

# Calcimimetic (Cinacalcet, Etelcalcetide)

## Criteria for Use

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VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

*The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.*

The Product Information should be consulted for detailed prescribing information.

## Exclusion Criteria

If the answer to the item below is met, then the patient should NOT receive an initial prescription for cinacalcet or etelcalcetide.

- Serum calcium less than the lower limit normal (e.g., < 8.4 mg/dL, corrected for serum albumin)

## Inclusion Criteria

The answers to one of the following must be fulfilled in order to meet criteria.

- Cinacalcet or etelcalcetide:** Secondary hyperparathyroidism in a patient with chronic kidney disease (CKD) **on chronic dialysis** with elevated intact plasma parathyroid hormone (iPTH) level (e.g., greater than 400 pg/ml or significant trend upwards within two to nine times the upper limit normal for the assay) despite management with standard therapy as appropriate (e.g., dietary phosphate restriction, phosphate binders [calcium-based or non-calcium based], calcitriol or vitamin D analogs [Refer to Issues for Consideration])
- Cinacalcet:** Hypercalcemia (e.g., > 12.5 mg/dl, or symptomatic and > 11.3 mg/dl; corrected for serum albumin) in a patient with primary hyperparathyroidism who is not a surgical candidate or with recurrence despite surgical intervention
- Cinacalcet:** Hypercalcemia (e.g., > 12.5 mg/dl, corrected for serum albumin) in a patient with parathyroid carcinoma despite standard therapy to control hypercalcemia prior to surgical intervention, or who is not a surgical candidate, or who has recurrence despite surgical intervention

Calculation for corrected total serum calcium = total calcium + 0.8 (4 - serum albumin). The normal serum albumin of 4.0gm/dl is based on measurements using bromocresol green. If the bromocresol purple method is used, the normal serum albumin should be adjusted accordingly (e.g., 3.5gm/dl). Local laboratory should be contacted to determine if this correction should be applied to the current result.

[4gm/dl (normal serum albumin) – most recent serum albumin]

Ex. Calcium 9.9mg/dl; albumin 3.2gm/dl

$[4 - 3.2] = 0.8; 0.8 \times 0.8 = 0.64$

$9.9 + 0.64 = 10.54$  (10.5mg/dl is the corrected serum calcium)

## Dosage and Administration

- Refer to Product Information

## Issues for Consideration

### Hypocalcemia

- Both cinacalcet and etelcalcetide lower serum calcium, leading to hypocalcemia, which can be severe. Severe hypocalcemia may cause paresthesias, myalgias, muscle spasms, seizures, QT interval prolongation and ventricular arrhythmia. Patients predisposed to QT interval prolongation, ventricular arrhythmias, or seizures may be at increased risk of these occurring if hypocalcemia develops with cinacalcet or etelcalcetide.
  - Close monitoring is recommended for development of hypocalcemia, with adjustment of other therapies (e.g., phosphate binders, calcitriol or vitamin D analogs) as indicated. Per the respective prescribing information, it is recommended that patients on a maintenance dose of cinacalcet should have serum calcium monitored approximately monthly if receiving treatment for secondary hyperparathyroidism with CKD on dialysis, and every 2 months for patients with parathyroid carcinoma or primary hyperparathyroidism; patients treated with etelcalcetide should have corrected serum calcium levels monitored within 1 week after initiation and dose adjustments, and every 4 weeks during maintenance therapy.
  - For patients on cinacalcet for management of secondary hyperparathyroidism with CKD on dialysis and calcium between 8.4 mg/dL and 7.5 mg/dL, calcium-based phosphate binders and/or vitamin D sterols can be used to increase calcium. If the calcium is below 7.5 mg/dL or the patient has symptoms of hypocalcemia, the dose of cinacalcet should be held until calcium is 8.0 mg/dL. Cinacalcet may be resumed at a lower dose once calcium is corrected.
  - For patients receiving etelcalcetide, the dose should be reduced when calcium is below the lower limit of normal but at or above 7.5 mg/dL. If the patient is symptomatic or the calcium is below 7.5 mg/dL, etelcalcetide should be discontinued. Once the calcium is corrected, etelcalcetide may be re-initiated at a dose of 2.5 mg for patients previously taking 2.5 or 5 mg, or 5 mg less than the previous dose for patients on higher doses.

### Management of CKD and mineral bone disorder (MBD)

- Treatment of CKD-MBD in patients on dialysis often involves the treatment of hyperphosphatemia with phosphate binders, while avoiding hypercalcemia. Phosphate binders, calcitriol or vitamin D analogs, are often listed as inclusion criteria or are part of baseline therapy in clinical trials of calcimimetics. Current guidelines recommend calcimimetics, calcitriol or vitamin D analogs, or a combination of calcimimetics with calcitriol or vitamin D analogs, in patients with CKD on dialysis requiring intervention to lower PTH; and consider calcimimetics, calcitriol, or vitamin D analogs acceptable first-line options for managing elevated PTH in patients with CKD on dialysis. Adjustments in the prescribed therapies will often be required in an attempt to maintain patients within the recommended laboratory target levels. As long-term outcome benefits have not been determined for either the calcimimetics or calcitriol or the vitamin D analogs, treatment selection should be patient specific and depend on laboratory parameters (e.g., iPTH, calcium, phosphorus), and current treatment for CKD-MBD.

## Calcimimetic selection for secondary hyperparathyroidism in CKD on dialysis

- Once the determination has been made for treatment with a calcimimetic, the selection of oral cinacalcet or IV etelcalcetide should depend on treatment response, tolerability, adherence, and cost. Patients adequately controlled on cinacalcet, who are tolerating therapy and adherent to the oral once daily treatment regimen, should remain on cinacalcet, due to limited data on risk vs. long-term outcome benefit (e.g., potential safety concerns including increased adverse event reports of a reduction in calcium and interventions for correction with etelcalcetide [68.9%] compared to cinacalcet [59.8%]; warnings and precautions for both agents for upper gastrointestinal bleeding, with additional evaluation on the potential association with etelcalcetide and fatal and non-fatal bleeding; and heart failure events with etelcalcetide [3.0%] vs. cinacalcet [0.6%]). Patients being switched from cinacalcet to etelcalcetide should have their cinacalcet discontinued for 7 days prior to initiation of etelcalcetide, ensuring that the corrected serum calcium is at or above the lower limit of normal prior to initiation.
- **It should be noted that concurrent use of calcimimetics could result in severe, life-threatening hypocalcemia; taking into consideration patient safety, it is recommended that cinacalcet and etelcalcetide not be used as concomitant therapy.**
- **Note: In order to avoid duplication of or concomitant calcimimetic therapy, VA facilities/pharmacies should coordinate care of Medicare or VA contract patients receiving dialysis at a non-VA dialysis center to ensure these patients are only prescribed/administered one calcimimetic (oral cinacalcet OR IV etelcalcetide), and that they receive their calcimimetic prescription from the non-VA dialysis center/related pharmacy.**

## FDA indications

- Cinacalcet
  - Secondary hyperparathyroidism in adult patients with CKD on dialysis. Limitations of Use: Cinacalcet is not indicated for use in patients with CKD not on dialysis.
  - Hypercalcemia in adult patients with parathyroid carcinoma.
  - Hypercalcemia in adult patients with primary hyperparathyroidism for whom parathyroidectomy would be indicated on the basis of serum calcium levels, but who are unable to undergo parathyroidectomy.
- Etelcalcetide
  - Secondary hyperparathyroidism in adult patients with CKD on hemodialysis. Limitations of Use: Etelcalcetide has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with CKD who are not on hemodialysis and is not recommended for use in these conditions.

### **Off-label use of cinacalcet**

- The long-term safety and efficacy of cinacalcet in patients with CKD not on dialysis has not been established; there may however be individual cases where treatment of a non-dialysis patient with markedly elevated iPTH (per the criteria above) might be considered. It should be noted that patients treated with cinacalcet who are not on dialysis may be at increased risk for the development of hypocalcemia (as noted in the Prescribing Information).
- Limited data have shown a reduction in hypercalcemia and iPTH with cinacalcet in patients with hyperparathyroidism after kidney transplantation. Further controlled clinical trials are needed to determine the long-term safety and efficacy in this patient population; appropriate treatment with cinacalcet should be determined on a case by case basis.

### **Pregnancy**

- Refer to the prescribing information for data on animal reproduction studies to determine use of cinacalcet or etelcalcetide in patients of child-bearing potential, and the need for contraceptive counseling and education on potential risk vs. benefit of taking cinacalcet or etelcalcetide if the patient were to become pregnant.

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