BONKY 1㎍ Injection

(Calcitriol)

Calcitriol is the active form of vitamin D_3(cholecalciferol). The natural of endogenous supply of vitamin D in man mainly depends on ultraviolet light for conversion of 7-dehydrocholesterol to vitamin D_3 in the skin. Vitamin D_3 must be metabolically activated in the liver and the kidney before it is fully active on its target tissues. The initial transformation is catalyzed by a vitamin D_3-25-hydroxylase enzyme present in liver, and the product of this reaction is 25-(OH)D_3(calcifediol). The latter undergoes hydroxylation in the mitochondria of kidney tissue, and this reaction is activated by the renal 25-hydroxyvitamin D_3-1-α-hydroxylase to product 1,25-(OH)2D_3(calcitriol), the active form of vitamin D_3.

The known sites of action of calcitriol are intestine, bone, kidney and parathyroid gland. Calcitriol is the most active known form of vitamin D_3 in stimulating intestinal calcium transport. In acutely uremic rats, calcitriol has been shown to stimulate intestinal calcium absorption. In bone, calcitriol, in conjunction with parathyroid hormone, stimulates resorption of calcium: and in the kidney, calcitriol increases the tubular reabsorption of calcium. In-vitro and in-vivo studies have shown that calcitriol directly suppresses secretion and synthesis of PTH. A vitamin d-resistant state may exist in uremic patients because of the failure of the kidney to adequately convert precursors to the active compound, calcitriol.

Calcitriol when administered by bolus injection is rapidly available in the blood stream. Vitamin D metabolites are known to be transported in blood, bound to specific plasma proteins. The pharmacologic activity of an administered dose of calcitriol is about 3 to 5 days. Two metabolic pathways for calcitriol have been identified, conversion to 1,24,25-(OH)3D_3 and to calcitroic acid.

Composition

Each 1ml ampoule contains
Active ingredient
Calcitriol(BP) ····· 1mcg
Non-active ingredient
Polysorbate (NF) ····· 4.0 ㎎
Sodium chloride (JP) ····· 1.5 ㎎
Sodium ascorbate (USP) ····· 10 ㎎
Disodium Edetate (JP) ····· 1.11 ㎎
Dibasic sodium phosphate anhydrous (USP) ··· 7.6 ㎎
Monobasic sodium phosphate monohydrate (USP) ··· 1.84 ㎎
Water for injection (JP) ····· 1 ㎖

Indications and usage

Bonky (calcitriol injection) is indicated in the management of hypocalcemia in patients undergoing chronic renal dialysis. It has been shown to significantly reduce elevated parathyroid hormone levels. Reduction of PTH has been shown to result in an improvement in renal osteodystrophy.

Description

Transparent, amber glass ampoule injection containing colorless to pale yellow solution

Dosage and Administration

The optimal dose of Bonky (calcitriol injection) must be carefully determined for each patient.

The effectiveness of Bonky therapy is predicated on the assumption that each patient is receiving an adequate and appropriate daily intake of calcium. The RDA for calcium in adults is 800mg. To ensure that each patient receives an adequate daily intake of calcium, the physician should either prescribe a calcium supplement or instruct the patient in proper dietary measures.

The recommended initial dose of Bonky is 0.5mcg (0.01mcg/kg) administered three times weekly, approximately every other day. Bonky can be administered as a bolus dose intravenously through the catheter at the end of hemodialysis, if a satisfactory response in the biochemical parameters and clinical manifestations of the disease state is not observed, the dose may be increased by 0.25 to 0.5mcg at two to four week intervals. During this titration period, serum calcium and phosphorus levels should be obtained at least twice weekly, and if hypercalcemia is noted, the drug should be immediately discontinued until normocalcemia ensues.

Most patients undergoing hemodialysis respond to doses between 0.5 and 3.0mcg(0.01 to 0.05mcg/kg) three times per week.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Discard unused portion.

Precautions

1. Contraindications
   1) Bonky (calcitriol injection) should not be given to patients with hypercalcemia or evidence of vitamin D toxicity.
   2) Patients with a history of hypersensitivity to this drug
2. Warnings
   Since calcitriol is the most potent metabolite of vitamin D available, vitamin D and its derivatives should be withheld during treatment. A non-aluminum phosphate-binding compound should be used to control serum phosphorus levels in patients undergoing dialysis.
   Overdosage of any form of vitamin d is dangerous (see also OVERDOSAGE). Progressive hypercalcemia due to overdosage of vitamin D and its metabolites may be so severe as to require emergency attention.
   Chronic hypercalcemia can lead to generalized vascular calcification, nephrocalcinosis and other soft-tissue calcification. the serum calcium times phosphate (Ca X P) product should not be allowed to exceed 70. Radiographic evaluation of suspect anatomical regions may be useful in the early detection of this condition.
3. Adverse reactions
   1) Hypersensitivity: Rarely hypersensitivity reactions including anaphylaxis and local reddening at injection site have been reported.
   2) Vitamin D toxicity
      Adverse effects of Bonky (calcitriol injection) are, in general, similar to those encountered with excessive vitamin D intake. The early and late signs and symptoms of vitamin D intoxication associated with hypercalcemia include.
      ① Early
         Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain and metallic taste.
      ② Late
         Polyuria, polydipsia, anorexia, weight loss, nocturia, conjuctivitis (calcific), pancreatitis, photophobia, rhinorrhea, pruritus, hyperthermia, decreased libido, elevated BUN, albuminura, hypercholest- erolemia, elevated AST and ALT, ectopic calcification, hypertension, cardiac arrhythmias and, rarely, overt psychosis.
   3)Occasional mild pain on injection have been observed.
4. Precautions
   1) Excessive dosage of Bonky (calcitriol injection) induces hypercalcemia and in some instances hypercalciuria: therefore, early in treatment during dosage adjustment, serum calcium and phosphorus should be determined at lease twice weekly. Should hypercalcemia develop, the drug should be discontinued immediately. Bonky should be given cautiously to patients on digitalis, because hypercalcemia in such patients may precipitate cardiac arrhythmias.
   2) Information for the patient
      The patient and his or her parents should be informed about adherence to instructions about diet and calcium supplementation and avoidance of the use of unapproved non-prescription drugs, including magnesium-containing antacids. Patients should also be carefully informed about the symptoms of hypercalcemia (see ADVERSE REACTIONS).
   3) Essential laboratory tests
      Serum calcium, phosphorus, magnesium and alkaline phosphatase and 24-hour urinary calcium and phosphorus should be determined periodically. during the initial phase of the medication, serum calcium and phosphorus should be determined more frequently (twice weekly)
   4) Because the effect of calcitriol in the treatment of bone loss after implantation has not been established, this drug should not be used.
   5) Because the effect of calcitriol in patients with post menopausal osteoporosis cause by decrease of estrogen have not been established, this drug should not be used.
5. Drug interactions
   1) Magnesium-containing antacids and Bonky should not be used concomitantly because such use may lead to the development of hypermagnesemia.
   2) When vitamin d derivatives and cardioglycosides have been administered concomitantly, cardiac arrhythmia may occur.
   3) Efficacy of vitamin D may be reduced in patients with barbiturates or anticonvulsants.
      0-4) Corticosteroids have been shown antagonization of vitamin D derivatives.
6. Use in pregnancy
   Calcitriol given orally has been reported to be teratogenic in rabbits when given in doses 4 and 15 times the dose recommended for human use. All 15 fetuses in 3 litters at these doses showed external and skeletal abnormalities. however, none of the other 23 letters (156 fetuses) showed significant abnormalities compared with controls. Teratology studies in rats showed no evidence of teratogenic potential.
   Safety and efficacy in pregnant women have not been established.
   Bonky should be used during pregnancy only if the potential benefit justifies potential risk to the fetus.
7. Nursing mothers
   It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reaction in nursing infants from calcitriol, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.
8. Pediatric use
   Safety and efficacy of Bonky in children have not been established.
9. Overdosage
   Administration of Bonky to patients in excess of their requirements can cause hypercalcemia, hypercalciuria and hyperphosphatemia. High intake of calcium and phosphate concomitant with Bonky may lead to similar abnormalities.
   1) Treatment of hypercalcemia and overdosage in patients on dialysis.
      General treatment of hypercalcemia (greater than 1mg/dl above the upper limit of normal range) consists of immediate discontinuation of Bonky therapy, institution of a low calcium diet and withdrawal of calcium supplements.
      Serum calcium levels should be determined daily until normocalcemia ensues.
      Hypercalcemia usually resolves in 2 to 7 days. When serum calcium levels have returned to within normal limits. Bonky therapy may be reinstituted at a dose 0.5mcg less than prior therapy. Serum calcium levels should be obtained at least twice weekly after all dosage changes.
      Persistent or markedly elevated serum calcium levels may be corrected by dialysis against a calcium-free dialysate.
   2) Treatment of accidental overdosage of calcitriol injection The treatment acute accidental overdosage of Bonky should consist of general supportive measures.
      Serial serum electrolyte determinations (especially calcium), rate of urinary calcium excretion and assessment of electrocardiographic abnormalities due to hypercalcemia should be obtained. Such monitoring is critical in patients receiving digitalis. Discontinuation of supplemental calcium and low calcium diet are also indicated in accidental overdosage. Due to the relatively short duration of the pharmacological action of calcitriol, further measures are probably unnecessary. should, however, persistent and markedly elevated serum calcium levels occur, there are a variety of therapeutic alternatives which may be considered, depending on the patients' underlying condition.
      An appropriate forced diuresis, peritoneal dialysis against a calcium-free dialysate, the use of drugs such as bisphosphonate, misramycin, calcitonin, glucocorticosteroids, nitrates and kalium have been reported.
10. Others: carcinogenesis, mutagenesis, impairment of fertility
    1) Long-term studies in animals have not been performed to evaluate the carcinogenic potential of Bonky (calcitriol)
    2) There was no evidence of mutagenicity as studies by the Ames Method.
    3) No significant effects of calcitriol on fertility were reported using oral calcitriol.

Storage

Store in light-resistant, hermetic container at below 30℃. Keep out of reach of children.

Package Units

10 Ampoules

Product Registration Holder :
Bio-Pharmaceuticals Sdn Bhd.
48-2 Jalan Sungai Burung AA32/AA, Section 32,
Bukit Rimau, 40460 Shah Alam, Selangor Malaysia

Product owner :
Yuyu pharma, Inc. ,94 Bio valley 1-ro, Jecheon-si, Chungcheongbuk-do, Republic of Korea

Manufactured for Yuyu pharma, Inc. by :
AJU pharm Co., Ltd., 23 Sandan-ro 121 Beon-gil, Pyeongtaek-si, Gyeonggi-do, Republic of Korea

Reg. No. : MAL20031763ACZ

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Yuyu Pharma

프로젝트 완료 시방서

작성자 / 작성완료일	김미영 / 2023.07.06
자재명/자재코드/개정번호/배율	본키주 (말레이시아) Insert / LT0948 / 05
규격(장폭고/두께)(mm)	115mm(가로) X 250mm(세로)
인쇄도수	1도 인쇄칼라 K100
용지/코팅/후가공	모조지 70g
수정내역	storage / Reg. No. 변경 inj.->Injection
자재업체(도안담당자)	
도안담당(디자인팀)	김미영 매니저 (02-6972-9032 / 내선번호 : 332)
도안확인(수출팀)	오민영 매니저 (02-6972-9175 / 내선번호 : 175)
도안확인(마케팅팀)	ETC
도안확인(QA)	임금희 주임 (043-653-9616 / 내선번호 : 957)

유유제약