GUIDELINES FOR THE TREATMENT OF HYPERPHOSPHATAEMIA & SECONDARY HYPERPARATHYROIDISM IN END STAGE RENAL FAILURE

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Transplantation, Urology & Nephrology Directorate

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Document Number:17/A	Reason for Change :Update
Original Date of Approval: January 2009	Originally Approved By: Renal guideline committee
Recent Date of Approval: May 2012	Approved By: Renal guideline committee
Date Effective From May 2012	Superseded Documents
Review Date: April 2014	

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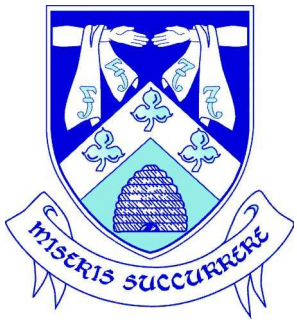

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SECTION 1

INTRODUCTION

Rationale: Chronic kidney disease is an international public health problem affecting 5-10 % of the world population. As kidney function declines, there is a progressive deterioration in mineral homeostasis, with a disruption of normal serum and tissue concentrations of phosphorus and calcium and changes in circulating levels of hormones. These include parathyroid hormone, 25-hydroxyvitamin D (25(OH) D), 1,25- dihydroxyvitamin D (1,25(OH)2D), and other vitamin D metabolites, fibroblast growthfactor - 23(FGF-23). As kidney function declines the ability of the kidneys to appropriately excrete a phosphate load is diminished, leading to hyperphosphataemia, elevated PTH, and decreased 1,25(OH)2D with associated elevations in the levels of FGF-23. The conversion of 25(OH)D to 1,25(OH)2D is impaired, reducing intestinal calcium absorption and increasing PTH. The kidney fails to respond adequately to PTH, which normally promotes phosphaturia and calcium reabsorption or to FGF-23 which also enhances phosphate excretion. Therapy is focused on correcting biochemical and hormonal abnormalities in an effort to limit their consequences.

Secondary hyperparathyroidism affects a significant number of haemodialysis patients, and metabolic disturbances associated with it may contribute to their higher mortality rate. This guideline has been formulated to provide a framework for medical, nursing staff and dieticians with regards to the treatment of hyperphosphataemia and secondary hyperparathyroidism in end stage renal disease.

Scope : This guideline is specifically for end stage renal failure ,CKD stage 5 on renal replacement therapy. It is a guide for the multidisciplinary team, doctors, nurses, dieticians. It requires a multidisciplinary approach. The nursing team in conjunction with the medical team will review blood levels and adjust/ change drug levels as necessary. Dietitian in conjunction with the nursing team will review and educate patients with regards to their diet.

Principles (Beliefs): The ultimate goal of treating SHPT is to normalise mineral metabolism, prevent bone disease and prevent extraskeletal manifestations of the altered biochemical process. It is important to identify SHPT early. Earlier identification and assessment of SHPT will improve bone and mineral metabolism in chronic kidney disease and reduce its associated complications such as fractures, pain and cardiovascular calcification.

SECTION 2

The statement of the standard that is to be achieved is as follows.

>IDENTIFY TARGET BLOOD RANGES FOR CKDMBD, STAGE 5 ON RENAL REPLACEMENT THERAPY.

>DISCUSS THE CONTROL OF SERUM PHOSPHATE.

> CALCIUM BASED PHOSPHATE BINDERS
>NON CALCIUM BASED PHOSPHATE BINDERS

>DISCUSS THE CONTROL OF SECONDARY HYPERPARATHYROIDISM

>**ACTIVE VITAMIN D ANALOUGES**

>CALCIMIMETIC

SECTION 3

If commencing or adjusting drug therapies consider previous trends and not single readings in isolation.

❖ Target Blood Ranges

Stage 5 CKD	Phosphate (mmol/L)	Corrected Calcium (mmol/L)	PTH Pg/ml
	0.8-1.5	2.2-2.6	150-500

❖ Control of Serum Phosphate

(1) Refer early for dietary advice. Dietary phosphate restriction is essential for phosphate control.

(2) Commence phosphate binders when dietary restrictions are unable to maintain serum phosphate < 1.6mmol/L.

❖ Calcium Based Phosphate Binders

- **Calcium containing phosphate binders are the initial binders of choice if calcium < 2.6**
- **Titrate up dose of calcium containing binders as required to achieve adequate phosphate control <1.5mmol/L**

Binder	Form / Elemental Ca^{2+}	Max Daily Dose	Starting Dose
Calcium Acetate (Phosex)	500mg tablet / 125 mg 1g tablet / 250mg	TTT QDS TT TDS	TT TDS T TDS
Calcium Acetate & Magnesium Carbonate (Osvaren)	435mg 235mg tab / 110 mg Ca, 60mg Mg	TTT QDS	T TDS *Monitor serum Mg*
Calcium carbonate (Calcichew)	Not routinely used		

- **Keep daily elemental calcium intake from binders to less than 1500 mg.**
- **Total elemental calcium from diet and binders not to exceed 2000mg/day.**

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❖ Non Calcium Based Phosphate Binders

Consider non-calcium containing binder therapy in following circumstances:

- **Baseline serum calcium > 2.6mmol/L.**
- **Baseline low PTH < 150pg/ml.**
- **Evidence of tissue/vascular calcification.**
- **As add on to calcium containing binder therapy if target phosphate not achieved despite maximum dose usage.**

Choice of binder depends or preparation the patient prefers to take.

Consider switching to alternate phosphate binder if poor compliance suspected or gastrointestinal side effects reported.

Binder	Form	Max Daily Dose	Starting Dose
Lanthanum Carbonate (Foznol – crush/chew**)**	250mg, 500mg, 750mg, 1g tablet	3750mg	500mg TDS *After meals*
Sevelamer Carbonate (Renvela – swallow whole)	800mg tablet 2400mg sachet	TTT TDS 3 sachets	TTT TDS T TDS
Sevelamer Hydrochloride (Renagel – swallow whole)	800mg tablet	TTT TDS	TTT TDS *With meals*

If dietary measures/binders fail to control phosphate effectively consider increasing frequency & duration of dialysis.

GUIDELINES FOR THE TREATMENT OF HYPERPHOSPHATAEMIA & SECONDARY HYPERPARATHYROIDISM IN END STAGE RENAL FAILURE

❖ Control of Secondary Hyperparathyroidism

Serial follow up of PTH levels should be performed at three month intervals to assess the continued control of disease

(1) Ensure optimal control of serum phosphate through dietary restrictions and phosphate binders.

(2) If PTH remains > 500pg/ml or fails to trend downwards despite achieving adequate phosphate control ie. <1.5mmol/L commence/increase active vitamin D analogues.

Vitamin D analogues should not be commenced until satisfactory phosphate control is achieved

❖ Active Vitamin D Analogues

- **Alphacalcidol (*One Alpha*) is the vitamin D analogue of choice in the treatment of secondary hyperparathyroidism.**
- **Initial dose of 0.25mcg, titrated up to 1mcg, if calcium remains within range.**
- **If PTH remains > 500pg/ml or fails to trend downwards despite use of alphacalcidol consider swapping to Paricalcitol, (on 2 consecutive readings).**
- **Consider using paricalcitol in preference to alphacalcidol if serum calcium levels are running at higher end of normal reference range**
- **Paricalcitol (*Zemplar*) should be administered orally.**

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Zemplar	Dose	Max Daily Dose	Starting Dose
Oral	1 mcg tablet 2 mcg tablet	4mcgs od	2 mcq od

- **Titrate dose of Paricalcitol upwards until PTH </= 500pg/ml**
- **Pre-dialysis calcium, phosphate should be monitored weekly once patients are commenced on paricalcitol.**
- **Monthly PTH serum readings should be taken once patients are commenced on paricalcitol.**
- **If PTH < 150pg/ml consider the following options, reduce or stop vitamin D therapy, switch to non-calcium containing binders, lower dialysate calcium concentration in order to avoid adynamic bone disease.**
- **If PTH remains above target and further dose escalation in vitamin D analogue limited by serum calcium > 2.6 consider the following options:**
  - **PTH > 500pg/ml or fails to trend downwards on 2 consecutive readings: consider adding cinacalcet to conventional therapy (binders/vitamin D).**
  - **Consider parathyroidectomy if refractory SHPT (PTH 1000pg/ml) despite cinacalcet use.**

GUIDELINES FOR THE TREATMENT OF HYPERPHOSPHATAEMIA & SECONDARY HYPERPARATHYROIDISM IN END STAGE RENAL FAILURE

❖ **Cinacalcet** *(Mimpara)*

- **Cinacalcet is indicated for treatment of SHPT.**
- **It is associated with less hypercalcaemia compared to vitamin D3 analogues.**
- **Cinacalcet should be considered in patients with PTH > 500pg/ml and in whom further dose escalation of vitamin D analogue is limited by elevated calcium (>2.6 mmol/L).**

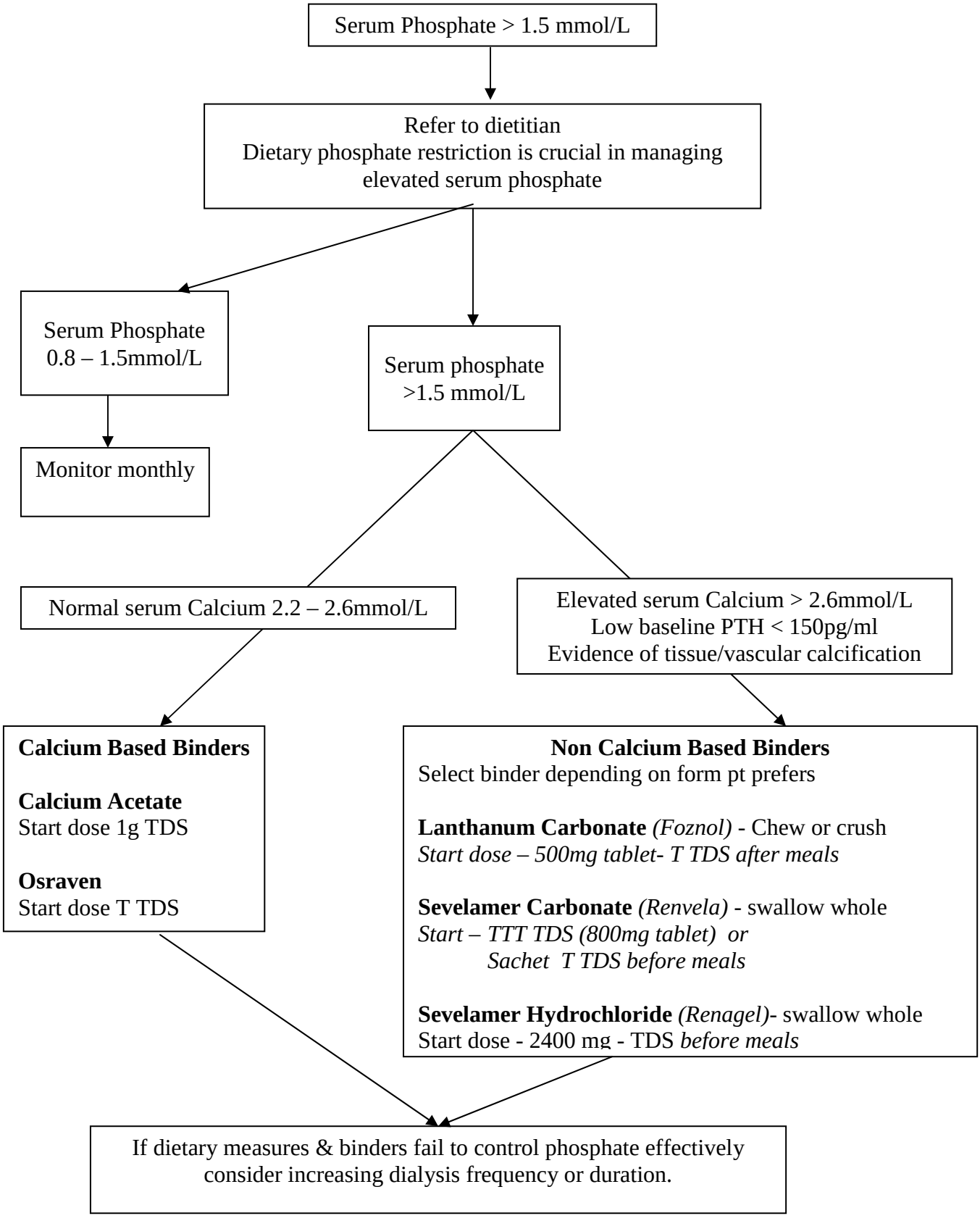
Mimpara	Dose	Max Daily Dose	Starting Dose
Oral	30mg 60mg 90mg	6 Tabs 3 Tabs 2 Tabs	30mg (od) Taken >12 hrs before blood draw

- **Starting dose 30mg od titrating upwards every 4 weeks until PTH </= 500pg/ml or pt on max dose 180mg od. Titrate downwards once satisfactory control is achieved.**
- **Pre-dialysis calcium/phosphate/magnesium should be monitored weekly once patients are commenced on cinacalcet.**
- **Monthly PTH serum readings should be taken once patients are commenced on cinacalcet.**
- **If on Zemplar and/or Mimpara and PTH low (<150):**
  - **Reduce/stop cincacalcet.**
  - **Switch to non-calcium containing binders.**
  - **Consider reduce/stop vitamin D analogue.**
  - **Use low calcium dialysate bath eg. 1mmol/L.**

If commencing or adjusting drug therapies consider result trends of a least two consecutive month readings. If changes are made in OPD appointments please inform nursing staff in the relevant HD or PD Unit.

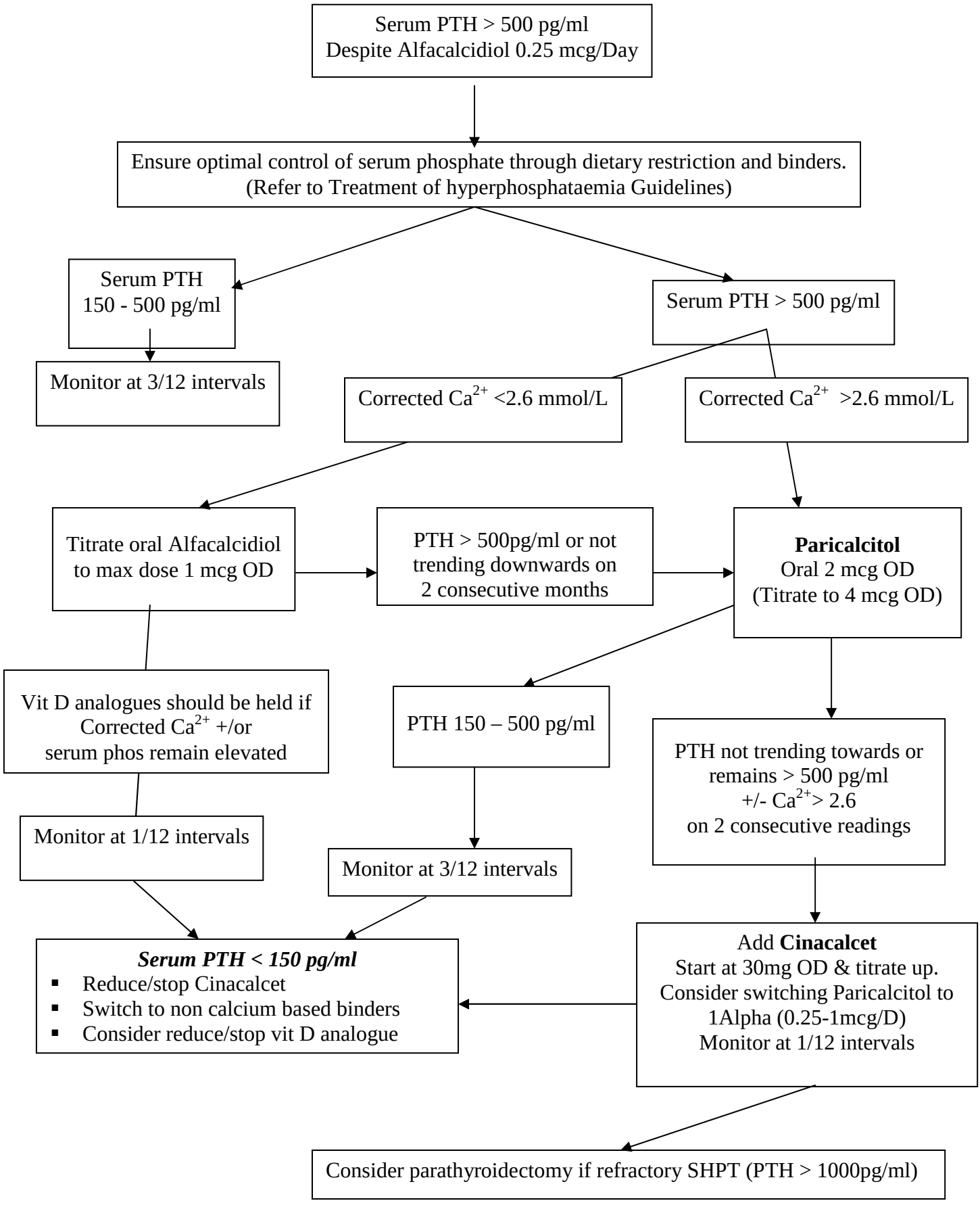
SECTION 4

Treatment of Hyperphosphataemia



GUIDELINES FOR THE TREATMENT OF HYPERPHOSPHATAEMIA & SECONDARY HYPERPARATHYROIDISM IN END STAGE RENAL FAILURE

TREATMENT OF ELEVATED PTH



SECTION 5

DISTRIBUTION

A copy of the guideline will be circulated to the relevant areas by the Divisional Nurse Manager and Consultants. The Clinical Nurse Manager in each area is responsible to ensure all staff access and read the guideline. The guideline will also be available on the renal intranet webpage. The Consultant staff are responsible to ensure that medical staff access and read the guideline.

SECTION 6

FILING

A copy will be filed in the guideline and procedure book folder in each unit. The master copy will be filed in the Divisional Nurse Managers office.

SECTION 7

REVIEW

This guideline will be reviewed in two years, Feburary 2013.

SECTION 8

SUPERSEDED/OBSOLETE DOCUMENTS

This is an updated version of Guidelines for Treatment of Hyperphosphataemia & SHPT and replaces all previous versions.

SECTION 9

DEVELOPMENT AND CONSULTATION PROCESS

CONSULTANT SUMMARY	
Informal meetings & emails between Caroline Brummel, Brian Carey & Oonagh Deeney following identification of required policy review.	March - November 2011
Subsequent development of treatment flow diagrams	
Informal meeting between Prof Conlon, Caroline Brummel, Brian Carey & Oonagh Deeney to discuss proposed policy & treatment flow diagrams.	December 2011
Draft 1 presented to Renal Guideline Committee. Await medical review of recently published IMPACT SHPT study	February 2012
Draft 2 presented to Renal Guideline Committee.	March 2012
Draft 3 presented to Renal Guideline Committee.	April 2012

Where Received	Summary of Feedback	Actions/Response

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SECTION 10

REFERENCE DOCUMENTS

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