

# References

## In this guide

### [In this guide](#)

1. [Calcidiol supplementation during pregnancy - Introduction and Background](#)
2. [Calcidiol supplementation during pregnancy - Toxicokinetics](#)
3. [Calcidiol supplementation during pregnancy - Toxicity](#)
4. [Calcidiol supplementation during pregnancy - Health based guidance values](#)
5. [Calcidiol supplementation during pregnancy - Exposure assessment](#)
6. [Calcidiol supplementation during pregnancy - Risk characterisation](#)
7. [Calcidiol supplementation during pregnancy - Conclusions and Questions](#)
8. [Calcidiol supplementation during pregnancy - List of Abbreviations and Technical terms](#)
9. [Calcidiol supplementation during pregnancy - References](#)
10. [Calcidiol supplementation during pregnancy - Search Terms](#)
11. [Calcidiol supplementation during pregnancy - Annex A](#)

Advisory Committee on Novel Foods and Processes (ACNFP). (2024). ACNFP Safety Assessment: Calcidiol (25-hydroxycholecalciferol monohydrate) as a novel food for use in food Supplements [ACNFP Safety Assessment: Calcidiol \(25-hydroxycholecalciferol monohydrate\) | Advisory Committee on Novel Foods and Processes](#)

Bañón, S., Rosillo, M., Gómez, A., Pérez-Elias, M.J., Moreno, S. and Casado, J.L. (2015). Effect of a monthly dose of calcidiol in improving vitamin D deficiency and secondary hyperparathyroidism in HIV-infected patients. *Endocrine*, 49, pp.528-537. [Relative effectiveness of oral 25-hydroxyvitamin D3 and vitamin D3 in raising wintertime serum 25-hydroxyvitamin D in older adults - ScienceDirect](#)

Barger-Lux MJ, Heaney RP, Dowell S, Chen TC, Holick MF. (1998). Vitamin D and its major metabolites: serum levels after graded oral dosing in healthy men. *Osteoporos Int* 8(3):222-230. [Vitamin D and its Major Metabolites: Serum Levels after Graded Oral Dosing in Healthy Men | Osteoporosis International](#)

Bates B, Lennox A, Prentice A, Bates C, Page P, Nicholson S, Swan G (2014). National Diet and Nutrition Survey Results from Years 1, 2, 3 and 4 (combined) of the Rolling Programme (2008/2009 - 2011/2012): [Main heading](#)

Bates, B.; Cox, L.; Nicholson, S.; Page, P.; Prentice, A.; Steer, T.; Swan, G. (2016) National Diet and Nutrition Survey Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013 - 2013/2014). [Main heading](#)

Bates, B.; Collins, D.; Jones, K.; Page, P.; Roberts, C.; Steer, T.; Swan, G. (2020) National Diet and Nutrition Survey Results from years 9, 10 and 11 (combined) of the Rolling Programme (2016/2017 to 2018/2019). [NDNS: results from years 9 to 11 \(2016 to 2017 and 2018 to 2019\) - GOV.UK](#)

Biondi, P., Pepe, J., Biamonte, F., Occhiuto, M., Parisi, M., Demofonti, C., Baffa, V., Minisola, S. and Cipriani, C. (2017). Oral calcidiol is a good form of vitamin D supplementation. *Clinical Cases in Mineral and Bone Metabolism*, 14(2), p.207.

Bischoff-Ferrari, H.A. and Dawson-Hughes, B. (2012). Stö ficklin E, Sidelnikov E, Willett WC, Orav EJ et al. Oral supplementation with 25 (OH) D3 versus vitamin D3: effects on 25 (OH) D levels, lower extremity function, blood pressure and markers of innate immunity. **J Bone Miner Res**, 27, pp.160-169. [Oral supplementation with 25\(OH\)D3 versus vitamin D3: effects on 25\(OH\)D levels, lower extremity function, blood pressure, and markers of innate immunity - PubMed](#)

Brandi, M.L. and Minisola, S. (2013). Calcidiol [25 (OH) D3]: from diagnostic marker to therapeutical agent. *Current medical research and opinion*, 29(11). pp.1565-1572.

Cashman, K.D., Seamans, K.M., Lucey, A.J., Stöcklin, E., Weber, P., Kiely, M. and Hill, T.R. (2012). Relative effectiveness of oral 25-hydroxyvitamin D3 and vitamin D3 in raising wintertime serum 25-hydroxyvitamin D in older adults. *The American journal of clinical nutrition*, 95(6), pp.1350-1356. [Relative effectiveness of oral 25-hydroxyvitamin D3 and vitamin D3 in raising wintertime serum 25-hydroxyvitamin D in older adults - PubMed](#)

Clausen I, Jakobsen J, Leth T and Ovesen L. (2003). Vitamin D3 and 25-hydroxyvitamin D3 in raw and cooked porkcuts. *Journal of Food Composition and Analysis*, 16, 575-585. [Vitamin D3 and 25-hydroxyvitamin D3 in raw and cooked pork cuts - ScienceDirect](#)

Committee on toxicity of chemicals in food, consumer products and the environment (COT). (2014). Statement on adverse effects of high levels of vitamin D. [\[ARCHIVED CONTENT\] UK Government Web Archive - The National Archives](#)

Committee on toxicity of chemicals in food, consumer products and the environment (COT) (2022). Statement on the potential effects of excess vitamin D intake during preconception, pregnancy and lactation [TOX-2021-45 Second draft statement Vitamin D V05](#)

Department of health (DH). (2012). Nutrient analysis of eggs Sampling Report. [Nutrient analysis of eggs - Sampling report \(publishing.service.gov.uk\)](#) Nutrient analysis of eggs - Sampling report (publishing.service.gov.uk).

EFSA (2021). Safety of calcidiol monohydrate produced by chemical synthesis as a novel food pursuant to Regulation (EU) 2015/2283. **EFSA Journal**, 19(7), p.e06660.

EFSA (2023a). Scientific opinion on the tolerable upper intake level for vitamin D, including the derivation of a conversion factor for calcidiol monohydrate. *EFSA Journal*, 21(8), p.e08145.

EFSA (2023b). Scientific and technical assistance to the evaluation of the safety of calcidiol monohydrate as a novel food. **EFSA Journal**, 22(1), p.e8520. [Scientific and technical assistance to the evaluation of the safety of calcidiol monohydrate as a novel food](#)

Gázquez, A., Sánchez-Campillo, M., Barranco, A., Rueda, R., Chan, J.P., Kuchan, M.J. and Larqué, E. (2022). Calcifediol during pregnancy improves maternal and fetal availability of vitamin D compared to vitamin D3 in rats and modifies fetal metabolism. *Frontiers in Nutrition*, 9, p.871632.

Gonnelli, S., Tomai Pitinca, M.D., Camarri, S., Lucani, B., Franci, B., Nuti, R. and Caffarelli, C., (2021). Pharmacokinetic profile and effect on bone markers and muscle strength of two daily dosage regimens of calcifediol in osteopenic/osteoporotic postmenopausal women. *Aging Clinical and Experimental Research*, pp.1-9. [Pharmacokinetic profile and effect on bone markers and muscle strength of two daily dosage regimens of calcifediol in osteopenic/osteoporotic postmenopausal women - PMC](#)

Graeff-Armas, L.A., Bendik, I., Kunz, I., Schoop, R., Hull, S. and Beck, M. (2020). Supplemental 25-hydroxycholecalciferol is more effective than cholecalciferol in raising serum 25-hydroxyvitamin D concentrations in older adults. **The Journal**

**of nutrition**, **150**(1), pp.73-81. [Supplemental 25-Hydroxycholecalciferol Is More Effective than Cholecalciferol in Raising Serum 25-Hydroxyvitamin D Concentrations in Older Adults - ScienceDirect](#)

Guerra López, P., Urroz Elizalde, M., Vega-Gil, N., Sánchez Santiago, B., Zorrilla Martínez, I., Jiménez-Mercado, M., Jódar, E., Landeta Manzano, A., Campo Hoyos, C. and Frías Iniesta, J. (2024). Efficacy and Safety of Calcifediol in Young Adults with Vitamin D Deficiency: A Phase I, Multicentre, Clinical Trial—POSCAL Study. *Nutrients*, *16*(2), p.306. [Efficacy and Safety of Calcifediol in Young Adults with Vitamin D Deficiency: A Phase I, Multicentre, Clinical Trial&mdash;POSCAL Study](#)

Guo, J., Lovegrove, J.A. and Givens, D.I. (2018). 25 (OH) D3-enriched or fortified foods are more efficient at tackling inadequate vitamin D status than vitamin D3. *Proceedings of the Nutrition Society*, *77*(3), pp.282-291. [25\(OH\)D3-enriched or fortified foods are more efficient at tackling inadequate vitamin D status than vitamin D3 - PMC](#)

Hard, G.C. (2014) Expert Review Of Histological Changes In Rat Kidney from a 90-Day Toxicity Study with Orally Administered DSM047117. Prepared for: DSM Nutritional Products AG, Wurmisweg 576, CH-4303 Kaiseraugst, Switzerland. Submitted as an appendix to Thiel et al, 2014c. DSM proprietary unpublished study.

Hathcock, J.N., Shao, A., Vieth, R. and Heaney, R., 2007. Risk assessment for vitamin D. **The American journal of clinical nutrition**, **85**(1), pp.6-18. [Risk assessment for vitamin D - ScienceDirect](#)

Heaney, R.P. (2008). Vitamin D: criteria for safety and efficacy. *Nutrition reviews*, *66*(suppl\_2), pp.S178-S181. [Vitamin D: criteria for safety and efficacy | Nutrition Reviews | Oxford Academic](#)

Institute Of Medicine (2011) Dietary Reference Intakes for Calcium and vitamin D. ISBN 978-0-309-16394-1. [Dietary Reference Intakes for Calcium and Vitamin D | The National Academies Press](#)

Jakobsen J and Saxholt E. (2009). Vitamin D metabolites in bovine milk and butter. *Journal of Food Composition and Analysis*, *22*, 472-478. [Vitamin D metabolites in bovine milk and butter - ScienceDirect](#)

Jetter, A., Egli, A., Dawson-Hughes, B., Staehelin, H.B., Stoecklin, E., Goessl, R., Henschkowski, J. and Bischoff-Ferrari, H.A. (2014). Pharmacokinetics of oral vitamin D3 and calcifediol. *Bone*, *59*, pp.14-19. [Pharmacokinetics of oral vitamin](#)

## [D3 and calcifediol - ScienceDirect](#)

Jones, G., Prosser, D.E. and Kaufmann, M. (2012). 25-Hydroxyvitamin D-24-hydroxylase (CYP24A1): its important role in the degradation of vitamin D. **Archives of biochemistry and biophysics**, **523**(1), pp.9-18.

Minisola, S., Cianferotti, L., Biondi, P., Cipriani, C., Fossi, C., Franceschelli, F., Giusti, F., Leoncini, G., Pepe, J., Bischoff-Ferrari, H.A. and Brandi, M.L., (2017). Correction of vitamin D status by calcidiol: pharmacokinetic profile, safety, and biochemical effects on bone and mineral metabolism of daily and weekly dosage regimens. *Osteoporosis International*, *28*, pp.3239-3249. [Correction of vitamin D status by calcidiol: pharmacokinetic profile, safety, and biochemical effects on bone and mineral metabolism of daily and weekly dosage regimens | Osteoporosis International](#)

Navarro-Valverde, C., Sosa-Henríquez, M., Alhambra-Expósito, M.R. and Quesada-Gómez, J.M. (2016). Vitamin D3 and calcidiol are not equipotent. *The Journal of Steroid Biochemistry and Molecular Biology*, *164*, pp.205-208. [Vitamin D3 and calcidiol are not equipotent - ScienceDirect](#)

NHS (2024). Meat in your diet. [Meat in your diet - NHS](#)

Occhiuto, M., Pepe, J., Colangelo, L., Lucarelli, M., Angeloni, A., Nieddu, L., De Martino, V., Minisola, S. and Cipriani, C. (2024). Effect of 2 Years of Monthly Calcifediol Administration in Postmenopausal Women with Vitamin D Insufficiency. *Nutrients*, *16*(11), p.1754. [Effect of 2 Years of Monthly Calcifediol Administration in Postmenopausal Women with Vitamin D Insufficiency](#)

Ovesen L, Brot C and Jakobsen J. (2003). Food contents and biological activity of 25-hydroxyvitamin D: a vitamin D metabolite to be reckoned with? *Annals of Nutrition and Metabolism*, *47*, 107–113. [Food contents and biological activity of 25-hydroxyvitamin D: a vitamin D metabolite to be reckoned with? - PubMed](#)

Pereda, C.A. and Nishishinya, M.B. (2022). Optimal dosage of vitamin D supplementation in obese patients with low serum levels of 25-Hydroxyvitamin D. A systematic review. *Obesity Medicine*, *29*, p.100381.

Pérez-Castrillón, J.L., Dueñas-Laita, A., Brandi, M.L., Jódar, E., del Pino-Montes, J., Quesada-Gómez, J.M., Cereto Castro, F., Gómez-Alonso, C., Gallego López, L., Olmos Martínez, J.M. and Alhambra Expósito, M.R., (2020). Calcifediol is superior to cholecalciferol in improving vitamin D status in postmenopausal women: a randomized trial. *Journal of Bone and Mineral Research*, *36*(10), pp.1967-1978.

[Calcifediol is superior to cholecalciferol in improving vitamin D status in postmenopausal women: a randomized trial | Journal of Bone and Mineral Research | Oxford Academic](#)

Quesada-Gomez, J.M. and Bouillon, R. (2023). Calcifediol cornerstone of the vitamin D endocrine system. *Nutrients*, 15(10), p.2290. [Calcifediol Cornerstone of the Vitamin D Endocrine System](#)

Remus T and Verspeek-Rip C. (2016). Evaluation of the mutagenic activity of DSM047117 in an in vitro mammalian cell gene mutation test with L5178Y mouse lymphoma cells (Study conducted at WIL Research Europe B.V., 5231 DD's Hertogenbosch, The Netherlands; WIL study number 511352). DSM Proprietary unpublished data.

Robbins, R.N., Serra, M., Ranjit, N., Hoelscher, D.M., Sweitzer, S.J. and Briley, M.E. (2022). Efficacy of various prescribed vitamin D supplementation regimens on 25-hydroxyvitamin D serum levels in long-term care. *Public Health Nutrition*, 25(1), pp.82-89. [Efficacy of various prescribed vitamin D supplementation regimens on 25-hydroxyvitamin D serum levels in long-term care | Public Health Nutrition | Cambridge Core](#)

Roberts, C.; Steer, T.; Maplethorpe, N.; Cox, L.; Meadows, S.; Page, P.; Nicholson, S.; Swan, G. (2018) National Diet and Nutrition Survey Results from Years 7 and 8 (combined) of the Rolling Programme (2014/2015 – 2015/2016) Available at: [National Diet and Nutrition Survey](#)

Ross, A.C., Manson, J.E., Abrams, S.A., Aloia, J.F., Brannon, P.M., Clinton, S.K., Durazo-Arvizu, R.A., Gallagher, J.C., Gallo, R.L., Jones, G. and Kovacs, C.S. (2011). The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *The Journal of Clinical Endocrinology & Metabolism*, 96(1), pp.53-58. [2011 Report on Dietary Reference Intakes for Calcium and Vitamin D from the Institute of Medicine: What Clinicians Need to Know | The Journal of Clinical Endocrinology & Metabolism | Oxford Academic](#)

Rossini, M., Viapiana, O., Gatti, D., James, G., Girardello, S. and Adami, S., (2005). The long term correction of vitamin D deficiency: comparison between different treatments with vitamin D in clinical practice. *Minerva medica*, 96, pp.1-7. [Short-Term Effects on Bone Turnover Markers of a Single High Dose of Oral Vitamin D3 | The Journal of Clinical Endocrinology & Metabolism | Oxford Academic](#)

Rossini, M., Adami, S., Viapiana, O., Fracassi, E., Idolazzi, L., Povino, M.R. and Gatti, D., (2012b). Dose-Dependent Short-Term Effects of Single High Doses of Oral Vitamin D 3 on Bone Turnover Markers. *Calcified Tissue International*, 91, pp.365-369. [Dose-Dependent Short-Term Effects of Single High Doses of Oral Vitamin D3 on Bone Turnover Markers | Calcified Tissue International](#)

Russo, S., Carlucci, L., Cipriani, C., Ragno, A., Piemonte, S., Fiacco, R.D., Pepe, J., Fassino, V., Arima, S., Romagnoli, E. and Minisola, S. (2011). Metabolic changes following 500 µg monthly administration of calcidiol: a study in normal females [Abstract]. *Calcified tissue international*, 89, pp.252-257. [Metabolic Changes Following 500 µg Monthly Administration of Calcidiol: A Study in Normal Females | Calcified Tissue International](#)

SACN. (2016). SACN vitamin D and health report. [SACN vitamin D and health report - GOV.UK](#)

Shieh, A., Ma, C., Chun, R.F., Witzel, S., Rafison, B., Contreras, H.T., Wittwer-Schegg, J., Swinkels, L., Huijs, T., Hewison, M. and Adams, J.S. (2017). Effects of cholecalciferol vs calcifediol on total and free 25-hydroxyvitamin D and parathyroid hormone. **The Journal of Clinical Endocrinology & Metabolism**, **102**(4), pp.1133-1140. [Effects of Cholecalciferol vs Calcifediol on Total and Free 25-Hydroxyvitamin D and Parathyroid Hormone | The Journal of Clinical Endocrinology & Metabolism | Oxford Academic.](#)

Stamp, T.C.B., Haddad, J.G. and Twigg, C.A. (1977). Comparison of oral 25-hydroxycholecalciferol, vitamin D, and ultraviolet light as determinants of circulating 25-hydroxyvitamin D. *The Lancet*, 309(8026). pp.1341-1343.

Vaes, A.M., Tieland, M., de Regt, M.F., Wittwer, J., van Loon, L.J. and de Groot, L.C. (2018). Dose-response effects of supplementation with calcifediol on serum 25-hydroxyvitamin D status and its metabolites: a randomized controlled trial in older adults. *Clinical nutrition*, 37(3), pp.808-814.

Verbaan, IAJ and Remus T. (2016). DSM047117: Micronucleus test in bone marrow cells of the rat. DSM Proprietary unpublished data.

Vicchio, D., Yergey, A., O'Brien, K., Allen, L., Ray, R. and Holick, M. (1993). Quantification and kinetics of 25-hydroxyvitamin D3 by isotope dilution liquid chromatography/thermospray mass spectrometry. *Biological mass spectrometry*, 22(1), pp.53-58.

Vieth, R. (2020). Vitamin D supplementation: cholecalciferol, calcifediol, and calcitriol. *European Journal of Clinical Nutrition*. 74(11), pp.1493-1497.

Weber E and Schulz M. (2005). Chromosome Aberration Test in Human

Lymphocytes in vitro with Calcifediol. DSM Proprietary unpublished data.

Wöhrle T and Sokolowski A. (2013). DSM047117: *Salmonella typhimurium* and *Escherichia coli* reverse mutation assay. (Study conducted at Harlan CCR; D64380 Rossdorf; Harlan CCR study Number 1533500). DSM Proprietary unpublished data.