AGIO PHARMACEUTICALS LTD.

ARTWORK OF PACK INSERT

Brand Name : KETOZAR Tablets	Generic Name : Alpha Ketoanalogue Tablet		Date : 24.05.2024
Name of Packing Material : PACK INSERT	Pack size & Type : 10x10 Tablets Alu-Alu Blister	Country : Philippines - Order	Design : ~~AGIO~~ / Party
Size : L-100mm x H-160mm	Size after folding : L-100mm x H-40mm	Specification : 57gsm ± 5% Map Litho paper	
New/revised artwork Code :	Colour : ■ Black		No. of colours: Single colour
Previous artwork Code : PPIPHK003	Registration No. : DRP-8515		
Change control No.:	Reason for revision :		
Trade Mark Status: ® Registered in country of Export ☐ / TM - Under registration in country of Export ☐ NA			Remark : Do not use any symbol

KETOANALOGUES + ESSENTIAL AMINO ACIDS

KETOZAR

Renal Nutrition Therapy
Film-Coated Tablet

℞

FORMULATION:
Each film-coated tablet contains:
Calcium-4-methyl-2-oxo-valerate
(α-ketoanalogue to leucine, calcium salt) ..... 101 mg
Calcium-3-methyl-2-oxo-butyrate
(α-ketoanalogue to valine, calcium salt) ..... 86 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-ketoanalogue to methionine, calcium salt) ..... 59 mg
L-Lysine Acetate USP ..... 105 mg
L-Threonine USP ..... 53 mg
L-Histidine USP ..... 38 mg
L-Tyrosine USP ..... 30 mg
L-Tryptophan USP ..... 23 mg
Colour : Titanium Dioxide BP

PRODUCT DESCRIPTION:
White to off white, capsule shaped, biconvex, film-coated tablets plain on both sides.

PHARMACOLOGICAL ACTION:
Pharmacodynamic properties:
Pharmacotherapeutic group: Amino acids, including combinations with polypeptides.
Alpha Ketoanalogue Tablets are administered for nutrition therapy in chronic kidney disease. Alpha Ketoanalogue Tablet allows the intake of essential amino acids while minimising the amino-nitrogen intake.
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 uremic toxins is reduced. Keto and hydroxy acids do not induce hyperfiltration of the residual nephrons. Ketoacid containing supplements exert a positive effect on renal hyperphosphatemia and secondary hyperparathyroidism. Moreover, renal osteodystrophy may be improved. The use of Alpha Ketoanalogue Tablets 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.

Pharmacokinetic Properties:
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 minutes, after oral administration. Increases of up to the 5-fold the baseline levels are achieved. Peak levels occur within 20-60 minutes, and after 90 minutes, 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.

INDICATIONS:
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:
Adults (70 kg/body weight): 4-8 tablets 3 times daily during meals.
There is no experience in children.
Administration: For oral use. Tablets may be taken during meals; should be swallowed whole.
Duration of Use: Alpha Ketoanalogue Tablets are given as long as the GFR is between 5 and about 15 mL/min.
Simultaneously for adults, food should contain ≤ 40 g/day of protein ie, generally in patients with glomerular filtration rate (GFR) between 5 and about 15 mL/min. Or as directed by the physician.

CONTRAINDICATIONS:
Hypercalcemia, disturbed amino acid metabolism.
In case of hereditary phenylketonuria, it has to be taken into account that Alpha Ketoanalogue Tablet contains phenylalanine.

WARNINGS AND PRECAUTIONS:
Alpha Ketoanalogue Tablet should be taken during meals to allow proper absorption and metabolism into the corresponding amino acids. The serum calcium levels should be monitored regularly.
Ensure the sufficient supply with calories.
Use in pregnancy: No experience has been made so far with the application in pregnancy.
Use in children: No experience has been made so far with the application in pediatry.

DRUG INTERACTIONS:
Simultaneous administration of medicaments containing calcium (eg, acetolyte) may lead to pathological increases of the serum calcium level or intensification. As the uremic symptoms improve under Alpha Ketoanalogue Tablet, a possible administration of aluminum hydroxide should be reduced. Pay attention to a reduction of serum phosphate.
Do not take drugs together with Alpha Ketoanalogue Tablet that form sparingly soluble compounds with calcium (eg, tetracyclines) in order not to interfere with absorption.

PREGNANCY AND LACTATION:
There are no adequate data from the use of Alpha Ketoanalogue Tablet in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal 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.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Alpha Ketoanalogue Tablet has no influence on the ability to drive and use machines.

ADVERSE DRUG REACTIONS:
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 of the product as well as the intake of any other calcium sources has to be reduced.

OVERDOSE AND TREATMENT:
No case of overdose has been reported.

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

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph.
Seek medical attention immediately at the first sign of any adverse drug reaction.

KEEP ALL MEDICINES OUT OF REACH OF CHILDREN.

STORAGE CONDITION:
Store at temperatures not exceeding 30°C in a dry place and Protect from Moisture.

ERP CODE

AVAILABILITY:
Alu/Alu Blister Pack x 10's (Box of 100's)

DRP-8515
Date of First Authorization: October 24, 2019
Date of Revision of Package Insert: May 23, 2024

Manufactured by:
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Prepared by (Name) : _____ Sign & date: _____