

# Case series; hypocalcaemia requiring hospitalisation following administration of Denosumab in Chronic Kidney Disease (CKD) patients

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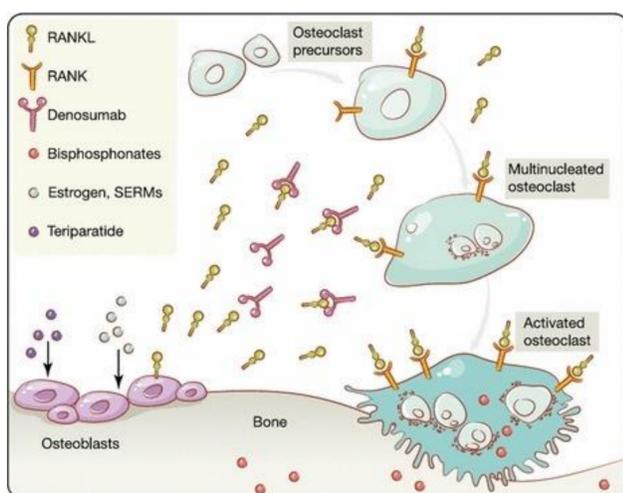
## Objective

This case series aims to raise awareness of the risk of hospital admission due to hypocalcaemia in this patient subset and highlight the role of the pharmacist in patients receiving denosumab.

## Background

Denosumab:

- Indications include; treatment of osteoporosis, to increase bone mass density with androgen deprivation therapy for prostate cancer. <sup>1,2,3</sup>
- Monoclonal antibody with high affinity and specificity for RANK Ligand. <sup>1,2,3</sup> Inhibition of osteoclast formation and activity decreases bone resorption thus increasing bone mass and strength. <sup>2,3</sup>
- Does not require dose adjustment in renal impairment. <sup>2,3</sup>
- Increased risk of hypocalcaemia with CrCl <30mL/min and dialysis; monitoring calcium concentrations is recommended with calcium nadir usually occurring 8-11 days after administration. <sup>2</sup>
- It can be missed off patient dispensing history and medication records as it is administered six monthly by the GP.



Denosumab mechanism of action.<sup>1</sup>

## Clinical features

Three individuals presented to our facility with severe hypocalcaemia after administration of denosumab; one with stage 4 CKD, one stage 5 CKD and the third receiving haemodialysis.

In each instance, recent administration of Denosumab by the patient's GP was identified by the pharmacist, in one case during the CKD clinic and the others during admission to the emergency department.

Patient No.	No. of days post Denosumab	cCa on admission	Calcitriol/ Calcium supplement dose on admission	Inpatient LOS	CKD Stage	Calcitriol/ Calcium supplement dose on Discharge
1	3 days	1.60	Calcium 2 BD (Phosphate Binder) Calcitriol 1 mane	2 days	ESKD HD	Calcium 2 TDS Calcitriol 2 mane
2	7 days	1.67	Nil	4 days	Stage 5 CKD	Calcium 1 mane
3	10 days	1.44	Nil	6 days	Stage 4 CKD	Calcium 1 mane

## Interventions, case progress and outcomes

The patients were treated with intravenous calcium and discharged on oral calcium supplements. Close monitoring of calcium levels was required both during the admission and on discharge.

Outpatient Medication Record: 23 Aug 2018		Clinic: Renal Medicine (inc renal OP clinics)					
If you have any questions, please phone 07 3646 1087							
Medicine Names	Brand Name	Used for	Directions	Daily Time Table			Changes
				Morning	Noon	Evening	
Calcium Carbonate 1250mg (500mg Calcium) Tablets	Cal-sup	Phosphate binder	Take 1 tablet THREE times a day with each of your main meals	1	1	1	Unchanged
Denosumab 60mg/mL Syringe	Prolia	Treat/prevent osteoporosis	To be injected by your doctor ONCE every 6 months. Last administered May 2018. Next due Nov 2018.	To be injected by your doctor ONCE every 6 months. Last administered May 2018. Next due Nov 2018.			Unchanged

Allergies and Adverse Drug Reactions:		
Date	Medicine / Causal Agent	Reaction
01/01/1999	Enalapril	Cough

An example of recording Denosumab on a general patients discharge medication list.

On discharge, Denosumab was ceased or with-held pending further review by their GP. In all 3 instances the suspected adverse drug reaction was reported to the Therapeutic Goods Administration.

### The pharmacist's role:

- Identified denosumab as probable cause of hypocalcaemia
- Assisted management of calcium replacement.
- Counselling patients on importance of taking calcium supplements away from food when used for supplementation rather than as a phosphate binder.
- Follow-up management of fracture risk with patient and GP

## Conclusions

Renal bone disease is a common complication of CKD and Denosumab is not indicated for this condition. CKD patients with osteoporosis who are treated with Denosumab are at increased risk of hypocalcaemia.

Caution and regular monitoring is required when administering this medication in this patient sub-group.

Clear documentation of Denosumab administration and calcium supplementation in a patient's medical history is important in identifying adverse drug reactions.

## References

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2. Australian Medicines Handbook. Adelaide: Australian Medicines Handbook Pty Ltd; 2018.
3. MIMS Australia 2018. Prolia – Product Information. (Last updated 01/08/2018). Retrieved from <http://mimsonline.com.au>

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