KDIGO CKD-MBD QUICK REFERENCE GUIDE

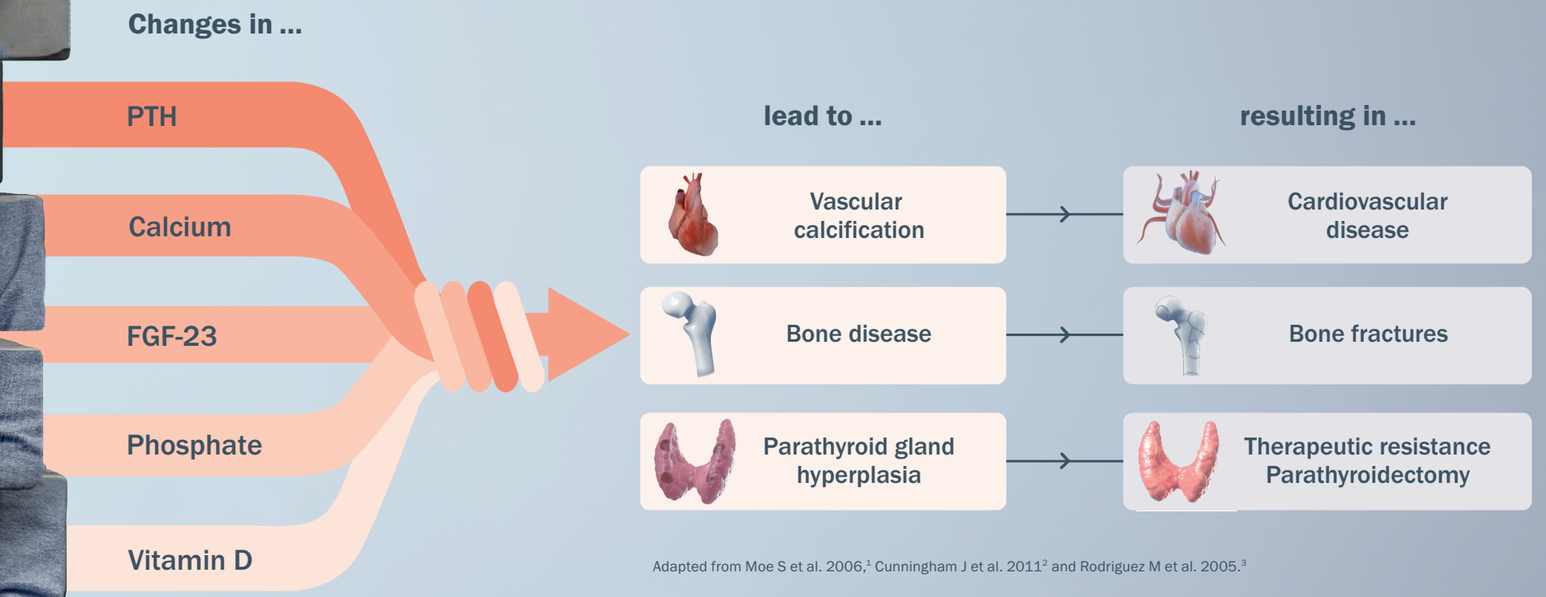
VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA

VIFOR PHARMA

This guide presents the recommendation statements (quoted in bold and starred ★) from the KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease - Mineral and Bone Disorder (CKD-MBD) with those that remained unchanged from the 2009 KDIGO Clinical Practice Guideline for the Diagnosis, Evaluation, Prevention, and Treatment of CKD-MBD.

CHRONIC KIDNEY DISEASE-MINERAL AND BONE DISORDER (CKD-MBD)

Figure 1



Adapted from Moe S et al. 2006,[1] Cunningham J et al. 2011[2] and Rodriguez M et al. 2005.[3]

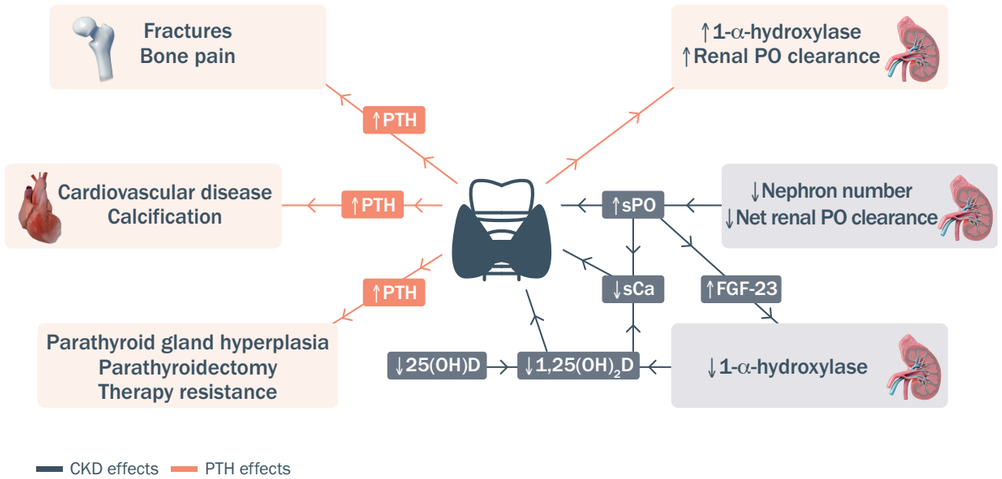
This figure illustrates the interrelated nature of biochemical abnormalities, bone diseases, vascular calcification and parathyroid gland hyperplasia in CKD-MBD. It is important to recognise that treatment of one abnormality could affect others and therefore it is critical to assess biochemical parameters together.[2] The 2017 KDIGO CKD-MBD update states:

"In patients with CKD Stages G3a–G5D, treatments of CKD-MBD should be based on serial assessments of PO, Ca and PTH levels considered together".[4]

Ca: Calcium; CKD: Chronic kidney disease; CKD-MBD: Chronic kidney disease-mineral and bone disorder; FGF-23: Fibroblast growth factor-23; PO: Phosphate; PTH: Parathyroid hormone.

PATHOPHYSIOLOGY OF SECONDARY HYPERPARATHYROIDISM (SHPT) IN CKD

Figure 2



Adapted from Cunningham J et al. 2011,[2] Rodriguez M et al. 2005,[3] Friedl C et al. 2017[5] and Wu W et al. 2018.[6]
FGF-23: Fibroblast growth factor-23; PO: Phosphate; PTH: Parathyroid hormone; sCa: Serum calcium; sPO: Serum phosphate; 25(OH)D: 25-hydroxyvitamin D; $1,25(OH)_2D$: 1,25-dihydroxyvitamin D.

As kidney function declines in CKD, there is a progressive deterioration in mineral homeostasis, with a disruption of normal serum and tissue concentrations of phosphate and calcium, and changes in circulating levels of parathyroid hormone (PTH) and $1,25(OH)_2D$ (calcitriol).[2]

There are increased levels of circulating FGF-23, possibly as an adaptive response to phosphate regulation, which suppress the 1-α hydroxylase. This, along with 25(OH)D insufficiency reduces vitamin D activation. Both the resultant reduction in circulating $1,25(OH)_2D$ and the associated decrease in gastrointestinal calcium absorption stimulate increased PTH secretion.[2,5]

Prolonged stimulation of the parathyroid glands leads to parathyroid hyperplasia, while increased levels of circulating PTH are associated with bone complications and vascular calcification, which are linked with increased morbidity and mortality.[2]

CONSEQUENCES OF SHPT AND TREATMENT OPTIONS

- In patients with CKD the estimated prevalence of SHPT is 56% overall in patients with Stage 3 to Stage 5 CKD, with prevalence increasing from 40–82% with progressive reduction in kidney function.[7]
- Higher levels of PTH are associated with increased disease progression, morbidity and mortality in patients with CKD.[8–11]
- The optimal PTH level is not known in patients with CKD G3a–G5 not on dialysis and modest increases in PTH may represent an appropriate adaptive response to declining kidney function.[4]
- However, Recommendation 4.2.1 suggests that patients with levels of intact PTH progressively rising or persistently above the upper normal limit for the assay be evaluated for modifiable factors, including hyperphosphatemia, hypocalcemia, high phosphate intake, and vitamin D deficiency.[4]
- Further, in adult patients, Recommendation 4.2.2 suggests $1,25(OH)_2D$ (calcitriol) and vitamin D analogues not be routinely used. It is reasonable to reserve the use of calcitriol and vitamin D analogues for patients with CKD G4–G5 with severe and progressive hyperparathyroidism.[4]
- An alternative to calcitriol and its analogues is ‘nutritional’ vitamin D supplementation (cholecalciferol and ergocalciferol); however, no studies of sufficient duration were identified, and so this therapy remains unproven.[4]

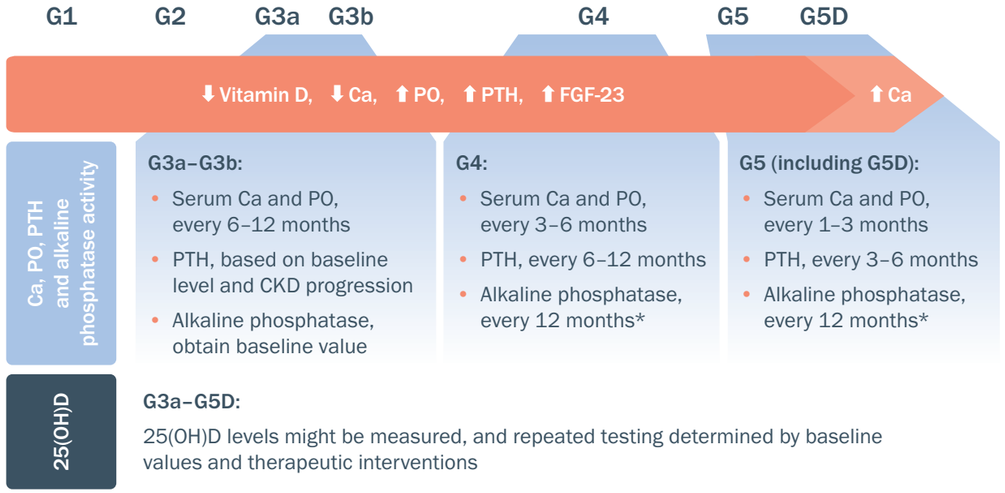
Glomerular Filtration Rate (GFR) categories – Description and range[4]

GFR category	GFR (mL/min/1.73 m^2)	Terms
G1	≥ 90	Normal or high
G2	60–89	Mildly decreased*
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	< 15	Kidney failure

*Relative to young adult level

CHAPTER 3.1 DIAGNOSIS OF CKD-MBD: BIOCHEMICAL ABNORMALITIES[4]

Frequency of monitoring: CKD G3a–G5D



*or more frequently in the presence of elevated PTH
No recommendation for FGF-23 to be measured in clinical practice
Ca: Calcium; FGF-23: Fibroblast growth factor 23; PTH: Parathyroid hormone; PO: Phosphate; 25(OH)D: 25-hydroxyvitamin D.

What the guideline statements say

In patients with CKD G3a–G5D:

(3.1.1) Recommend monitoring serum levels of calcium, phosphate, PTH, and alkaline phosphatase activity beginning in CKD G3a. (1C)

(3.1.2) It is reasonable to base the frequency of monitoring serum calcium, phosphate, and PTH on the presence and magnitude of abnormalities, and the rate of progression of CKD. (Not Graded)

(3.1.3) Suggest that 25(OH)D levels might be measured, and repeated testing determined by baseline values and therapeutic interventions. (2C). Suggest that vitamin D deficiency and insufficiency† be corrected using treatment strategies recommended for the general population. (2C)

(3.1.4) Recommend that therapeutic decisions be based on trends rather than on a single laboratory value, taking into account all available CKD-MBD assessments. (1C)

(3.1.5) Suggest that individual values of serum calcium and phosphate, evaluated together, be used to guide clinical practice rather than the mathematical construct of calcium–phosphate product (Ca x PO). (2D)

(3.1.6) Recommend that clinical laboratories inform clinicians of the actual assay method in use and report any change in methods, sample source (plasma or serum), or handling specifications to facilitate the appropriate interpretation of biochemistry data. (1B)

†Most studies define deficiency as serum 25(OH)D <10 ng/mL and insufficiency ≥10 but <20–32 ng/mL. There is no consensus on what defines 'adequate' or toxic vitamin D levels.

CHAPTER 3.2 DIAGNOSIS OF CKD-MBD: BONE[4]

What the guideline statements say

In patients with CKD G3a–G5D:

(3.2.1) With evidence of CKD-MBD and/or risk factors for osteoporosis, suggest bone mineral density (BMD) testing to assess fracture risk if results will impact treatment decisions. (2B)

(3.2.2) It is reasonable to perform a bone biopsy if knowledge of the type of renal osteodystrophy will impact treatment decisions. (Not Graded)

(3.2.3) Suggest that measurements of serum PTH or bone-specific alkaline phosphatase can be used to evaluate bone disease because markedly high or low values predict underlying bone turnover. (2B)

(3.2.4) Suggest not to routinely measure bone-derived turnover markers of collagen synthesis and breakdown. (2C)

Rationale for guideline update

3.2.1 BMD testing

2009 guidance	2017 update
3.2.2 … BMD testing should not be perfomed routinely …	**3.2.1** In patients with CKD G3a–G5D with evidence of CKD-MBD and/or risk factors for osteoporosis, test BMD to assess fracture risk if results will impact treatment decisions (2B)

Multiple new prospective studies have documented that lower DXA (dual-energy X-ray absorptiometry) BMD predicts incident fractures in patients with CKD G3a–G5D. The order of these first 2 recommendations was changed because a DXA BMD result might impact the decision to perform a bone biopsy.

3.2.2 Bone biopsy

2009 guidance	2017 update
3.2.1 … perform a bone biopsy… prior to therapy with bisphosphonates	**3.2.2** In patients with CKD G3a–G5D, it is reasonable to perform a bone biopsy if knowledge of the type of renal osteodystrophy will impact treatment decisions (Not Graded)

The primary motivation for this revision was the growing experience with osteoporosis medications in patients with CKD, low BMD, and a high risk of fracture. The inability to perform a bone biopsy may not justify withholding antiresorptive therapy from patients at high risk of fracture.

CHAPTER 3.3 DIAGNOSIS OF CKD-MBD: VASCULAR CALCIFICATION[4]

What the guideline statements say

In patients with CKD G3a–G5D:

(3.3.1) Suggest that a lateral abdominal radiograph can be used to detect the presence or absence of vascular calcification, and an echocardiogram can be used to detect the presence or absence of valvular calcification, as reasonable alternatives to computed tomography-based imaging. (2C)

(3.3.2) Suggest that patients with known vascular/valvular calcification be considered at highest cardiovascular risk. (2A) It is reasonable to use this information to guide the management of CKD-MBD. (Not Graded)

CHAPTER 4.1 TREATMENT OF CKD-MBD: SERUM PHOSPHATE AND CALCIUM[4]

What the guideline statements say

In patients with CKD G3a–G5D:

(4.1.1) Treatments of CKD-MBD should be based on serial assessments of phosphate, calcium and PTH levels, considered together. (Not Graded)

(4.1.2) Suggest lowering elevated phosphate levels towards the normal range. (2C)

(4.1.3) Suggest avoiding hypercalcaemia in adult patients. (2C)

(4.1.4) Suggest using a dialysate calcium concentration between 1.25 and 1.50 mmol/L (2.5 and 3.0 mEq/L). (2C)

(4.1.5) Decisions about phosphate-lowering treatment should be based on progressively or persistently elevated serum phosphate. (Not Graded)

(4.1.6) In adult patients receiving phosphate-lowering treatment, suggest restricting the dose of calcium-based phosphate binders. (2B)

(4.1.7) Recommend avoiding the long-term use of aluminum-containing phosphate binders and, in patients on dialysis, recommend avoiding dialysate aluminum contamination to prevent aluminum intoxication. (1C)

(4.1.8) Suggest limiting dietary phosphate intake in the treatment of hyperphosphataemia alone or in combination with other treatments. (2D) It is reasonable to consider phosphate source (e.g. animal, vegetable, additives) in making dietary recommendations. (Not Graded)

(4.1.9) In patients on dialysis, suggest increasing dialytic phosphate removal in the treatment of persistent hyperphosphataemia. (2C)

Rationale for guideline update

4.1.1 Treatment decisions based on serial lab results

2009 guidance	2017 update
Not in guideline	**4.1.1** In patients with CKD G3a–G5D, treatments of CKD-MBD should be based on serial assessments of phosphate, calcium and PTH levels considered together (Not Graded)

This new recommendation was provided in order to emphasise the complexity and interaction of CKD-MBD laboratory parameters.

4.1.2 Treatment goals for hyperphosphataemia

2009 guidance	2017 update
4.1.1 In patients with CKD G3a–G5, maintain serum phosphate in the normal range	**4.1.2** In patients with CKD G3a–G5D, lower elevated phosphate levels towards the normal range (2C)

There is an absence of data supporting that efforts to maintain phosphate in the normal range are of benefit to CKD G3a–G4 patients, including some safety concerns. Treatment should aim at overt hyperphosphataemia.

4.1.3 Treatment goals for hypercalcaemia

2009 guidance	2017 update
4.1.2 In patients with CKD G3a–G5D, maintain serum calcium in the normal range	**4.1.3** In adult patients with CKD G3a–G5D, avoid hypercalcaemia (2C)

Mild and asymptomatic hypocalcaemia (e.g. in the context of calcimimetic treatment) can be tolerated in order to avoid inappropriate calcium loading in adults.

4.1.5 Phosphate-binding agents in hyperphosphataemia

2009 guidance	2017 update
4.1.4 In patients with CKD G3a–G5 (2D) and G5D (2B) use phosphate-binding agents in the treatment of hyperphosphataemia	**4.1.5** In adult patients with CKD G3a–G5D, decisions about phosphate-lowering treatment should be based on progressively or persistently elevated serum phosphate (Not Graded)

Emphasises the perception that early 'preventive' phosphate-lowering treatment is currently not supported by data. The broader term 'phosphate-lowering' treatment is used instead of phosphate-binding agents because all possible approaches (i.e. binders, diet, dialysis) can be effective.

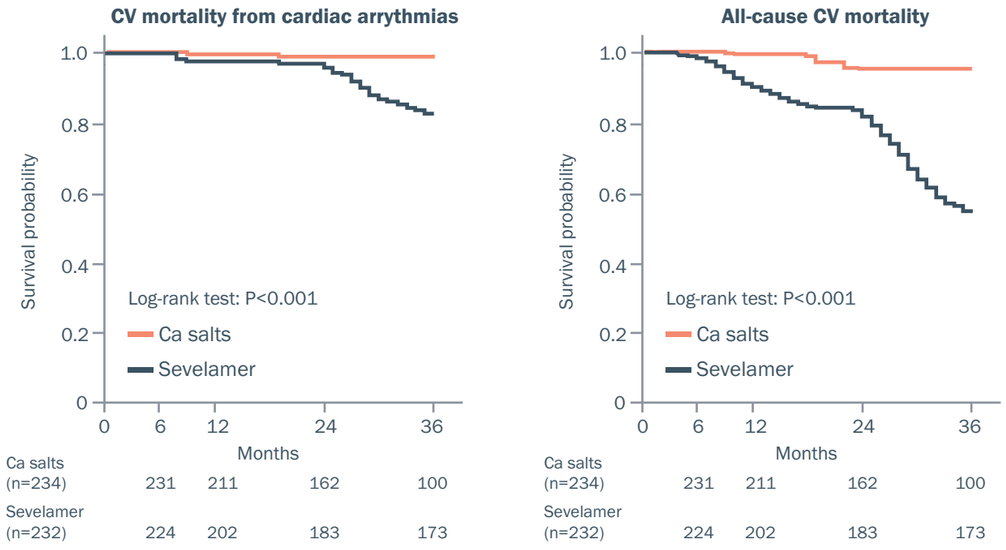
4.1.6 Restricted use of calcium-based phosphate binders

2009 guidance	2017 update
4.1.5 … restrict the dose of Ca-based phosphate binders in the presence of persistent or recurrent hypercalcaemia (1B) … arterial calcification and/or adynamic bone disease and/or if serum PTH levels are persistently low (2C)	**4.1.6** In adult patients with CKD G3a–G5D receiving phosphate-lowering treatment, restrict the dose of Ca-based phosphate binder (2B)

New evidence from 3 RCTs supports a more general recommendation to restrict calcium-based phosphate binders in hyperphosphataemic patients, across all severities of CKD.

Evidence to support the guideline update:[12]

Open-label, randomised, controlled, parallel-group study of Ca-based vs Ca-free phosphate binder* in dialysis-dependent CKD patients (N=466)



*Sevelamer vs Ca carbonate
Republished with permission of Elsevier on behalf of the National Kidney Foundation from Di Iorio B et al. Am J Kidney Dis. 2013;62:771–8.
Ca: Calcium; CV: Cardiovascular.

Patients receiving the Ca-based binder experienced higher CV mortality due to cardiac arrhythmias, all-cause CV mortality and all-cause mortality vs. patients receiving the Ca-free binder, even when adjusted for confounding variables

4.1.8 Limiting dietary phosphate intake

2009 guidance	2017 update
4.1.7 … limit dietary phosphate intake in the treatment of hyperphosphataemia alone or in combination with other treatments	**4.1.8** In patients with CKD G3a–G5D, limit dietary phosphate intake in the treatment of hyperphosphataemia alone or in combination with other treatments (2D). It is reasonable to consider phosphate source (e.g. animal, vegetable, additives) in making dietary recommendations (Not Graded)

New data on phosphate sources were deemed to be included as an additional qualifier to the previous recommendation.

CHAPTER 4.2 TREATMENT OF ABNORMAL PTH LEVELS IN CKD-MBD[4]

What the guideline statements say

In patients with CKD G3a–G5 not on dialysis:

(4.2.1) The optimal PTH level is not known. However, it is suggested that patients with levels of intact PTH progressively rising or persistently above the upper normal limit (ULN) for the assay be evaluated for modifiable factors, including hyperphosphataemia, hypocalcaemia, high phosphate intake, and vitamin D deficiency. (2C)

(4.2.2) In adult patients, it is suggested that calcitriol and vitamin D analogues not be routinely used. (2C) It is reasonable to reserve the use of calcitriol and vitamin D analogues for patients with CKD G4–G5 with severe and progressive hyperparathyroidism. (Not Graded)

In patients on dialysis:

(4.2.3) Suggest maintaining intact PTH levels in the range of approximately two to nine times the upper normal limit for the assay. (2C) Suggest that marked changes in PTH levels in either direction within this range prompt an initiation or change in therapy to avoid progression to levels outside of this range. (2C)

(4.2.4) For those requiring PTH-lowering therapy, suggest calcimimetics, calcitriol, or vitamin D analogues, or a combination of calcimimetics with calcitriol or vitamin D analogues. (2B)

(4.2.5) In patients with CKD G3a–G5D with severe hyperparathyroidism who fail to respond to medical/pharmacological therapy, suggest parathyroidectomy. (2B)

Rationale for update

4.2.1 Evaluation for modifiable risk factors in pre-dialysis patients with abnormal PTH levels

2009 guidance
4.2.1
In patients with levels of intact PTH above the ULN, first evaluate for hyperphosphataemia, hypocalcaemia and vitamin D deficiency (2C)

2017 update
4.2.1
In patients with CKD G3a–G5 not on dialysis, the optimal PTH level is not known. However, patients with levels of intact PTH progressively rising or persistently above the ULN for the assay should be evaluated for modifiable factors, including hyperphosphataemia, hypocalcaemia, high phosphate intake, and vitamin D deficiency (2C)

The Work Group felt that modest increases in PTH may represent an appropriate adaptive response to declining kidney function and has revised this statement to include 'persistently' above the upper normal PTH level as well as 'progressively rising' PTH levels, rather than 'above the upper normal limit.' That is, treatment should not be based on a single elevated value.

4.2.2 Use of calcitriol and vitamin D analogues pre-dialysis

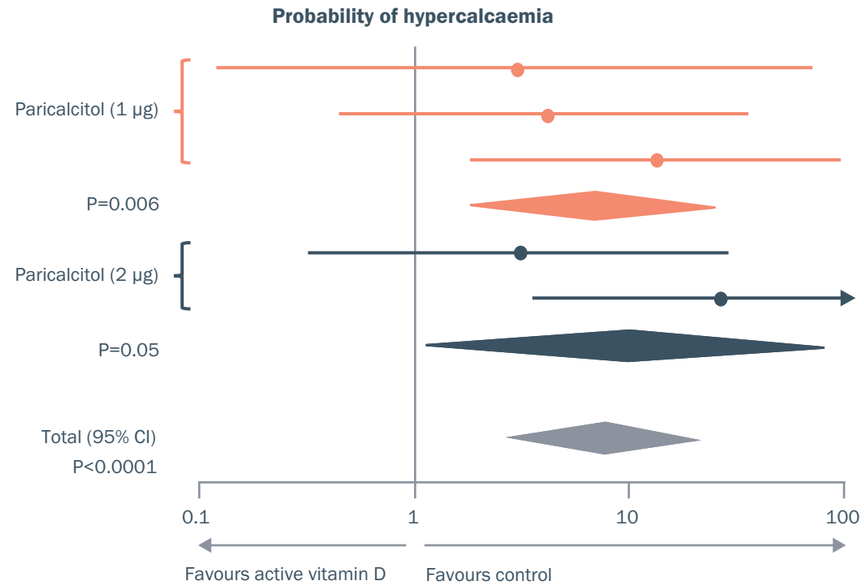
2009 guidance
4.2.2
… serum PTH is progressively rising and remains persistently above the ULN for the assay despite correction of modifiable factors, treat with calcitriol or vitamin D analogues

2017 update
4.2.2
In adult patients with CKD G3a–G5 not on dialysis, do not routinely use calcitriol and vitamin D analogues (2C). It is reasonable to reserve the use of calcitriol and vitamin D analogues for patients with CKD G4–G5 with severe and progressive hyperparathyroidism (Not Graded)

Recent RCTs of vitamin D analogues failed to demonstrate improvements in clinically relevant outcomes but did demonstrate increased risk of hypercalcaemia.

Evidence to support the guideline update:[13]

Systematic review and meta-analysis to evaluate the effect of active vitamin D on CV outcomes in pre-dialysis CKD patients



Republished with permission of John Wiley and Sons on behalf of the Asian Pacific Society of Nephrology from Li X-H et al. Nephrology. 2015;20:706–14.

Active vitamin D treatment did not alter left ventricular mass index and systolic function, but was associated with an increased risk of hypercalcaemia vs control (RR, 7.85; 95% CI, 2.92–21.10)

4.2.4 Treatment of SHPT in dialysis patients

2009 guidance
4.2.4
In patients with CKD G5D and elevated or rising PTH, we suggest calcitriol, or vitamin D analogues, or calcimimetics, or a combination of calcimimetics and calcitriol or vitamin D analogues to lower PTH …

2017 update
4.2.4
In patients with CKD G5D requiring PTH-lowering therapy, use calcimimetics, calcitriol, or vitamin D analogues, or a combination of calcimimetics and calcitriol or vitamin D analogues (2B)

Recommendation was re-evaluated due to a series of secondary and post-hoc publications of the EVOLVE trial. Although EVOLVE did not meet its primary endpoint, the majority of the Work Group members were reluctant to exclude potential benefits of calcimimetics for G5D patients based on subsequent pre-specified analyses. The Work Group, however, decided not to prioritise any PTH-lowering treatment at this time because calcimimetics, calcitriol, or vitamin D analogues are all acceptable first-line options in G5D patients.

CHAPTER 4.3 TREATMENT OF BONE WITH BISPHOSPHONATES, OTHER OSTEOPOROSIS MEDICATIONS, AND GROWTH HORMONE[4]

What the guideline statements say

In patients with CKD G1–G2 with osteoporosis and/or high risk of fracture, as identified by World Health Organization (WHO) criteria:

(4.3.1) Recommend management as for the general population. (1A)

In patients with CKD G3a–G3b with PTH in the normal range and osteoporosis and/or high risk of fracture, as identified by WHO criteria:

(4.3.2) Suggest treatment as for the general population. (2B)

In patients with CKD G3a–G5D with biochemical abnormalities of CKD-MBD and low BMD and/or fragility fractures:

(4.3.3) **Suggest that treatment choices take into account the magnitude and reversibility of the biochemical abnormalities and the progression of CKD, with consideration of a bone biopsy. (2D)**

Rationale for update

4.3.3 Treatment considerations in patients with biochemical abnormalities and fracture risk

2009 guidance
4.3.3
In patients with CKD G3a–G3b with biochemical abnormalities of CKD-MBD and low BMD and/or fragility fractures …

2017 update
4.3.3
In patients with CKD G3a–G5D with biochemical abnormalities of CKD-MBD and low BMD and/or fragility fractures, treatment choices should take into account the magnitude and reversibility of the biochemical abnormalities and the progression of CKD, with consideration of a bone biopsy (2D)

Recommendation 3.2.2 now addresses the indications for a bone biopsy prior to antiresorptive and other osteoporosis therapies. Therefore, 2009 Recommendation 4.3.4 has been removed and 2017 Recommendation 4.3.3 is broadened from CKD G3a–G3b to CKD G3a–G5D.

CHAPTER 5 KIDNEY TRANSPLANT BONE DISEASE[4]

What the guidelines statements say

In patients in the immediate post-kidney-transplant period:

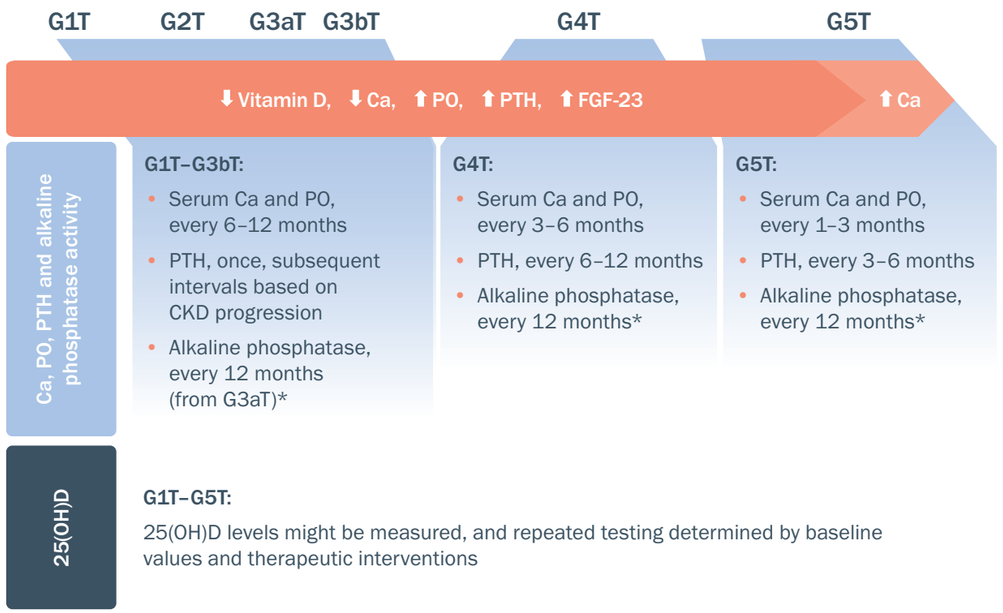
(5.1) Recommend measuring serum calcium and phosphate at least weekly, until stable. (1B)

In patients after the immediate post-kidney-transplant period:

(5.2) It is reasonable to base the frequency of monitoring serum calcium, phosphate, and PTH on the presence and magnitude of abnormalities, and the rate of progression of CKD. (Not Graded)

Frequency of monitoring

Frequency of monitoring: CKD G3a–G5D



*or more frequently in the presence of elevated PTH
No recommendation for FGF-23 to be measured in clinical practice
Ca: Calcium; FGF-23: Fibroblast growth factor 23; PTH: Parathyroid hormone; PO: Phosphate; 25(OH)D: 25-hydroxyvitamin D.

In patients with CKD G1T–G5T:

(5.3) Suggest that 25(OH)D levels might be measured, and repeated testing determined by baseline values and interventions. (2C)

(5.4) Suggest that vitamin D deficiency and insufficiency be corrected using treatment strategies recommended for the general population (2C)

(5.5) In those with risk factors for osteoporosis, suggest that BMD testing be used to assess fracture risk if results will alter therapy. (2C)

5.5 BMD testing in transplant patients at risk of fractures

2009 guidance
5.5
In patients with an estimated GFR >~30 mL/min/1.73 m²... measure BMD... if have risk factors for osteoporosis ...
5.7
In patients with CKD G4T–G5T, BMD testing should not be performed routinely ...

2017 Update
5.5
In patients with G1T–G5T with risk factors for osteoporosis, use BMD testing to assess fracture risk if results will alter therapy (2C)

There is growing evidence that DXA BMD predicts fractures across the spectrum of CKD severity (see Recommendation 3.2.1), with limited data suggesting these findings extend to transplant recipients. The 2009 Recommendations 5.5 and 5.7 were therefore combined to give Recommendation 5.5.

What the guidelines say about treatment

In patients in the first 12 months after kidney transplant with an estimated glomerular filtration rate greater than approximately 30 mL/min/1.73 m² and low BMD:

(5.6) Suggest that treatment with vitamin D, calcitriol/alfacalcidol, and/or antiresorptive agents be considered. (2D)

- **Suggest that treatment choices be influenced by the presence of CKD-MBD, as indicated by abnormal levels of calcium, phosphate, PTH, alkaline phosphatases, and 25(OH)D. (2C)**
- **It is reasonable to consider a bone biopsy to guide treatment. (Not Graded)**

There are insufficient data to guide treatment after the first 12 months.

In patients with CKD G4T–G5T:

(5.7) Suggest management as for patients with CKD G4–G5 not on dialysis, as detailed in Chapters 4.1 and 4.2. (2C)

Rationale for update

5.6 Treatment of biochemical abnormalities in transplant patients

2009 guidance
5.6
... consider a bone biopsy to guide treatment, specifically before the use of bisphosphonates

2017 update
5.6
In patients in the first 12 months after kidney transplant with an estimated GFR >~30 mL/min/1.73 m² and low BMD, consider treatment with vitamin D, calcitriol/alfacalcidol, and/or antiresorptive agents (2D)

- Treatment choices should be influenced by the presence of CKD-MBD, as indicated by abnormal levels of calcium, phosphate, PTH, alkaline phosphatases and 25(OH)D (2C)
- Consider a bone biopsy to guide treatment (Not Graded)

There are insufficient data to guide treatment after the first 12 months

The second bullet is revised, consistent with the new bone biopsy recommendation (Recommendation 3.2.2).

PAEDIATRIC CKD-MBD[4]

What the guideline statements say

Diagnosis of CKD-MBD: Biochemical Abnormalities

(3.1.1) In children, suggest monitoring serum levels of calcium, phosphate, PTH, and alkaline phosphatase activity beginning in CKD G2. (2D)

Diagnosis of CKD-MBD: Bone

(3.2.5) Recommend that infants with CKD G2–G5D have their length measured at least quarterly while children with CKD G2–G5D should be assessed for linear growth at least annually. (1B)

Treatment of CKD-MBD: Serum Phosphate and Calcium

(4.1.3) In children with CKD G3a–G5D, suggest maintaining serum calcium in the age-appropriate normal range. (2C)

(4.1.6) In children with CKD G3a–G5D, it is reasonable to base the choice of phosphate-lowering treatment on serum calcium levels. (Not Graded)

Treatment of CKD-MBD: Serum PTH

(4.2.2) In children, calcitriol and vitamin D analogues may be considered to maintain serum calcium levels in the age-appropriate normal range. (Not Graded)

Treatment of CKD-MBD: Bone Disease

(4.3.4) In children and adolescents with CKD G2–G5D and related height deficits, recommend treatment with recombinant human growth hormone when additional growth is desired, after first addressing malnutrition and biochemical abnormalities of CKD-MBD. (1A)

CKD-MBD GUIDELINE UPDATE HIGHLIGHTS[4]

- BMD testing is now suggested in patients with CKD-MBD and/or osteoporosis risk factors, if the results will impact future treatment. Multiple new prospective studies have documented that lower DXA BMD predicts incident fractures in patients with CKD G3a–G5D.
- Trends—rather than single values of serum phosphate, calcium, and PTH—should be considered together to make treatment decisions for CKD-MBD.
- Phosphate-lowering therapies (e.g. diet, binders, dialysis) should be based on progressive or persistent elevated serum phosphate. Elevated serum phosphate levels should be lowered towards the normal range.
- Avoid hypercalcaemia in adults, since new evidence links higher calcium concentrations to increased mortality and nonfatal cardiovascular events in adults with CKD.
- Restrict the dose of calcium-based phosphate binders across all severities of CKD. New evidence suggests that excess exposure to exogenous calcium in adults may be harmful in all severities of CKD, regardless of other risk markers.
- When limiting dietary phosphate intake, the source of phosphate (e.g. animal, vegetable, additives) should be considered, since restricting dietary phosphate must not compromise adequate protein intake.
- Patients with intact PTH levels that are progressively rising or persistently above the upper normal limit for the assay should be evaluated for modifiable factors, including hyperphosphataemia, hypocalcaemia, high phosphate intake, and vitamin D deficiency.
- Routine use of calcitriol or its analogues in CKD G3a–G5 is no longer recommended. It is reasonable to reserve the use of calcitriol and its analogues for patients with CKD G4–G5 with severe and progressive hyperparathyroidism. Recent studies failed to demonstrate improvements in clinically relevant outcomes (cardiovascular) but did demonstrate increased risk of hypercalcaemia.
- Treatment choices should take into account the magnitude and reversibility of biochemical abnormalities and CKD progression, with consideration of a bone biopsy in patients with CKD G3a–G5D with CKD-MBD and low BMD and/or fragility fractures.

References: 1. Moe S et al. Kidney Int. 2006;69:1945–53. **2.** Cunningham J et al. Clin J Am Soc Nephrol. 2011;6:913–21. **3.** Rodriguez M et al. Am J Renal Physiol. 2005;288:F253–64. **4.** Kidney Disease: Improving Global Outcomes (KDIGO) Work Group. Kidney Int Suppl. 2017;7:1–59. **5.** Friedl C et al. Int J Nephrol Renovascular Dis. 2017;10:109–22. **6.** Wu W et al. Exp Dermatol. 2018;27:1201–09. **7.** Levin A et al. Kidney Int. 2007;71:31–8. **8.** Geng G et al. Osteoporos Int. 2019;30:2019–25. **9.** Xu Y et al. Clin Kidney J. 2021;14(10):2213–20. **10.** Kovesdy CP et al. Kidney Int. 2008; 73:1296–302. **11.** Schumock G et al. Curr Med Res Opin. 2008;24:3037–48. **12.** Di Iorio B et al. Am J Kidney Dis. 2013;62:771–8. **13.** Li X et al. Nephrology. 2015;20:706–14.

KDIGO Clinical Practice Guidelines are based upon the best information available at the time of publication. This Guide is designed to provide information and assist decision-making. It is not intended to define a standard of care, and should not be interpreted as prescribing an exclusive course of management. Variations in practice will inevitably and appropriately occur when clinicians consider the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Healthcare professionals using these recommendations should decide how to apply them to their own clinical practice.

This guide was developed through the support of Vifor Fresenius Medical Care Renal Pharma.

VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA

VIFOR PHARMA

MED-HQ-NA-2200027 Date of preparation: June 2022
Vifor Fresenius Medical Care Renal Pharma Ltd