Chronic kidney disease–mineral bone disorder (CKD-MBD) is a universal complication of advanced chronic kidney disease, and is characterized by bone disease, calcification of extraskelatal tissue, and multiple biochemical abnormalities.

Specific CKD-MBD laboratory abnormalities, such as hyperphosphatemia, hyperparathyroidism, hypocalcemia, and elevated fibroblast growth factor 23 levels, are each independently associated with mortality in dialysis patients (1, 2).

Management of CKD-MBD
Treatment for CKD-MBD generally starts with counseling about a low-phosphorus diet and phosphate binders to limit gastrointestinal phosphorus absorption (3–5). Clinically meaningful reductions in serum phosphorus levels can also be achieved by increasing weekly dialysis time. Next, calcitriol or another active vitamin D agent is typically started to reduce parathyroid hormone (PTH) levels to goal. Neither the Kidney Disease Outcomes Quality Initiative nor the Kidney Disease Improving Global Outcomes (KDIGO) guidelines give preference to any specific active vitamin D agent.

Calcimimetics in January 2018.

Calcimimetics
Cinacalcet, fractures, and parathyroidectomy
Dialysis patients have a higher incidence of fractures, with increased morbidity and mortality compared with the general population (14). Secondary hyperparathyroidism is a major contributor to bone disease in ESRD, and treatment with cinacalcet improves histopathologic changes seen on bone biopsy (15). In the EVOLVE Trial, the effect of cinacalcet on clinical fracture was not statistically significant (relative hazard, 0.89; 95% confidence interval, 0.75 to 1.07) (11). However, when accounting for differences in baseline characteristics, multiple fractures, and/or events prompting discontinuation of study drug, cinacalcet reduced the rate of clinical fracture by 10% to 29% (16). Furthermore, parathyroidectomy occurred in 7% of cinacalcet-treated patients and 14% of placebo-treated patients (relative hazard, 0.44; 95% confidence interval, 0.36 to 0.54). Independent predictors of parathyroidectomy included younger age, female gender, geographic region, and absence of history of peripheral vascular disease (11).

Challenges and new developments
There are multiple practical challenges to current successful calcimimetic prescribing. Prescribers often encounter barriers owing to insurance prior authorization policies. Cinacalcet often comes at significant patient cost under Medicare Part D, and some patients are unable to afford copays. The wholesale annual cost of cinacalcet dosed at 30 to 60 mg per day ranges from $10,000 to $19,400, respectively. Gastrointestinal side effects of cinacalcet also limit patient adherence.

Calcimimetics
In January 2018, dialysis providers became responsible for providing both cinacalcet and etelcalcetide for Medicare patients and likely, many private insurers as well. This represents an opportunity to address many of the practical prescribing issues noted here.

In conclusion:
- Management of CKD-MBD in ESRD includes dietary phosphorus restriction, phosphate binders, active vitamin D agents, and calcimimetics.
- Cinacalcet use is associated with lower rates of parathyroidectomy and possibly, fewer bone fractures.
- Data on the effect of cinacalcet on cardiovascular disease and mortality remain uncertain.
- Compared with cinacalcet, etelcalcetide more effectively lowers PTH, with a similar incidence of nausea and vomiting but higher rates of hypercalcemia.
- Physicians will need to individualize CKD-MBD care by carefully evaluating the value and benefit against the risks and costs of different approaches as dialysis facilities began taking on the provision of calcimimetics in January 2018.

References
1. Block GA, et al. Mineral metabolism, mortality, and

Calcimimetics in End Stage Renal Disease
By Susan Ziolkowski and Graham Abra
Table 1. Cinacalcet vs. etelcalcetide in CKD-MBD

<table>
<thead>
<tr>
<th>Mechanism of Action</th>
<th>SENSIPAR (cinacalcet)</th>
<th>PARSABIV (etelcalcetide)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route</td>
<td>Oral</td>
<td>Intravenous</td>
</tr>
<tr>
<td>Efficacy: % of patients with &gt;30% iPTH reduction</td>
<td>63.9%</td>
<td>77.9%</td>
</tr>
<tr>
<td>Safety: % patients with Adverse Reactions</td>
<td>cCa decrease 68.9%</td>
<td>Nausea 18.3%</td>
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