of concomitant administration of aluminium hydroxide

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USE IN SPECIFIC POPULATION:
There are no adequate data from the use in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women. No experience has been made so far with the use during lactation. Ketorite has no influence on the ability to drive and use machines.

ADVERSE REACTIONS:
Adverse effect frequencies are ranked as follows:
Very common (≥ 1/10) Common (≥ 1/100 to < 1/10) Uncommon (≥ 1/1,000 to < 1/100) Rare (≥ 1/10,000 to < 1/1,000) Very rare (<1/10,000) Not known (cannot be estimated from the available data).
Metabolism and nutrition disorders very rare:
Hypercalcaemia.

If hypercalcaemia occurs, the intake of vitamin D should be reduced. In case of persisting hypercalcaemia, the dose as well as the intake of any other calcium sources has to be reduced.

OVER DOSAGE: No case of overdose has been reported.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:
Ketorite Tablet : Pack of 10 x 10 tablets.

FOR FURTHER INFORMATION PLEASE CONTACT:

CCL
Manufactured by :
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

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