HOW DOES VITAMIN D DEFICIENCY IMPACT HEALTHCARE?

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Why do we need vitamin D?
What do guidelines recommend?
What is the impact of vitamin D deficiency on the NHS?

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What is vitamin D?

Vitamin D is a fat-soluble pro-hormone[1,2]

Produced in the skin through sunlight or ingested from the diet[1,2]

Vitamin D is essential for bone and muscle health[1]

Vitamin D deficiency in adults can:

- precipitate or exacerbate osteopenia and osteoporosis[1]
- cause osteomalacia and muscle weakness[1]
- increase the risk of fracture[1]

Vitamin D deficiency has been implicated as a possible risk factor for falls and fractures in the elderly[3]

1. Holick MF N Engl J Med 2007;357:266-81.
2. Public Health England. The Scientific Advisory Committee on Nutrition (SACN) recommendations on vitamin D. 2016. Available at: https://www.gov.uk/government/publications/sacn-vitamin-d-and-health-report [Last accessed March 2021].
3. Dretakis OE et al. J Int Med Res 2010; 38: 1824–34.

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Guideline recommendations

Royal Osteoporosis Society[1*]

Recommend testing and treatment for vitamin D deficiency if patients have:

- Fragility fracture/osteoporosis/ high fracture risk
- Drug treatment for bone disease
- Symptoms suggestive of vitamin D deficiency
- Increased risk of developing vitamin D deficiency e.g. Reduced UV exposure, raised parathyroid hormone, treatment with anticonvulsants or glucocorticoids, malabsorption.

Vitamin D is indicated for:[1–7]

- The treatment and prevention of vitamin D deficiency
- As an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency

*This guideline applies ONLY to adult patients with, or at risk of developing, bone disease The guideline does not address the management of vitamin D deficiency in; childhood, pregnancy, or patients with severe or end-stage chronic kidney disease (CKD Stages 4–5)

1. Royal Osteoporosis Society. Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. Feb 2020. Available at: https://theros.org.uk/clinical-publications-and-resources/ [Last accessed March 2021].
2. Meda Pharmaceuticals. Desunin. SPC. Available at: https://www.medicines.org.uk/emc/ [Accessed March 2021].
3. Accord UK Ltd. Plenachol. SPC. Available at: https://www.medicines.org.uk/emc/ [Accessed March 2021].
4. Internis Pharmaceuticals Ltd. Fultium-D3. SPC. Available at: https://www.medicines.org.uk/emc/ [Accessed March 2021].
5. Kyowa Kirin Ltd. Stexerol-D3 Tablets. SPC. Available at: https://www.medicines.org.uk/emc/ [Accessed March 2021].
6. Strides Pharma UK Ltd. STRIVIT-D3. SPC. Available at: https://www.medicines.org.uk/emc/ [Accessed March 2021].
7. Galen Limited. THORENS. SPC. Available at: https://www.medicines.org.uk/emc/ [Accessed March 2021].
8. Accord UK Ltd. Plenachol. SPC. Available at: https://www.medicines.org.uk/emc/ [Accessed March 2021].
9. Consilient Health Ltd. InVita D3 SPC..Available at: https://www.consilienthealth.co.uk/branded-pharmaceuticals/#products-pharma [Accessed March 2021].

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Guideline recommendations

NICE recommend before treatment for;

(1) primary prevention of fragility fractures in postmenopausal women who have osteoporosis[1], or

(2) secondary prevention of fragility fractures in postmenopausal women who have osteoporosis and have sustained a clinically apparent osteoporotic fragility fracture[2]

……women are vitamin D replete, or

vitamin D supplementation should be considered[1,2]

Scottish Intercollegiate Guidelines Network[3]

Calcium and vitamin D treatment may be considered for frail older people, for example nursing care residents, who are at high risk of vitamin D deficiency to reduce the risk of non-vertebral fractures.

1. NICE Raloxifene for the primary prevention of osteoporotic fragility fractures in postmenopausal women (TA160). 2018. www.nice.org.uk/guidance/ta160
2. NICE Raloxifene and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women (TA161). 2019. www.nice.org.uk/guidance/ta161
3. SIGN 142. Management of osteoporosis and the prevention of fragility fractures. June 2020.

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Epidemiology and costs: Fragility fractures

Over **300,000 patients** present to hospitals in the UK with fragility fractures each year[1]

Around **£2 billion** in medical and social care costs – most of which relate to hip fracture care[1]

Is osteoporosis a new epidemic?

1. British Orthopaedic Association September 2007. The care of patients with fragility fracture. https://www.sign.ac.uk/our-guidelines/management-of-osteoporosis-and-the-prevention-of-fragility-fractures/ [Last accessed April 2021]

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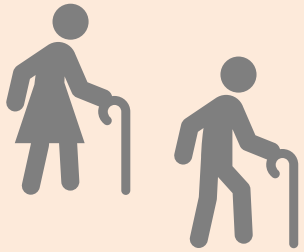
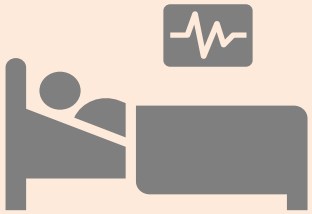
Challenges to healthcare systems



Increased hospitalisation of older adults was prospectively associated with vitamin D deficiency, independent of markers of physical and cognitive frailty ($p < 0.001$).[1]

Increased hospital length of stay was directly associated with low vitamin D levels in nursing home residents admitted to a community hospital ($p=0.002$).[2]



Increased length of ICU stay was associated with vitamin D deficiency in critically ill surgical patients ($P=0.003$).[3]

1. Beirne A, et al. Nutrients 2021;13(2):616.
2. Mc Williams C, et al. J Community Hosp Intern Med Perspect. 2011;1(3).
3. Alizadeh N, et al. J Res Pharm Pract. 2015;4(4):193-8.

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What would be the impact on health resource utilization of treating vitamin D deficiency?

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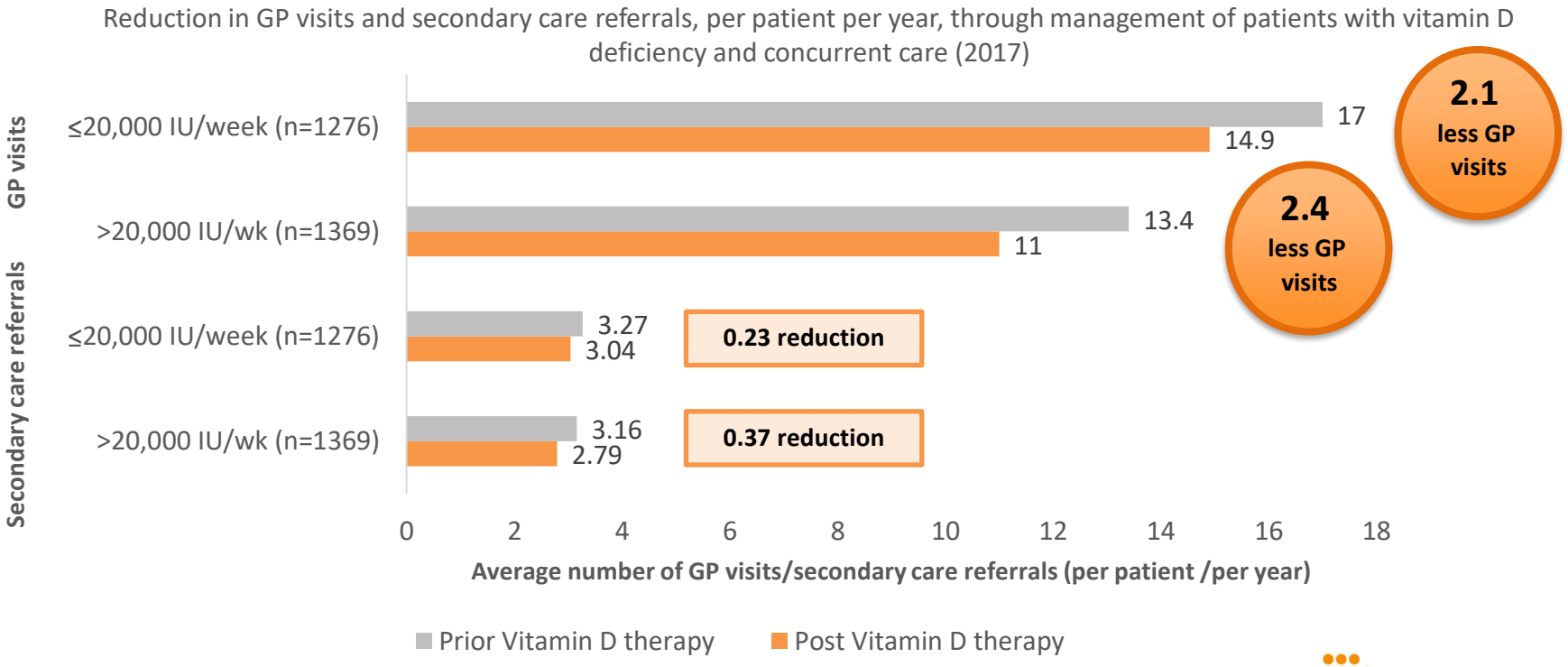
Vitamin D status and healthcare utilization: UK RWD

In the 12 months following initiation of therapy, there was a reduction in the number of GP visits and secondary care referrals for patients prescribed vitamin D[1]



The assumption has been made that 1 prescription per treatment course in the THIN database = 1 patient.

The data extraction was sponsored by Consilient Health Ltd. Mark Evans from Harvey Walsh Limited provided the data and Jane Griffin from Jane Griffin Associates contributed to the development of the analyses and report.

1. Adapted from: Consilient Health Ltd. Poster presented at the RCGP Annual Primary Care Conference & Exhibition. Glasgow. 2018. Consilient data on file available upon request.

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How do we test for vitamin D deficiency?
Who is at risk and high risk?
How do we treat vitamin D deficiency?

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Testing for vitamin D deficiency

Levels of vitamin D are clinically assessed by measuring blood serum levels of the major metabolite of vitamin D; 25(OH)D[1,2]

Recommended UK vitamin D thresholds[1]

Definition	Serum 25(OH)D
Deficient	**<25 nmol/L**
Inadequate (in some people)	25–50 nmol/L
Sufficient (almost the whole population)	>50 nmol/L

1. Royal Osteoporosis Society. Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. Feb 2020. Available at: https://theros.org.uk/clinical-publications-and-resources/ [Last accessed March 2021].
2. Holick MF. J Investig Med. 2011;59(6):872–80.

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Royal Osteoporosis Society*: Guidance for screening patients

Who should be routinely tested for vitamin D deficiency?

Patients with bone diseases that may be improved with vitamin D treatment	✓
Patients with bone diseases where correcting vitamin D deficiency prior to specific treatment would be appropriate	✓
Patients with musculoskeletal symptoms that could be attributed to vitamin D deficiency	✓
Asymptomatic individuals at higher risk of vitamin D deficiency#	✗
Asymptomatic healthy individuals	✗

In some areas, requests are made to measure plasma 25(OH)D for unclear clinical indications, resulting in large numbers of tests[1]

*This guideline applies ONLY to adult patients with, or at risk of developing, bone disease The guideline does not address the management of vitamin D deficiency in; childhood, pregnancy, or patients with severe or end-stage chronic kidney disease (CKD Stages 4–5)
#These individuals are more likely to be vitamin D- deficient and current UK guidance from the Department of Health and Social Care recommends that these individuals have a higher intake of vitamin D
25(OH)D, 25 hydroxyvitamin D.

1. Royal Osteoporosis Society. Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. Feb 2020. Available at: https://theros.org.uk/clinical-publications-and-resources/ [Last accessed March 2021].

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Other at-risk groups

Department of Health
People at risk of vitamin D deficiency[1]

All pregnant and breastfeeding women, especially teenagers and young women

Infants and young children under 5 years of age

Older people aged 65 years and over

People who have low or no exposure to the sun, for example those who cover their skin for cultural reasons, who are housebound or confined indoors for long periods

People who have darker skin, for example people of African, African-Caribbean and South Asian origin, because their bodies are not able to make as much vitamin D

1. Department of Health. Vitamin D - advice on supplements for at risk groups. 2012. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213703/dh_132508.pdf [Last accessed March 2021].

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Royal Osteoporosis Society*
Managing Vitamin D deficiency

Treatment

In patients with symptomatic disease or about to start treatment with a potent antiresorptive agent (zoledronate or denosumab)[1]

Loading dose
A loading regimen to provide a total of approximately 300,000 IU vitamin D
Given orally either as separate weekly or daily doses over 6 to 10 weeks

Maintenance

Where correction of vitamin D deficiency is less urgent and when co-prescribing vitamin D supplements with an oral antiresorptive agent, maintenance therapy may be started without the use of loading doses[1]

Maintenance dose
Maintenance therapy comprising of vitamin D in doses equivalent to 800–2000 IU daily
Occasionally up to 4,000 IU daily – given either daily or intermittently at a higher equivalently dose

*This guideline applies ONLY to adult patients with, or at risk of developing, bone disease The guideline does not address the management of vitamin D deficiency in; childhood, pregnancy, or patients with severe or end-stage chronic kidney disease (CKD Stages 4–5)

1. Royal Osteoporosis Society. Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. Feb 2020. Available at: https://theros.org.uk/clinical-publications-and-resources/ [Last accessed March 2021].

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Using InVita D3 to follow the ROS treatment recommendations

TREATMENT

1 X 50,000 IU
soft capsule or oral solution weekly for 6 weeks [1,2]

Treatment cost £9.90 or £12.50[3]

Followed by

MAINTENANCE

therapy of 400-1,000 IU/day such as:

DAILY
1 X 800 IU
soft capsule [4]

£2.50 per pack (4 weeks supply)[3]

1. Consilient Health Ltd. InVita D3 50,000 IU soft capsules. Summary of Product Characteristics.
2. Consilient Health Ltd. InVita D3 50,000 IU oral solution. Summary of Product Characteristics.
3. MIMS, June 2019.
4. Consilient Health Ltd. InVita D3 800 IU soft capsules. Summary of Product Characteristics.

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What about licensed medicines and over-the-counter medicines?

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Licensed medicine and OTC medicines

Licensed medicines

General Medical Council[1]

Unlicensed medicines should only be prescribed where-

"...there is no suitably licensed medicine that will meet the patient's need."

Over-the-counter medicine

NHS England[2]

Advise CCGs to support prescribers that vitamins and minerals should not be routinely prescribed in primary care due to limited evidence of clinical effectiveness

Exception[2]

Calcium and vitamin D for osteoporosis
Medically diagnosed deficiency

NB: maintenance or preventative treatment is not an exception

1. General Medical Council. Good practice in prescribing and managing medicines and devices. 2013. Available at http://www.gmc-uk.org/guidance/ethical_guidance/14316.asp. [Last accessed March 2021].
2. NHS England. Conditions for which over the counter items should not routinely be prescribed in primary care: Guidance for CCGs. 2018. Available at https://www.england.nhs.uk/wp-content/uploads/2018/03/otc-guidance-for-ccgs.pdf [Last accessed March 2021].

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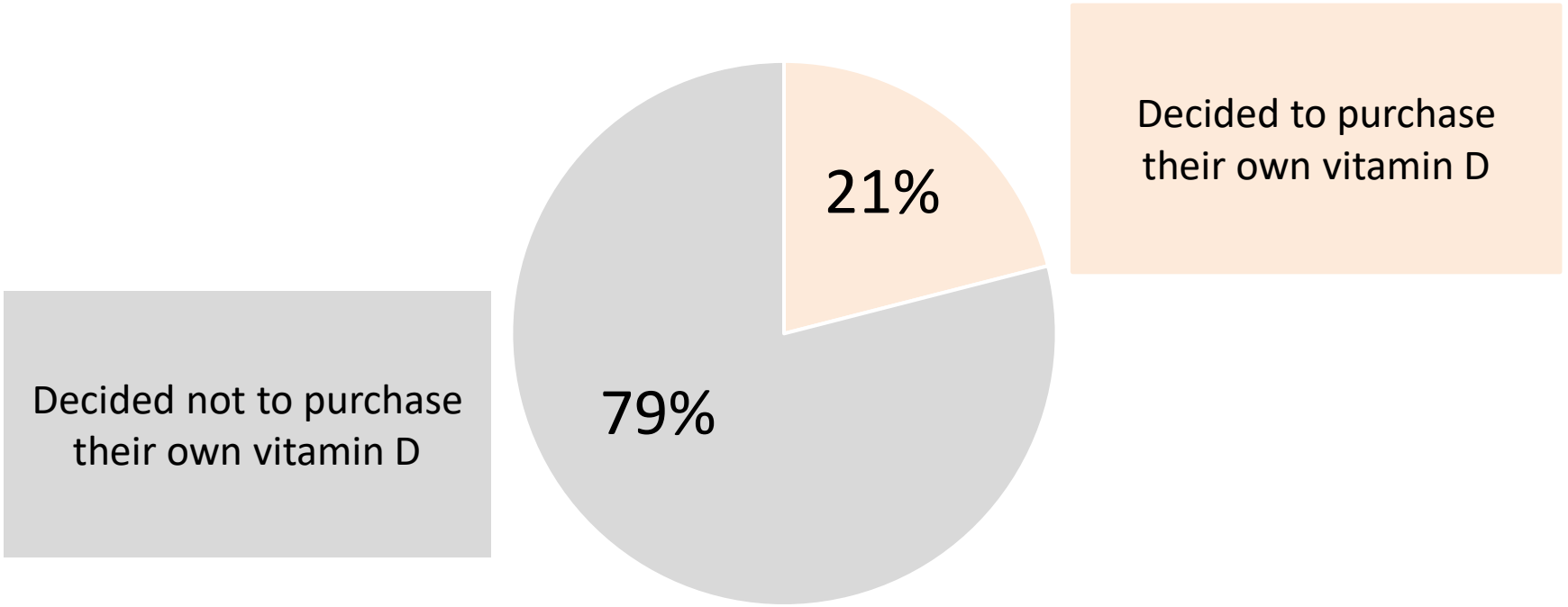
How likely are patients to purchase their own vitamin D supplements?

In a 2018 survey of 109 patients who had previously been prescribed vitamin D but were no longer being prescribed it[1]



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1. Consilient Health. TalkHealth Data on File. 2018.

Appropriate use of vitamin D: summary

- Vitamin D deficiency is associated with bone deformities and an increased risk of fracture in adults[1]
- Vitamin D deficiency has been associated with
  - increased hospitalisation[2]
  - increased length of stay[3]
- UK RWD shows a reduction in healthcare utilisation in the 12 months following initiation of vitamin D[4]
- The InVita D3 portfolio offers treatment and maintenance aligned to the Royal Osteoporosis Society guidelines[5, 6–8]

1. Holick MF. J Investig Med. 2011;59(6):872–80; 2. Beirne A, et al. Nutrients 2021;13(2):616.; 3. Mc Williams C, et al. J Community Hosp Intern Med Perspect. 2011;1(3).; 4. Consilient Health Ltd. Poster presented at the RCGP Annual Primary Care Conference & Exhibition. Glasgow. 2018. Consilient data on file available upon request.; 5. Royal Osteoporosis Society. Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. Feb 2020. Available at: https://theros.org.uk/clinical-publications-and-resources/ [Last accessed March 2021]; 6. Consilient Health Ltd. InVita D3 50,000 IU oral solution Summary of Product Characteristics; 7. Consilient Health Ltd. InVita D3 50,000 soft capsules Summary of Product Characteristics; 8.Consilient Health Ltd. InVita D3 25,000 IU oral solution Summary of Product Characteristics.

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InVita D3 prescribing information

InVitaD3 (colecalciferol) Abbreviated Prescribing Information - for full prescribing information, including side effects, precautions and contra-indications, see Summaries of Product Characteristics (SmPC).

Product name and Composition: InVita D3 50,000 IU oral solution: 1 ml solution (1 single-dose oral solution) contains 1.25 mg colecalciferol, equivalent to 50,000 IU vitamin D3. **InVita D3 50,000 IU soft capsules:** each capsule contains 50,000 IU colecalciferol, equivalent to 1.25 mg vitamin D3. **InVita D3 25,000 IU oral solution:** 1 ml solution (1 single-dose oral solution) contains 0.625 mg cholecalciferol, equivalent to 25,000 IU vitamin D. **InVita D3 25,000 IU soft capsules:** each capsule contains 25,000 IU colecalciferol, equivalent to 0.625 mg vitamin D3. **InVita D3 5,600 IU soft capsules:** each capsule contains colecalciferol 5,600 IU, equivalent to 0.14 mg vitamin D3. **InVita D3 2,400 IU/ml oral drops, solution:** 1 ml solution (36 drops) contains 0.06 mg colecalciferol, equivalent to 2,400 IU vitamin D3. **InVita D3 800 IU soft capsules:** each capsule contains colecalciferol 800 IU (equivalent to 0.02 mg vitamin D3. **InVita D3 400 IU soft capsules:** each capsule contains 400 IU colecalciferol, equivalent to 0.01 mg vitamin D3. **Indications: InVita D3 50,000 IU oral solution, InVita D3 50,000 IU soft capsules:** The treatment of vitamin D deficiency. **InVita D3 25,000 IU oral solution:** The prevention and treatment of vitamin D deficiency. As an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency. **InVita D3 25,000 IU soft capsules:** Prophylaxis and treatment of vitamin D deficiency in adults and adolescents with an identified risk. As an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency. **InVita D3 5,600 IU soft capsules:** Prophylaxis and treatment of vitamin D deficiency in adults and adolescents with an identified risk. As an adjunct to specific therapy for osteoporosis in patients at risk of vitamin D deficiency, preferably in combination with calcium. **InVita D3 2,400 IU/ml oral drops, solution:** Prevention of vitamin D deficiency in infants and children. Prevention of vitamin D deficiency in pregnant and breast-feeding women. **InVita D3 800 IU soft capsules:** Prophylaxis and treatment of vitamin D deficiency in adults and adolescents with an identified risk. As an adjunct to specific therapy for osteoporosis in patients at risk of vitamin D deficiency, preferably in combination with calcium. **InVita D3 400 IU soft capsules:** Prophylaxis and treatment of vitamin D deficiency in children and adolescents with an identified risk. Prophylaxis of vitamin D deficiency in adults, pregnant and breast-feeding women with an identified risk. As an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D deficiency. **Dosage and administration: InVita D3 50,000 IU oral solution, InVita D3 50,000 IU soft capsules:** Infants and children: Due to a lack of clinical data, not recommended in the paediatric population. Pregnancy and breastfeeding: Due to a lack of clinical data, not recommended. Adults: 50,000 IU/week (1 single-dose oral solution or 1 capsule) for 6-8 weeks, followed by maintenance therapy (equivalent to 1400-2000 IU/day, such as 1 single-dose 50,000 IU oral solution or capsule per month) may be required; check 25(OH)D measurements 3-4 months after starting maintenance therapy. Higher doses and monitoring of serum 25(OH)D may be required in populations at high risk of vitamin D deficiency (including those who are institutionalised or hospitalised, dark skinned, obese, being evaluated for osteoporosis, with limited effective sun exposure due to protective clothing or consistent use of sun screens, using certain concomitant medication e.g. anticonvulsants or glucocorticoids, with malabsorption, including inflammatory bowel disease and coeliac disease and recently treated for vitamin D deficiency, and requiring maintenance therapy). Renal impairment: should not be used in combination with calcium in patients with severe renal impairment. Take orally, preferably with food, capsules swallowed whole and oral solution either directly or by mixing with a small amount of cold or lukewarm food or drink immediately prior to use. **InVita D3 25,000 IU oral solution, InVita D3 25,000 IU soft capsules:** Infants and children: *Prevention of deficiency*, 0-1 year 25000 IU (1 single-dose oral solution) every 8 weeks; 1-18 years 25000 IU (1 single-dose oral solution) every 6 weeks; 10-18 years 25000 IU (1 capsule) every 6 weeks. *Treatment of deficiency*, 0-18 years 25000 IU (1 single-dose oral solution) once every 2 weeks for 6 weeks followed by maintenance therapy of 400-1000 IU/day such as 25000 IU (1 single-dose oral solution) per month; 10-18 years 25000 IU (1 capsule) every 2 weeks for 6 weeks followed by maintenance therapy of 400 – 1000 IU per day such as 25000 IU (1 capsule) per month. Pregnancy and breastfeeding: not recommended. Adults: *Prevention of deficiency*, 25000 IU (1 single-dose oral solution or capsule) per month; higher doses and monitoring of serum 25(OH) D may be required in populations at high risk of vitamin D deficiency (including those who are institutionalised or hospitalised, dark skinned, obese, being evaluated for osteoporosis, with limited effective sun exposure due to protective clothing or consistent use of sun screens, using certain concomitant medication e.g. anticonvulsants or glucocorticoids, with malabsorption, including inflammatory bowel disease and coeliac disease and recently treated for vitamin D deficiency, and requiring maintenance therapy). *Adjunct to specific therapy for osteoporosis*, 25000 IU (1 single-dose oral solution) per month. *Treatment of vitamin D deficiency (<25 ng/ml)*, 50000 IU/week (2 single-dose oral solutions or 2 capsules) for 6-8 weeks, followed by maintenance therapy of 1400-2000 IU/day such as 50000 IU (2 single-dose oral solutions or 2 capsules) per month may be required; check 25(OH)D measurements 3-4 months after starting maintenance therapy). Renal impairment: InVita D3 should not be used in combination with calcium in patients with severe renal impairment. **InVita D3 5,600 IU soft capsules:** One capsule per week; increase if necessary to achieve desirable serum levels of 25-hydroxycolecalciferol (25(OH)D). The weekly dose should not exceed 5 capsules. Renal impairment: InVita D3 should not be used in patients with severe renal impairment. Paediatric population: InVita D3 is not recommended in children under 12 years of age. The capsules should be swallowed whole with water. **InVita D3 2,400 IU/ml oral drops, solution:** Infants and Children: Age 0-1 years 400 IU/day (6 drops); Age 1-18 years 600 IU/day (9 drops). Pregnancy and breastfeeding: 400 IU/day (6 drops). Special populations renal impairment: no specific adjustment required. Obese patients, patients with malabsorption syndromes, and patients on medications affecting vitamin D metabolism: higher doses are required for the treatment and prevention of vitamin D deficiency (2-3 times higher). Take InVita D3 orally, preferably with food, either directly or by mixing with a small amount of cold or lukewarm food immediately prior to use. Ensure that the entire dose is taken. For children who are not breastfeeding, the prescribed dose should be administered with a meal. **InVita D3 800 IU soft capsules:** One capsule (800 IU) per day; increase if necessary for treatment of vitamin D deficiency, with dose adjusted according to desirable serum levels of 25-hydroxycolecalciferol (25(OH)D), the severity of the disease and the patient's response to treatment. The daily dose should not exceed 4,000 IU (5 capsules per day). Renal impairment: Do not use in patients with severe renal impairment. Paediatric population: Not recommended in children under 12 years of age. The capsules should be swallowed whole with water. **InVita D3 400 IU soft capsules:** Paediatric: *Prevention of deficiency, 10-18 years* 800 IU/day (2 capsules); increase to maximum 1200 IU/day (3 capsules) if required. *Treatment of deficiency, 10-18 years* 2000 IU/day (5 capsules) for 6 weeks, followed by maintenance therapy of 400-1200 IU/day (1-3 capsules). Pregnancy and breastfeeding: *Prevention of deficiency*, 400 IU/day (1 capsule); increase up to 2000 IU/day (5 capsules) if required. Even higher doses may be required during breast-feeding if women choose not to give the infant a vitamin D3 supplement. Adults: *Prevention of deficiency*, 800 IU/day (2 capsules); higher doses and monitoring of serum 25(OH)D may be required in populations at high risk of vitamin D deficiency (including those who are institutionalised or hospitalised, dark skinned, obese, being evaluated for osteoporosis, with limited effective sun exposure due to protective clothing or consistent use of sun screens, using certain concomitant medication e.g. anticonvulsants or glucocorticoids, with malabsorption, including inflammatory bowel disease and coeliac disease and recently treated for vitamin D deficiency, and requiring maintenance therapy). *Adjunct to specific therapy for osteoporosis*, 800 IU/day (2 capsules). Take InVita D3 orally with water, preferably with food. **Contraindications: InVita D3 50,000 IU oral solution, InVita D3 50,000 IU soft capsules, InVita D3 25,000 IU oral solution, InVita D3 25,000 IU soft capsules, InVita D3 400 IU soft capsules:** Hypersensitivity to the active substance or to any of the excipients; hypercalcaemia and/or hypercalciuria; nephrolithiasis and/or nephrocalcinosis; serious renal impairment; hypervitaminosis D; pseudohypoparathyroidism; InVita D3 25,000 IU soft capsules only, pregnancy. **InVita D3 5,600 IU soft capsules, InVita D3 800 IU soft capsules:** Hypersensitivity to the active substance or to any of the excipients; hypercalcaemia and/or hypercalciuria; nephrolithiasis and/ or nephrocalcinosis; hypervitaminosis D. **InVita D3 2,400 IU/ml oral drops, solution:** Hypersensitivity to the active substance or to any of the excipients; hypercalcaemia and/or hypercalciuria; hypervitaminosis D; kidney stones (nephrolithiasis, nephrocalcinosis) in patients with current chronic hypercalcaemia. **Warnings and precautions: InVita D3 50,000 IU oral solution, InVita D3 50,000 IU soft capsules, InVita D3 25,000 IU oral solution, InVita D3 25,000 IU soft capsules, InVita D3 400 IU soft capsules:** Use with caution in impaired renal function; monitor effect on calcium and phosphate levels. Consider the risk of soft tissue calcification. Exercise caution in patients receiving treatment for cardiovascular disease as concomitant administration of vitamin D with drugs containing digitalis and other cardiac glycosides may increase risk of digitalis toxicity and arrhythmia; strict medical supervision is needed, with serum calcium concentration and electrocardiographic monitoring if necessary. Use with caution in patients with sarcoidosis due to possible increase in vitamin D metabolism; monitor serum and urinary calcium levels in these patients. Allow for the total dose of vitamin D where patients consume treatments and / or foodstuffs enriched with vitamin D and for the patient's level of sun exposure. Possible risk of renal stones, especially with concomitant calcium supplementation; consider the need for additional calcium supplementation for individual patients. Calcium supplements should be given under close medical supervision. **InVita D3 5,600 IU soft capsules, InVita D3 800 IU soft capsules:** Use with caution in impaired renal function; monitor effect on calcium and phosphate levels. Consider the risk of soft tissue calcification. In patients with severe renal insufficiency, colecalciferol is not metabolised normally and other forms of vitamin D should be used. During long-term treatment, monitor serum calcium levels and renal function (via serum creatinine measurements). Monitoring is especially important in elderly patients on concomitant treatment with cardiac glycosides or diuretics and in patients with a high tendency to calculus formation. In case of hypercalciuria (exceeding 300 mg (7.5 mmol)/24 hours) or signs of impaired renal function the dose should be reduced or the treatment discontinued. Use with caution in patients with sarcoidosis due to possible increase in vitamin D metabolism; monitor serum and urinary calcium levels in these patients. Allow for the total dose of vitamin D where patients consume treatments containing vitamin D. Additional doses of vitamin D should be taken under close medical supervision; monitor serum calcium levels and urinary calcium excretion frequently. InVita D3 5,600 IU soft capsules contain Allura Red AC (E129) and Sunset Yellow FCF (E110) which may cause allergic reactions. **Undesirable effects:** All presentations: *Uncommon (>1/1,000, <1/100):* Hypercalcaemia and hypercalciuria. *Rare (>1/10,000, <1/1,000):* pruritus, rash, urticaria. **Additionally, for InVita D3 5,600 IU soft capsules, InVita D3 800 IU soft capsules:** *Not known (cannot be estimated from the available data):* Hypersensitivity reactions such as angio-oedema or laryngeal oedema. **NHS Price: InVita D3 50,000 IU oral solution:** £6.25 per pack of 3 x 1ml ampoules. **InVita D3 50,000 IU soft capsules:** £4.95 per pack of 3 capsules. **InVita D3 25,000 IU oral solution:** £4.45 per pack of 3 x 1ml ampoules. **InVita D3 25,000 IU soft capsules:** £3.95 per pack of 3 capsules. **InVita D3 5,600 IU soft capsules:** £2.50 per pack of 4 capsules. **InVita D3 2,400 IU/ml oral drops, solution:** £3.60 per 10ml bottle. **InVita D3 800 IU soft capsules:** £2.50 per pack of 28 capsules. **InVita D3 400 IU soft capsules:** £1.85 per pack of 28 tablets. **Legal Classification:** POM. **MA number: InVita D3 50,000 IU oral solution:** PL 24837/0076. **InVita D3 50,000 IU soft capsules:** PL 24837/0074. **InVita D3 25,000 IU oral solution:** PL 24837/0039. **InVita D3 25,000 IU soft capsules:** PL 24837/0073. **InVita D3 5,600 IU soft capsules:** PL 24837/0077. **InVita D3 2,400 IU/ml oral drops, solution:** PL 24837/0046. **InVita D3 800 IU soft capsules:** PL 24837/0070. **InVita D3 400 IU soft capsules:** PL 24837/0069. **Marketing Authorisation Holder:** Consilient Health Limited, 5th Floor, Beaux Lane House, Mercer Street Lower, Dublin 2, Ireland. Further information is available on request from Consilient Health (UK) Ltd, 1 Church Road, Richmond upon Thames, Surrey, TW9 2QE or drugsafety@consilienthealth.com. **Job Code:** UK-INV-270. **Date of preparation or last revision of PI:** June 2021.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Consilient Health (UK) Ltd, Ground Floor, No. 1 Church Road, Richmond upon Thames, Surrey TW9 2QE UK or drugsafety@consilienthealth.com or on +44(0)203 751 1882

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Licensed medicine for vitamin D deficiency