

Vitamin D Deficiency in Children

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Note:

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Explanation of the aboriginal artwork:

The aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant woman. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.



Cultural safety enhances clinical safety.

To secure the best health outcomes, clinicians must provide a culturally safe health care experience for Aboriginal children, young people and their families. Aboriginal children are born into strong kinship structures where roles and responsibilities are integral and woven into the social fabric of Aboriginal societies.

Australian Aboriginal culture is the oldest living culture in the world, yet Aboriginal people currently experience the poorest health outcomes when compared to non-Aboriginal Australians.

It remains a national disgrace that Australia has one of the highest youth suicide rates in the world. The over representation of Aboriginal children and young people in out of home care and juvenile detention and justice system is intolerable.

The accumulative effects of forced removal of Aboriginal children, poverty, exposure to violence, historical and transgenerational trauma, the ongoing effects of past and present systemic racism, culturally unsafe and discriminatory health services are all major contributors to the disparities in Aboriginal health outcomes.

Clinicians can secure positive long term health and wellbeing outcomes by making well informed clinical decisions based on cultural considerations.

The term 'Aboriginal' is used to refer to people who identify as Aboriginal, Torres Strait Islanders, or both Aboriginal and Torres Strait Islander. This is done because the people indigenous to South Australia are Aboriginal and we respect that many Aboriginal people prefer the term 'Aboriginal'. We also acknowledge and respect that many Aboriginal South Australians prefer to be known by their specific language group(s).

Vitamin D Deficiency in Children

Purpose and Scope

This Vitamin D Deficiency in Children Clinical Guideline is primarily aimed at medical staff working in any of primary care, local, regional, general or tertiary hospitals, however may be utilised or guide the care provided by other clinicians such as nurses. The information is current at the time of publication and provides a minimum standard for the assessment (including investigations) and management of Vitamin D Deficiency; it does not replace or remove clinical judgement or the professional care and duty necessary for each specific case.

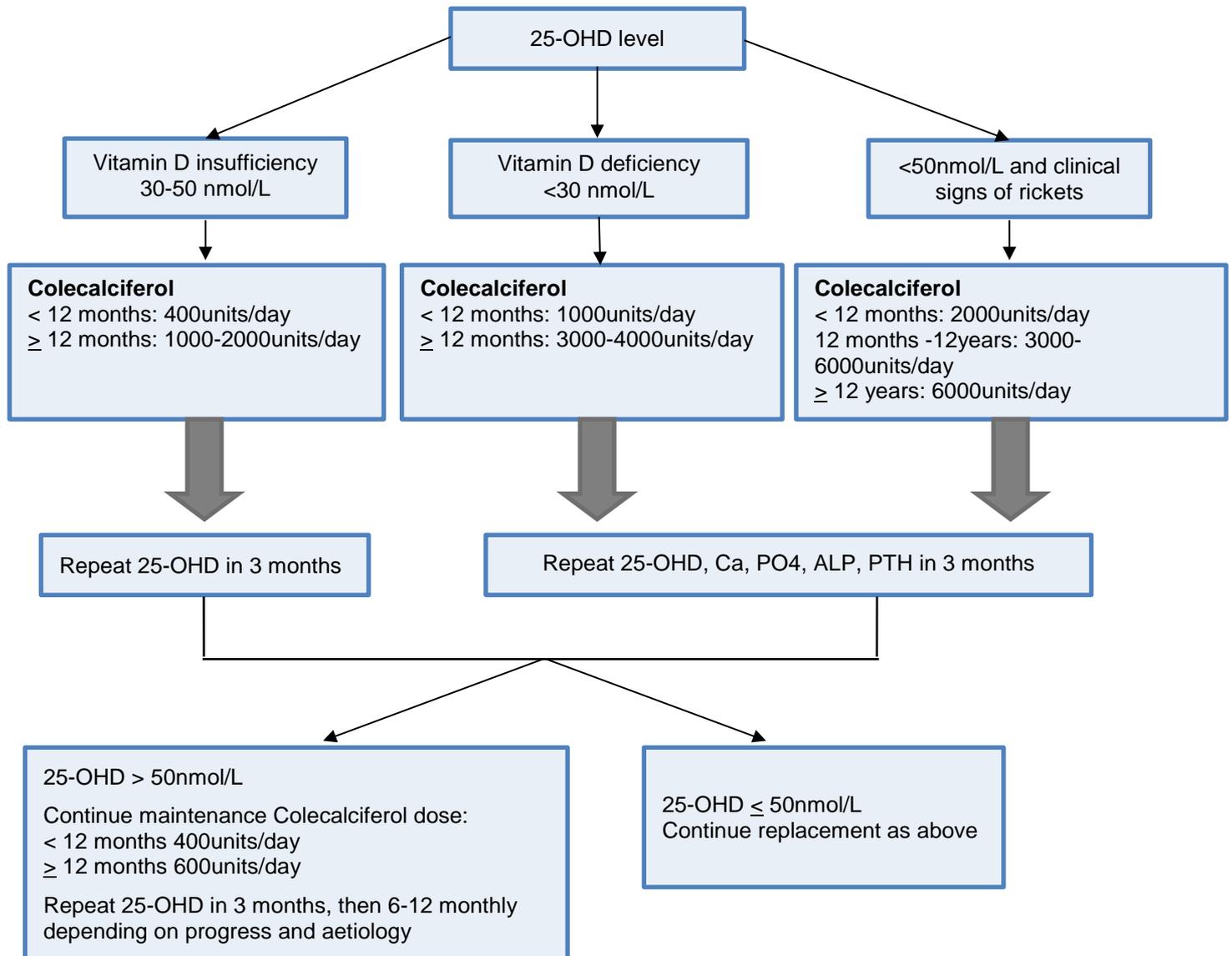
Table of Contents

Purpose and Scope	2
Management summary and flowchart for vitamin D deficiency	3
Important points	4
Abbreviations	4
Definitions	4
Introduction	5
Assessment	6
Common presentations of vitamin D deficiency	6
Investigations after confirmation of vitamin D deficiency.....	6
Differential diagnosis for rickets and hypocalcaemia: laboratory results.....	7
Management.....	7
Stoss therapy (high dose vitamin D therapy)	7
Calcium supplementation	8
Recommended daily calcium intake	8
Exposure to sunlight	8
Individual cases	8
Prevention of rickets and osteomalacia with vitamin D	8
Follow-up	8
References.....	9
Information for parents.....	11
Appendices	12
Acknowledgements.....	13



Vitamin D Deficiency in Children

Management summary and flowchart for vitamin D deficiency



Follow-up

- Follow-up should be with the General Practitioner in mild cases with an obvious cause
- If 25OHD remains less than 50nmol/L after 6 months of treatment, consider non-compliance and exclude other causes such as malabsorption
- If significant bowing of limbs or other nutritional deficiencies, refer to General Paediatric clinic
- If secondary fractures/hypocalcaemia/not responsive to vitamin D replacement, refer to Endocrine clinic

Vitamin D Deficiency in Children

Important points

- > Children in 'at risk' populations should be screened for vitamin D deficiency.
- > Ongoing monitoring is required and care should be taken when giving high doses of vitamin D.
- > Stoss therapy (high dose vitamin D) can be considered but caution must be taken in those with elevated PTH levels due to the increased risk of hypervitaminosis D leading to hypercalcaemia.
- > This guideline is not relevant for children with Cystic Fibrosis.

Abbreviations

nmol/L	nanomole/litre
mg/day	milligram(s)
Ca	Calcium Catecholamine
PO ₄	Phosphate
ALP	Alkaline phosphatase
PTH	parathyroid hormone
units/d	Units/day (page 6)
1,25-[OH] ₂ D, or calcitriol	1,25 Dihydroxyvitamin D
25-OHD	serum 25 hydroxyvitamin D

Definitions

Vitamin D	<ul style="list-style-type: none">> Refers to levels of serum 25 hydroxyvitamin D (25-OHD) which reflects total body stores.> Colecalciferol (vitamin D3) and ergocalciferol (vitamin D2) from sunlight are converted to 25-hydroxyvitamin D (25-OHD) in the liver. To convert ng/mL to nmol/L multiply by 2.496.
1,25 Dihydroxyvitamin D	<ul style="list-style-type: none">> In the kidney, 25-OHD is hydroxylated to produce the biologically active form of vitamin D, 1,25-dihydroxyvitamin D (1,25-[OH]₂D, or calcitriol). This step requires the activity of parathyroid hormone (PTH).> The actions of 1,25-[OH]₂D are to: (i) enhance absorption of calcium and phosphate from the small intestine; (ii) modify serum calcium concentration both directly and through parathyroid hormone; and (iii) promote skeletal mineralisation.> Even in severe vitamin D deficiency, levels of 1,25-[OH]₂D can be normal due to compensatory elevation of PTH. Therefore it is of no value in making the diagnosis of nutritional vitamin D deficiency but may be helpful in other less common causes of rickets.
Parathyroid hormone	<ul style="list-style-type: none">> Parathyroid hormone (PTH) is produced in the parathyroid glands and is required to convert the inactive form of vitamin D (25-OHD) to the active form, 1,25-[OH]₂D.> Elevated levels of PTH often occur in severe or chronic vitamin D deficiency, or when dietary calcium is inadequate.



Vitamin D Deficiency in Children

Vitamin D Deficiency	<ul style="list-style-type: none"> > Recommended guidelines for defining vitamin D deficiency in children and adolescents (Munns 2016) > Reference ranges for children differ to those in adults. A vitamin D level above 60nmol/L is considered normal in adults. <table border="1" data-bbox="804 398 1355 589"> <thead> <tr> <th>Vitamin D status</th> <th>25-OHD level (nmol/L)</th> </tr> </thead> <tbody> <tr> <td>Sufficiency</td> <td>> 50</td> </tr> <tr> <td>Insufficiency</td> <td>30-50</td> </tr> <tr> <td>Deficiency</td> <td>< 30</td> </tr> </tbody> </table>	Vitamin D status	25-OHD level (nmol/L)	Sufficiency	> 50	Insufficiency	30-50	Deficiency	< 30
Vitamin D status	25-OHD level (nmol/L)								
Sufficiency	> 50								
Insufficiency	30-50								
Deficiency	< 30								
Nutritional Rickets	<ul style="list-style-type: none"> > Vitamin D deficiency and/or low calcium intake with clinical/radiological evidence of rickets. 								
ALP	<ul style="list-style-type: none"> > ALP is produced by bone and is elevated in conditions of increased bone turnover. This is often associated with calcium deficiency, vitamin D deficiency, and elevated PTH. 								

Introduction

- > Vitamin D deficiency and nutritional rickets are re-emerging as common paediatric health issues.
- > Sunlight is the main source of vitamin D - colecalciferol (vitamin D3) and ergocalciferol (vitamin D2).
- > Reduced sun exposure (e.g. use of sunscreen, wearing a veil for cultural reasons, more time spent indoors) results in decreased production of vitamin D from sunlight. This is particularly evident in dark skinned individuals with increased skin pigment who may require up to 6 times more sun exposure than light skinned individuals.
- > Other 'at-risk' populations include infants of vitamin D deficient mothers, dietary deficiency (e.g. prolonged breast feeding), small bowel disorders (e.g. coeliac disease), pancreatic insufficiency (e.g. cystic fibrosis), chronic liver/renal disease, and medications (e.g. anticonvulsants).
- > Although vitamin D deficiency has been associated with conditions such as type 1 diabetes, respiratory illness, cardiovascular disease, altered immunity, and cancer (to name a few), there is limited outcome data to show vitamin D to be causally related in children.
- > Numerous preparations of vitamin D are available over the counter and high doses are easily obtained through compounding pharmacies. The aim of this guideline is to ensure that children and adolescents with vitamin D deficiency are adequately replaced and are not given excessive doses of vitamin D.
- > Children with radiographically confirmed rickets have an increased risk of fracture. Children with simple vitamin D deficiency are not at increased risk of fracture.



Assessment

Risk factors for vitamin D deficiency

- > Infant of vitamin D deficient mother.
- > Dietary deficiency (e.g. prolonged breastfeeding). Minimal vitamin D is available in the diet (breast milk 25 units/L, milk formula 400units/L, oily fish, eggs, butter, and margarine 50-100units/day).
- > Dark skin colour – Individuals with increased skin pigment may require up to 6 times more sun exposure than light skinned individuals.
- > Reduced sun exposure (e.g. use of sunscreen, extent of clothing covering body).
- > Small bowel disorders (e.g. coeliac disease, inflammatory bowel disease).
- > Pancreatic insufficiency (e.g. cystic fibrosis).
- > Chronic liver/renal disease.
- > Medications (e.g. anticonvulsants, rifampicin, isoniazid, chronic glucocorticoids).
- > Obesity (reduces bioavailability of vitamin D).
- > Disabled children (often have poor sun exposure and increased anticonvulsant use).

Common presentations of vitamin D deficiency

- > Hypocalcaemia seizures or tetany, often in the neonatal period
- > Incidental finding on screening investigations
- > Vitamin D deficient rickets - swelling of wrists and ankles, rachitic rosary, genu varum/valgum, frontal bossing, limb pain and fracture, craniotabes
- > Other less common presentations - myopathy, delayed fontanelle closure, delayed tooth eruption, enamel hypoplasia, raised ICP, brown tumour (osteoclastoma) secondary to hyperparathyroidism

Investigations after confirmation of vitamin D deficiency

- > **Insufficiency** (25-OHD 30-50nmol/L): no further investigations are required unless symptomatic
- > **Deficiency** (25-OHD <30nmol/L): the following blood investigations should be considered.
 - Blood: calcium, phosphate, ALP. Check PTH if has clinical rickets or history suggests low calcium intake
 - If patient is <1 month old, maternal blood should also be taken
 - Calcium and phosphate may be normal or low, ALP may be elevated, PTH may be normal or high
 - Prolonged deficiency may result in high phosphate due to PTH resistance
 - Infants of vitamin D deficient mothers may have high phosphate due to inadequate PTH release or inadequate renal responsiveness to PTH
- > **Radiology:** If there is a clinical suspicion of vitamin D deficient rickets, x-rays of the wrists or knees should be requested (cupping, splaying, fraying, coarse trabecular pattern of metaphysis, osteopaenia, fractures)
- > If the results do not suggest nutritional vitamin D deficiency, refer to the following table for a differential diagnosis. If a cause other than vitamin D deficiency is suspected then appropriate investigation and management for that condition should be instituted



Vitamin D Deficiency in Children

Differential diagnosis for rickets and hypocalcaemia: laboratory results

Causes	Ca	PO ₄	ALP	PTH	25OHD	1,25OHD
Vitamin D deficiency	↓ / N	↓ / N	↑	N / ↑	↓	↓ / N
Hypoparathyroidism	↓	↑	↓ / N	↓ / N	N	↓
Pseudo hypoparathyroidism	↓	↑	N / ↑	↑	N	↓
Vitamin D Resistant Rickets	↓	↓	↑	↑	N	↑
Familial Hypophosphataemic Rickets	N	↓	↑	N	N	↓ / N
Vitamin D Dependent Rickets	↓	↓	↑	↑	N	↓

Management

Standard replacement of Vitamin D

- > Oral daily colecalciferol replacement should be commenced if 25OHD <50nmol/L as outlined in the [management flowchart](#).

Stoss therapy (high dose vitamin D therapy)

- > High dose vitamin D therapy (Stoss therapy) can be considered in patients with poor compliance, recalcitrant vitamin D deficiency or vitamin D deficient rickets
- > There are many stoss regimens with doses ranging from 100,000–600,000 units given as single or divided doses. There is currently no consensus on the most effective and safest regimen and until this is studied further, a conservative approach is recommended
- > Vitamin D toxicity (25-OHD > 250nmol/L) may result in hypercalcaemia, hypercalciuria and suppressed PTH. The main symptoms of vitamin D overdose are those of hypercalcemia: anorexia, nausea and vomiting can occur, followed by polyuria, polydipsia, weakness, nervousness, pruritus, renal stones and renal failure
- > **Stoss therapy should not be given if the PTH is elevated due to the increased risk of vitamin D toxicity. Elevated PTH is more likely to be seen if 25-OHD <25nmol/L and/or dietary calcium is inadequate.**
- > To replenish vitamin D stores using stoss therapy orally as a single dose
 - 3-12 months - 50,000units
 - >12 months - 150,000units

A range of concentrated colecalciferol products are available from public hospitals and local pharmacies, [see Appendix 1](#).

- > Repeat doses can be given after 6 – 12 weeks depending on the clinical situation.
- > Calcium, phosphate and ALP should be checked in 2 months, and 25-OHD should be re-measured in 3 months
- > Care in dosing and monitoring is essential
- > Simultaneous calcium supplementation should be considered if dietary intake is inadequate due to the risk of hypocalcaemia from remineralisation of bone.

Vitamin D Deficiency in Children

Calcium supplementation

- > Low dietary calcium intake contributes to rickets and low bone density and may also be a cause for raised PTH levels.
- > If dietary intake is poor, calcium supplementation is recommended
- > For calcium preparations, [see Appendix 1](#).

Recommended daily calcium intake

Age	Calcium (mg/day)
0-6 months	200
6-12 months	260
1-3 years	500-700
4-8 years	800-1000
9-18 years	1100-1300

Exposure to sunlight

- > A balance needs to be struck between sufficient sun exposure and minimising the risk of skin cancer.

No paediatric data is available but in adults the recommended daily sun exposure time in Australia ranges from 5 minutes in summer to 40 minutes in winter.

Individual cases

- > Individual cases may require modification of above guidelines.
- > Mild vitamin D deficiency associated with underlying medical conditions such as malabsorption, low bone density, or elevated PTH, may require higher doses of vitamin D.
- > Children with Cystic Fibrosis require other management and a specific protocol is available at the Women's and Children's Hospital.

Prevention of rickets and osteomalacia with vitamin D

- > Recent global consensus guidelines (Munns 2016) recommend that **all** infants from birth to 12 months of age, independent of their mode of feeding are treated with colecalciferol 400units/day to prevent rickets. The Australian and New Zealand position statement (Paxton 2013) recommends supplementation of only those at risk.
- > Further studies are required to confirm whether universal supplementation will reduce the risk of nutritional rickets in Australia and New Zealand.

Follow-up

- > Follow-up should be with the General Practitioner in mild cases with an obvious cause.
- > If 25OHD remains less than 50nmol/L after 6 months of treatment, consider non-compliance and exclude other causes such as malabsorption.
- > If significant bowing of limbs or other nutritional deficiencies, refer to General Paediatric clinic.
- > If secondary fractures / hypocalcaemia / not responsive to vitamin D replacement, refer to Endocrine clinic.



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Vitamin D Deficiency in Children

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Several guideline sites were consulted for existing guidelines regarding “vitamin D deficiency” and “children”, including:

- > National Guideline Clearing House <http://www.guideline.gov/>
- > National Institute for Health and Clinical Excellence (NICE) <http://guidance.nice.org.uk/CG/published>
- > New Zealand Guidelines Group <http://www.nzgg.org.nz/>
- > Scottish Intercollegiate Guidelines network <http://www.sign.ac.uk/guidelines/published/>
- > British Medical Journal <http://bmj.bmjournals.com/cgi/collection/guidelines>
- > National Institute of Clinical Studies <http://www.nhmrc.gov.au/nics/index.htm>
- > National Health and Medical Research Council <http://www.nhmrc.gov.au/publications/index.htm>
- > Royal College of Nursing Guidelines <http://www.rcna.org.au/Default.aspx?SiteSearchID=360&ID=/results>
- > Royal Australian College of Physicians <http://www.racp.edu.au/page/search>
- > NHS National Library of Guidelines <http://www.library.nhs.uk/guidelinesfinder/>
- > Starship Children’s Hospital http://www.starship.org.nz/index.php/pi_pageid/1065
- > John Hunter Hospital intensive Care Guidelines <http://www.philippelefevre.com/JHH-ICU-guidelines/index.php>
- > Royal Children’s Hospital – Melbourne Clinical Practice Guidelines <http://www.rch.org.au/clinicalguide/>
- > Princess Margaret Hospital Clinical Practice Guidelines



Vitamin D Deficiency in Children

http://www.pmh.health.wa.gov.au/development/manuals/clinical_practice_guidelines/

The following guideline was also found to be suitable:

- > RCH guidelines http://www.rch.org.au/immigranthealth/resources.cfm?doc_id=10782

Information for parents

- > Parenting and Child Health, Women's and Children's Health Network
<http://www.cyh.com/HealthTopics/HealthTopicDetails.aspx?p=114&np=304&id=1855>



Vitamin D Deficiency in Children

Appendices

APPENDIX 1 – Vitamin & Calcium Preparations

Care should be taken when selecting preparations as there are multiple colecalciferol and calcium preparations available with varying concentrations.

The following products are available at the time of publishing; it is recommended to consult *MIMS* prior to prescribing.

SA Health clinicians should also consult the *SA Medicines Formulary* for product availability.

Colecalciferol single ingredient preparations	
1000 units / capsule	Ostelin®
1000 units / tablet	OsteVit-D® (Note tablets may be halved, crushed and dispersed in water)
1000 units / 0.5 mL	Ostelin Vitamin D Liquid®
1000 units / 0.2 mL	OsteVit-D Liquid®
Stoss Therapy (High dose)	
1000 units / 0.045 mL	BioCeuticals D3 Drops Forte
50,000 units / 2.25 mL (available via public hospital SA Pharmacy sites only)	WCH High Dose Vitamin D (Stoss)
50,000 units / capsule (available via public hospital SA Pharmacy sites only)	Biological Therapies® (Note capsules may be opened and contents dispersed in water)
Multivitamins containing colecalciferol	
400 units / 0.45 mL	Pentavite Infant Drops®
200 units / 5 mL	Penta-Vite Liquid Multivitamins with Iron®
440 units / capsule	VitABDECK®
Calcium single ingredient preparations (elemental calcium)	
Calcium (as citrate) 250 mg / tablet	Citracal®
Calcium (as carbonate) 500 mg / tablet	Cal-Sup® (Note Chewable tablet and dispersible in water)
Calcium (as carbonate) 600 mg / tablet	Calci-Tabs®, Caltrate®
Calcium (as carbonate and lactate gluconate) 1000 mg / tablet	CalSource Ca1000 Effervescent tablets®

Combination colecalciferol and calcium preparations are available; consult the [SA Medicines Formulary](#) or [MIMS](#) prior to prescribing



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Approval Date	Version	Who approved New/Revised Version	Reason for Change
05/07/18	V3	SA Health Safety & Quality Strategic Governance Committee	Formally reviewed in line scheduled timeline for review. Management flowchart now includes nutritional rickets and changing of definition of insufficiency vs deficiency and change in stoss dosing as per recent global consensus guidelines 2016. Also included are recommendation that all infants 0-12 months be supplemented with colecalciferol, not only the 'at risk' infants and guidance as to whether follow up is appropriate with general practitioner, general paediatrician, or endocrinologist.
01/07/13	V2	SA Health Safety & Quality Strategic Governance Committee	Formally reviewed in line scheduled timeline for review.
24/01/12	V1	SA Health Portfolio Executive	Original Portfolio Executive approved version.

