4.75"

7.15"

Citriol Injection 1µg/ml

(C a l c i t r i o l)

سیٹرِاول انجیکشن ۱ مائیکروگرام/ملی لیٹر

(کیلسی ٹرائیول)

COMPOSITION:
Each ml contains:
Calcitriol 1µg
(USP Specifications)

DESCRIPTION:
Calcitriol is the active form of vitamin D3 (cholecalciferol). The natural or 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 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) D3 (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 produce 1, 25—(OH) 2D3 (calcitriol), the active form of vitamin D_3.

INDICATIONS:
CITRIOL (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.

DOSAGE AND ADMINISTRATION:
The optimal dose of **CITRIOL** (calcitriol injection) must be carefully determined for each patient.
The effectiveness of 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 **CITRIOL** is 0.5µg (0.01 µg /kg) administered three times weekly, approximately every other day. **CITRIOL** 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 0.5µg 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 normal calcium level is maintained. Most patients undergoing hemodialysis respond to doses between 0.5 and 3.0 µg (0.01 to 0.05 µg /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.

WARNINGS & PRECAUTIONS:
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. Over dosage of any form of vitamin D is dangerous.
Progressive hypercalcemia due to over dosage 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.
Excessive dosage of **CITRIOL** (calcitriol injection) induces hypercalcemia and in some instances hypercalciuria: therefore, early in treatment during dosage adjustment, serum calcium and phosphorus should be determined at least-twice weekly. If hypercalcemia develop, the drug should be discontinued immediately. **CITRIOL** should be given cautiously to patients on digitalis, because hypercalcemia in such patients may precipitate cardiac arrhythmias.

ADVERSE REACTIONS:
Hypersensitivity
Rarely hypersensitivity reactions including anaphylaxis and local reddening at injection site have been reported.
Vitamin D toxicity
Adverse effects of **CITRIOL** (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:
Early
Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain and metallic taste.
Late
Polyuria, polydipsia, anorexia, weight loss, nocturia, conjunctivitis (calcific), pancreatitis, photophobia, rhinorrhea, pruritus, hyperthermia, decreased libido, elevated BUN (Blood uva nitrogen), albuminuria, hypercholesterolemia, elevated AST and ALT, ectopic calcification, hypertension, cardiac arrhythmias and, rarelyovert psychosis.
Occasional mild pain on injection has been observed.

DRUG INTERACTIONS:
Magnesium-containing antacids and **CITRIOL** should not be used concomitantly because such use may lead to the development of When vitamin D derivatives and cardio glycosides have been administered concomitantly, cardiac arrhythmia may occur.
Efficacy of vitamin D may be reduced in patients with barbiturates or anticonvulsants.
Corticosteroids have been shown antagonization of vitamin D derivatives.
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 liters 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.
CITRIOL should be used during pregnancy only if the potential benefit justifies potential risk to the fetus.
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.
Pediatric use
Safety and efficacy of **CITRIOL** in children have not been established.

OVERDOSAGE:
Administration of **CITRIOL** to patients in excess of their requirements can cause hypercalcemia, hypercalciuria and hyperphosphatemia. High intake of calcium and phosphate concomitant with **CITRIOL** may lead to similar abnormalities.
Treatment of hyper calcemia and over dosage in patients on dialysis.
Treatment of hypercalcemia (greater than 1mg/dl above the upper limit of normal range) consists of immediate discontinuation of **CITRIOL** therapy, institution of a low calcium diet and withdrawal of calcium supplements.
Serum calcium levels should be determined daily until normocalcemia ensures.
Hypercalcemia usually resolves in 2 to 7 days. When serum calcium levels have returned to within normal limits, **CITRIOL** therapy may be reinstituted at a dose 0.5 ug 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.

CONTRAINDICATIONS:
CITRIOL (calcitriol injection) should not be given to patients with hypercalcemia or evidence of vitamin D toxicity.
Patients with a history of hypersensitivity to this drug.

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 nonprescription drugs, including magnesium.
Carefully informed about the symptoms of hypercalcemia, essential laboratory tests i.e. 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).
Because the effect of calcitriol in the treatment of bone loss after implantation has not been established, this drug should not be used.
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.

DOSAGE & INSTRUCTIONS:
As directed by the physician. For further details, see the enclosed leaflet. Store between 15-25°C in cool and dry place. Protect from heat & sunlight. Keep away from the reach of children. Do not use the injection if any particulate matter is present, container is leaking or solution is cloudy. To be sold on the prescription of a registered medical practitioner only.

خوراک وطریقہ استعمال:
ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
مزید تفصیلات کیلئے ڈبے میں موجود پرچہ ملاحظہ کریں۔

ہدایات:
دوا کو ۱۵ - ۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان ٹھنڈی اور خشک جگہ پر رکھیں۔ دھوپ اور گرمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔ انجکشن کے ایک ہونے دھندلا ہونے یا اس میں ذرات نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔
صرف متعدد ڈاکٹر کے نسخے پر فروخت کریں۔

HOW SUPPLIED:
Citriol injection
1ml x 10's Ampoules.

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549, Sundar Industrial Estate,
Lahore, Pakistan.