Ketoanalogues + Essential Amino Acids

Alfaren™

Film-Coated Tablet
Renal Nutirition Therapy

FORMULATION:
Each film-coated tablet contains:

Calcium-4-methyl-2-oxo-valerate (α-ketoanalogue to leucine, calcium salt)	101 mg
Calcium-2-oxo-3-phenylpropionate (α-ketoanalogue to phenylalanine, calcium salt)	68 mg
Calcium-3-methyl-2-oxo-valerate (α-ketoanalogue to isoleucine, calcium salt)	67 mg
Calcium-DL-2-hydroxy-4-(methylthio)butyrate (α-hydroxyanalogue to methionine, calcium salt)	59 mg
L-Lysine Acetate	105 mg
L-Threonine	53 mg
L-Histidine	38 mg
L-Tyrosine	30 mg
L-Tryptophan	23 mg

Total nitrogen content per tablet: 36 mg. Calcium content per tablet: 1.25 mmol ≈50 mg.

INDICATION:
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 40g/day or less (adults). Usually this applies to patients whose glomerular filtration rate (GFR) is less than 25mL/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.

For oral use.

DESCRIPTION:
Ketoanalogues + Essential Amino Acids (Alfaren) is a combined preparation for the full supply of indispensable amino acids, with minimum nitrogen. It contains all amino acids essential for uremic patients, five of them are keto or hydroxyanalogues in the form of calcium salts, thus allowing reduction in the nitrogen supply and providing calcium. It s a medication for the treatment of chronic kidney disease patients on conservative management therapy (CKD stage I, II, III). In combination with very low protein diet, it helps in delaying the progression of kidney disease in the predialysis period.

CLINICAL PHARMACOLOGY:
Pharmacodynamics:

Following ingestion, the ketoanalogues are transaminated by taking nitrogen from non-essential amino acids, thereby decreasing the formation of urea by re-using the amino group. Ketoacid-containing supplements have a positive influence on the renal hyperphosphatemia and secondary hyperparathyroidism and can improve renal osteodystrophy.

Pharmacokinetics:
In normal individuals, there is an increase in the plasma level of ketoanalogues, 10 min after oral ingestion. These levels reach values that are approximately 5 times higher than the initial level. Peak levels are reached within 20-60 min, and normal levels are reached again after 90 min. G.I. absorption is thus very rapid.

In the plasma, a simultaneous increase in levels of the keto-analogue and the corresponding amino acid show that transamination of the keto-analogues is very rapid. Due to the natural pathways of disposal of α-ketonic acids, it is probable that exogenous intakes are very rapidly integrated into metabolic cycles. Ketoacids follow the same catabolic pathways as the classical amino acids. No specific study on ketoacid excretion has been performed to date.

ADVERSE EFFECTS:
Ketoanalogues + Essential Amino Acids (Alfaren) is tolerated well. Hypercalcemia may develop during the therapy. If hypercalcemia develops, it is recommended to decrease vitamin D intake. If it persists, the dosage of Ketoanalogues + Essential Amino Acids (Alfaren) needs to be reduced, as well as any other source of calcium. Ketoanalogues + Essential Amino Acids (Alfaren) is tolerated well. Hypercalcemia may develop during the therapy. If hypercalcemia develops, it is recommended to decrease vitamin D intake. If it persists, the dosage of Ketoanalogues + Essential Amino Acids (Alfaren) needs to be reduced, as well as any other source of calcium.

CONTRAINDICATION:
Allergy and hypersensitivity to any component of this drug.
Hypercalcemia due to any cause.
Patients of phenylketonuria.
Disturbed amino acid metabolism.

PRECAUTIONS:
The serum calcium level should be monitored regularly. Care to be taken when concomitant administration of calcium required.

EFFECTS ON ABILITY TO DRIVE AND OPERATE MACHINE:
Adverse effects such as sedation, dizziness, difficulty in driving and operating machineries has not been reported with Ketoanalogues + Essential Amino Acids (Alfaren).

DRUG INTERACTIONS:
Concomitant administration of drugs containing calcium, can increase the serum calcium levels.

Concomitant administration of antacids containing aluminum hydroxide should be avoided.

Antimicrobials like tetracyclines, ciprofloxacin, norfloxacin and iron preparations can interfere with the absorption of Ketoanalogues + Essential Amino Acids (Alfaren).

OVERDOSE:
Preclinical data revealed no toxicity based on acute and repeated dose toxicity, safety pharmacology and genotoxicity, but the data in human beings is lacking. No symptoms of toxicity have been observed to date.

USE IN SPECIAL POPULATION:
Pregnancy:
The data on efficacy and safety of Ketoanalogues + Essential Amino Acids (Alfaren) in pregnant women is not well established. Use during pregnancy is based on physician's discretion.

Lactation:
The data on efficacy and safety of Ketoanalogues + Essential Amino Acids (Alfaren) in nursing mothers is not well established. Use during lactation is based on physician's discretion.

Children:
Efficacy and safety in children is not established.

Renal Insufficiency:

Stage	GFR	Supplementation
	(mL/min/1.73 m²)	
1	≥ 90	Not required
2	60 - 89	Not required
3	39 - 59	4 - 8 tabs 3x/day
4	15 - 29	4 - 8 tabs 3x/day
5	< 10 - 15	
	- Not yet under dialysis	4 - 8 tabs 3x/day
	- Under dialysis	4 - 8 tabs 3x/day

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

STORAGE CONDITIONS:
Store at temperatures not exceeding 25°C at a cool, dry place. KEEP MEDICINE OUT OF REACH OF CHILDREN.

Reg. No. : DRP-7884

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Senator Gil Puyat Ave., Brgy. Bel-Air, Makati, Metro Manila
Distributed by:
UNILAB, INC.
No. 66 United Street, Mandaluyong City
Metro Manila, Philippines

BIM173698IN01
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