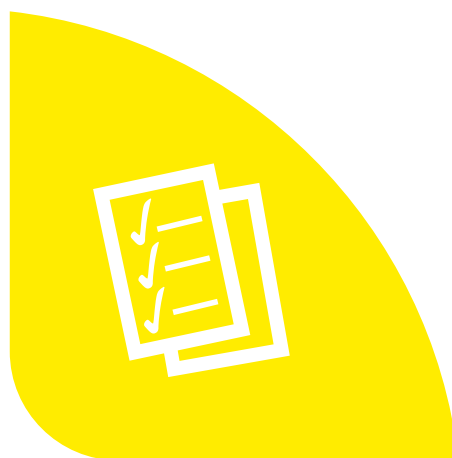


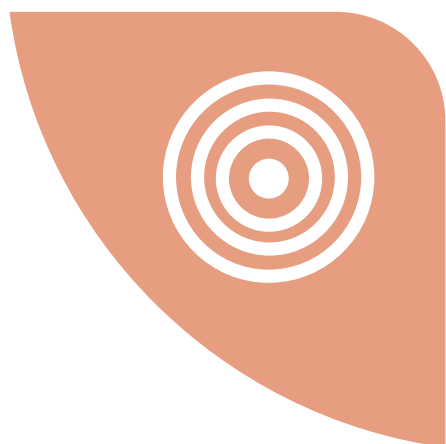
CONSIDER THE ADCAL D₃ RANGE

in the medicines
optimisation process
for osteoporotic patients



Adcal-D₃[®]

CALCIUM CARBONATE AND COLECALCIFEROL

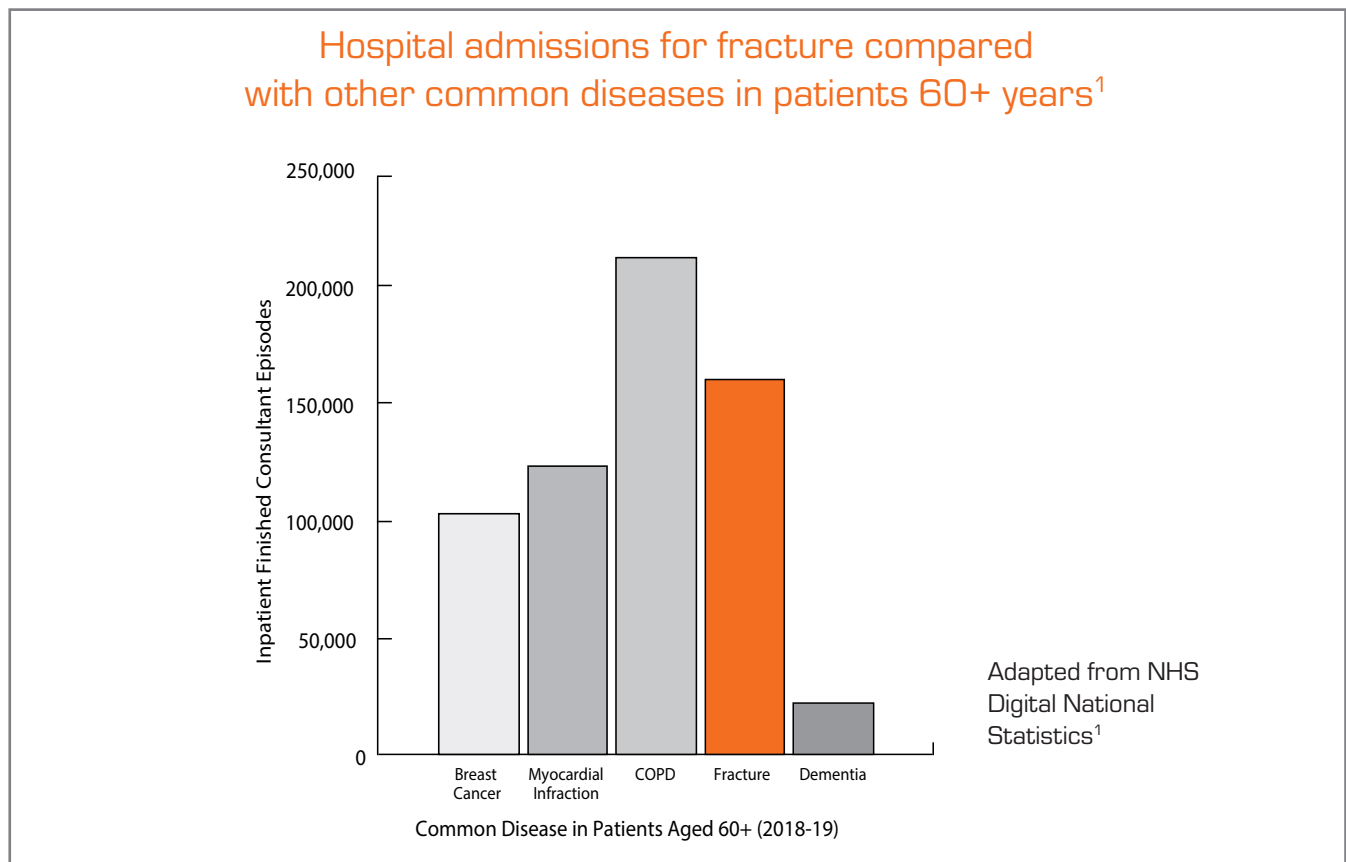


OSTEOPOROSIS: THE BURDEN ON THE NHS

The burden on the NHS impacts both primary and secondary care

Hospital admissions

In those patients over 60, the number of finished consultant episodes (FCEs) due to the major fractures (wrist, vertebral and hip), when combined, is greater than the number of FCEs of some other common diseases (i.e. myocardial infarction, breast cancer, and dementia) (see below).¹



Primary Care

Fractures also have a significant impact on primary care, with GP consultations hugely increased in those patients with osteoporotic fractures.²

Hip fractures are associated with significant healthcare costs

Audited figures from 2012/13 showed that the average cost of treating a hip fracture was £14,163 and £2,139 in the first and second year following fracture respectively.³

The impact of falls

A 2013 study analysed the costs of older people admitted to hospital, both 12 months before and 12 months after their fall (n=421 aged 65+).

The study found:⁴

- Hospital, community and social care costs for each patient were almost 4 x more in the 12 months after admission for a fall as the costs of the admission itself.
- When comparing the 12 months before and after a fall, there was an increase of:



Osteoporosis: a growing problem

The UK population is the largest it's ever been. Combined with a growing ageing population, this is expected to increase the prevalence of chronic conditions such as osteoporosis.^{5,6}

Over ½ million people receive hospital treatment every year in the UK because of a fragility fracture.⁷

2017 UK projection figures estimate that osteoporotic fractures will increase by 27%, and the associated fracture costs by over 30% by 2030.⁸

With the number of fractures increasing and 'prevention' introduced as part of the 2017 NHS General Practice 10 point action plan,⁹ now is the time to take action and reduce the consequences of fragility fractures for both the NHS and patients.

MEDICINES OPTIMISATION

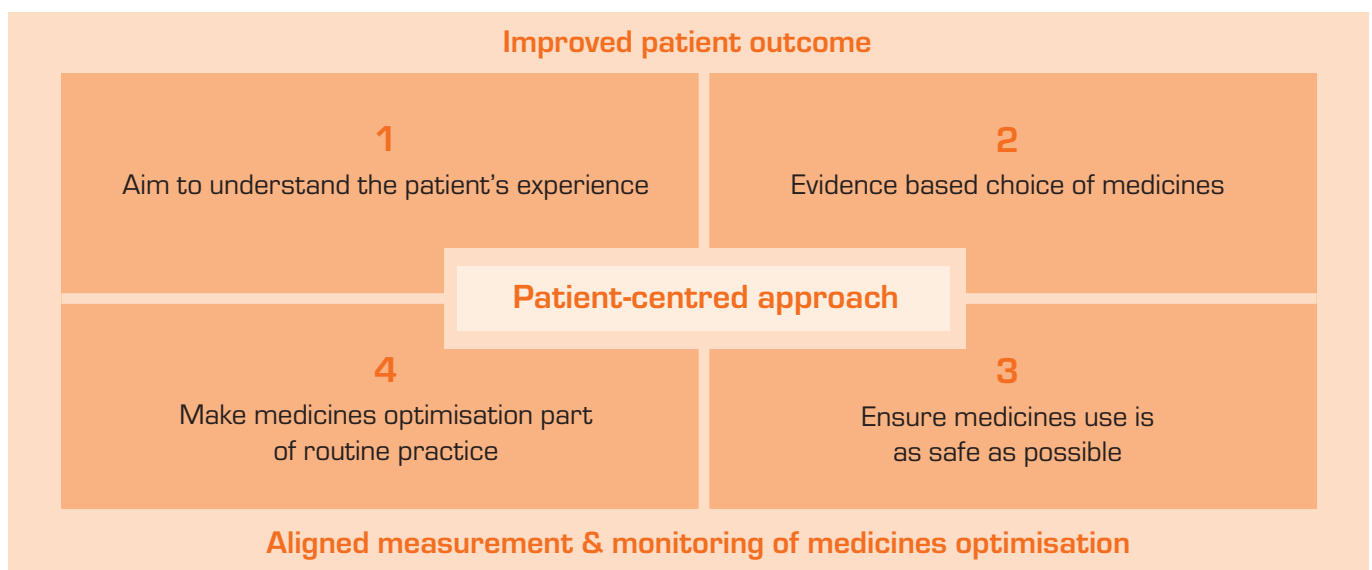
Getting the most out of medicines for both patients and the NHS

Medicines optimisation¹⁰⁻¹²

- Evaluates the value which medicines deliver
- Ensures medicines are both clinically-effective and cost-effective
- Provides patients with the right choice of medicines, at the right time
- Allows patients to be engaged in the process by their clinical team

A person-centred approach to safe and effective medicines use, to ensure people obtain the best possible outcomes from their medicines.

NICE Guideline 2015¹²



As the NHS faces financial challenges over the coming years, medicines optimisation can not only improve patient outcomes, but it may also help reduce costs in relation to both healthcare professionals' time and medicines wastage.¹⁰⁻¹³

The estimated national figure of pharmaceutical waste is **£300 million** per year or £1 in every £25 in primary care.¹³

THE ADCAL D₃ RANGE

1. Aim to understand each patient's experience

Designed to facilitate patient adherence through formulation choice, disease awareness and patient support initiatives.^{14,15}



2. Evidence based choice of medicines

Provides patients with an evidence-based dose as an adjunct in the treatment of osteoporosis.^{16,17}



Adcal-D₃^{*}

4. Make Adcal-D₃ part of your routine optimisation practice

Competitively priced range plus an evidence-based dose, allows you to offer a large choice of presentations with patient support initiatives.¹⁴⁻¹⁷

28 day packaging.¹⁴



3. Ensure appropriate use of medicines

28 day calendar packaging to support consistent administration and tracking.

28 day compatibility with compliance aids.^{18*}



* 28 day compatibility with compliance aids: available for Adcal-D₃ Caplet, Adcal-D₃ and Adcal-D₃ Lemon.



THE ADCAL D₃ RANGE

Designed to facilitate patient adherence

Designed to facilitate adherence through presentation choice

Patients have different preferences, abilities, cultural and religious backgrounds, and prescribing from a range with a large selection of preparations can help support patient choice.

The Adcal-D₃ range provides:

- The UK's largest choice of calcium and vitamin D preparations^{14,15}
 - Adcal-D₃, Adcal-D₃ Lemon, Adcal-D₃ Dissolve, Adcal-D₃ Caplets
- Adcal-D₃ Caplets:
 - Film coated caplets¹⁹ for ease of swallowing
 - The smallest high dose calcium and vitamin D₃ tablet available^{19,20}
 - Gelatin and soya free formulation¹⁹
 - Halal and Kosher certified^{21,22}



The problems with patient adherence

- 10 days after starting a medicine for a chronic condition, almost one third of patients are already non-adherent (n=226).²³
- Patient adherence to medicines such as calcium and/or vitamin D supplementation is historically low. One study showed that after 24 months, only 55% of patients were still adhering to their medication (n=5,292).²⁴
- High adherence (≥80%) to calcium & vitamin D supplementation was associated with a 24% fracture risk reduction in patients (p<0.0001). This is contrasted with a reduction of only 12% in studies where compliance was under 80% (p=0.0004, n=52,625 from 17 randomised trials).¹⁷

To address this Kyowa Kirin has a number of measures and initiatives in place to support patient adherence.



Patient education

Kyowa Kirin offers a patient educational leaflet on calcium and vitamin D to help awareness and to provide an understanding of the importance of these two essential nutrients in bone health.

Calendar packaging

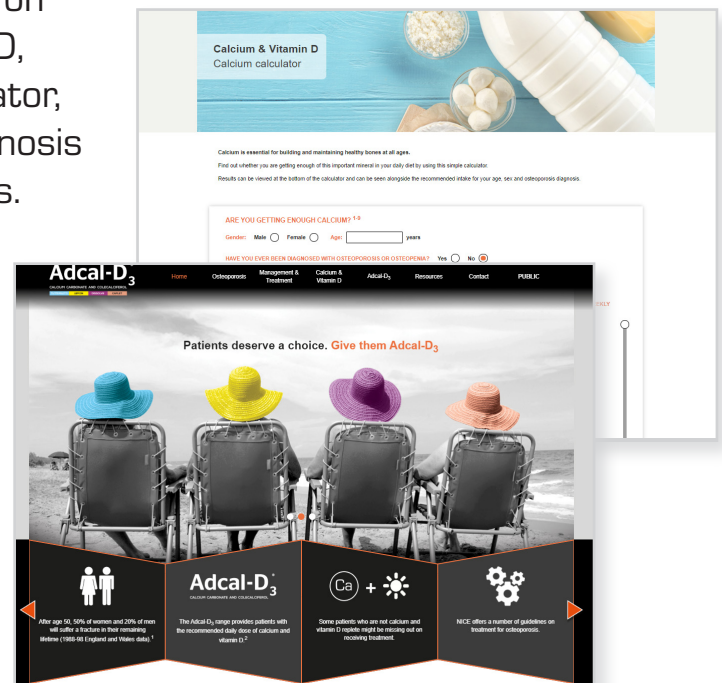
Adcal-D₃ also provides 28 day calendar packaging for the entire range, with the aim of improving adherence by allowing patients to keep track of when they have taken their Adcal-D₃.



Adcal-D₃ website

The Adcal-D₃ website is now available, which provides a variety of information on osteoporosis and calcium and vitamin D, including an easy-to-use calcium calculator, simple recipes and information on diagnosis and treatment options for osteoporosis.

Please visit www.adcal.co.uk to find out more.





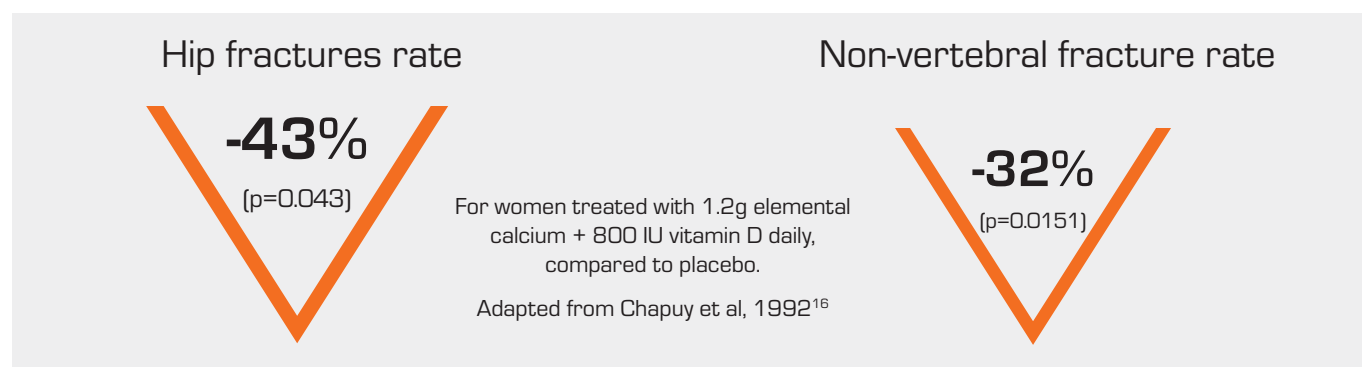
THE ADCAL D₃ RANGE

Providing patients with an evidence-based dose of calcium and vitamin D

Not all calcium and vitamin D formulations provide an evidence based dose for the effective treatment of osteoporosis

A randomised placebo-controlled trial of 3,270 healthy, ambulatory elderly women (mean age 84) demonstrated that:

- 1,200mg elemental calcium and 800 IU vitamin D₃ daily significantly reduced hip fractures and non-vertebral fractures vs. placebo over 18 months.¹⁶



- Not all calcium and vitamin D doses have been shown to reduce hip fracture rates, but the dose used in the Adcal-D₃ range has been clinically proven to reduce both hip and non-vertebral fractures.^{16,17}
 - 1,000mg calcium and 800 IU vitamin D₃ have **not** been shown to significantly reduce fracture rates.^{24,27,28}

Saving hospital beds in the NHS

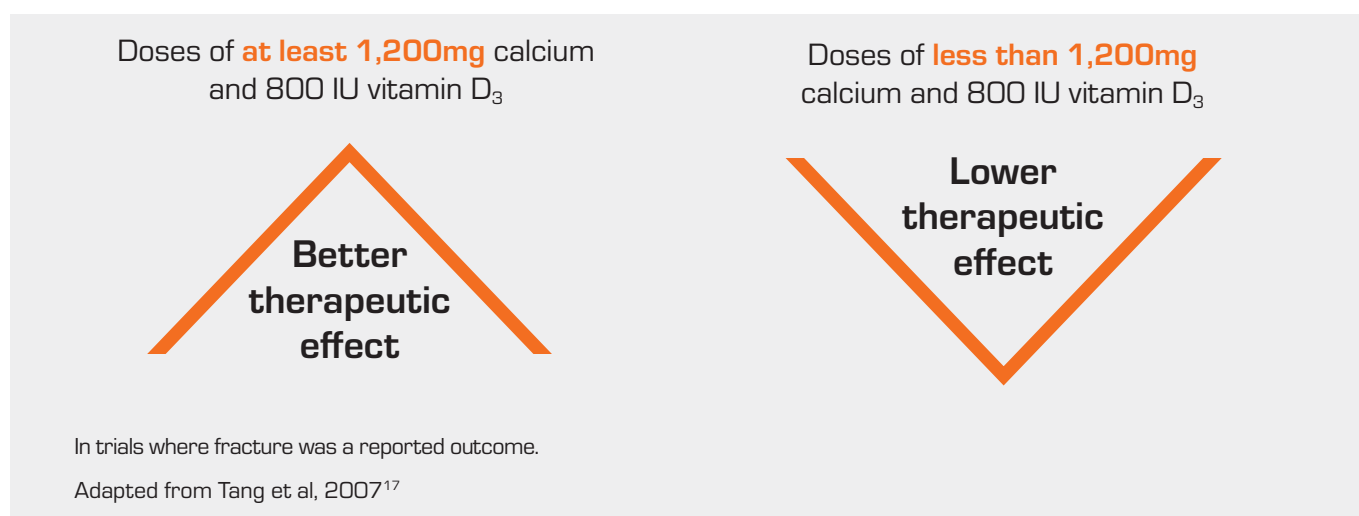
NHS England is looking into beds blocked by delayed transfers related to social care with an aim to free up 2,000 - 3,000 hospital beds.²⁹ How can fracture prevention contribute to saving hospital beds?

- In 2017, the length of stay per hip fracture was 20 days, resulting in 3,614 beds being occupied (data from England, N Ireland and Wales).³⁰
- Treating 30 patients with a daily dose of at least 1,200mg calcium and 800 IU vitamin D for 3.5 years prevents one hip fracture from occurring (patients >70 at risk of osteoporosis who are compliant with supplementation).¹⁷
- This can also result in reduced GP and consultant appointments.^{2,31}



In a meta-analysis involving 29 randomised clinical trials and 63,897 subjects, the authors concluded that:

- Daily doses of > 1,200mg calcium or > 800 IU vitamin D₃ have been shown to achieve better therapeutic effects than lower doses.¹⁷



Calcium and vitamin D supplementation is also an important adjunct to many osteoporosis treatments, including bisphosphonates.³²

The cost of fracture to the NHS

Osteoporosis is a major burden for the NHS, including primary care services.

- Audited figures show that the mean censor-adjusted cost of treating a hip fracture reached £14,163 and £2,139 in the first and second years following fracture respectively (using 2012/13 unit costs).³
- The Royal Osteoporosis Society published an estimate of the total hospital and social care costs of managing hip fractures in 2009; the figure quoted is approximately £2 billion.³³
- Fractures also have a significant impact on primary care, with GP consultations hugely increased in those patients with osteoporotic fractures compared to age and sex matched controls.²

THE ADCAL D₃ RANGE

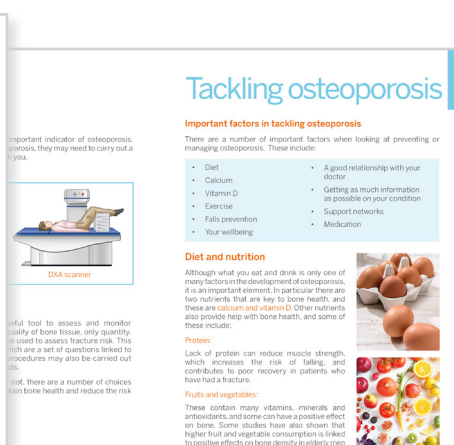
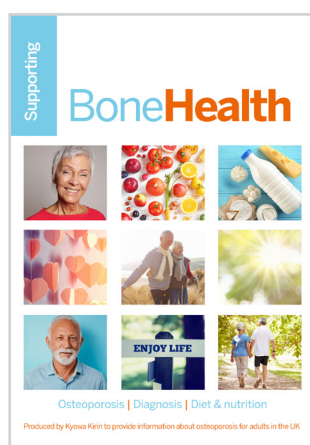
Helping patients understand their condition, medication and administration

Kyowa Kirin is committed to helping patients understand their condition and medication

Helping patients to understand more about osteoporosis, their medication and how to take it, can help them understand the importance of correct dosing and administration of Adcal-D₃.

Our initiatives include:

- 28 day calendar packaging for the entire range, which aims to help improve adherence by allowing patients to keep track of when they have taken their Adcal-D₃.
 - Calendar packaging is used on both the outer packaging (so patients can record when they take their Adcal-D₃) and the inner blister strips (which has the days of the week printed on the foil above each tablet).
 - 28 day packaging helps patient understanding of when medicine packaging/prescription will finish.
- Easy to understand patient education and information leaflets on osteoporosis.
- Adcal-D₃, Adcal-D₃ Lemon and Adcal-D₃ Caplets have all been stability tested for 28 days in compliance aids.¹⁸





THE ADCAL D₃ RANGE

Providing healthcare professionals with a range of options for their calcium & vitamin D prescriptions

By prescribing Adcal-D₃, healthcare professionals can ensure they are prescribing a range of calcium and vitamin D formulations which is both clinically-effective and competitively priced

- Adcal-D₃ offers a competitively priced calcium and vitamin D range:
 - Adcal-D₃ Caplets are now £2.95 per 28 day pack.¹⁴
 - With an evidence-based dose for the entire range, you can prescribe a calcium and vitamin D supplement at a dose that has a clinically proven risk reduction record for both hip and non-vertebral fractures.
- With the UK's largest choice of calcium and vitamin D presentations, healthcare professionals can provide a wide selection of variants for their patients.^{14,15} This can help them cater for different patients and their different needs/taste preferences, which may then help with adherence.
- Our 28 day packaging enables simple and straightforward four-week prescribing blocks.



References

1. NHS Digital, National Statistics. Hospital admitted patient care activity, 2018-19.
2. Dolan P and Torgerson DJ. Osteoporos Int 1998; 8: 611–617.
3. Leal J, et al. Osteoporos Int. 2016; 27(2): 549-58.
4. Yang T, et al. Exploring the system-wide costs of falls in older people in Torbay. The King's Fund, 2013.
5. Overview of the UK population: January 2021, ONS: <https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/articles/overviewoftheukpopulation/january2021> Last accessed May 2021.
6. Sözen T, et al. Eur J Rheumatol 2017; 4: 46-56.
7. Osteoporosis, NHS Choices: <https://www.nhs.uk/Conditions/Osteoporosis/> Last accessed May 2021.
8. Broken bones, broken lives: a roadmap to solve the fragility fracture crisis in Europe. IOF Report 2018.
9. General Practice – Developing confidence, capability and capacity, 2017. NHS England.
10. Medicines optimisation. NHS England. <https://www.england.nhs.uk/medicines/medicines-optimisation/> Last accessed May 2021.
11. Medicines optimisation (QS120). NICE Quality standard, March 2016.
12. Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes. NICE Guideline, March 2015.
13. Hazell B, Robson R. Pharmaceutical waste reduction in the NHS. Version 1. June 2015.
14. eMIMS, May 2021.
15. eMC, Calcium and Calcium & Vitamin D supplements SPCs. www.medicines.org.uk/emc. Last accessed: May 2021.
16. Chapuy M et al. N Engl J Med 1992; 327: 1637-1642.
17. Tang B et al. Lancet 2007 Aug 25; 370(9588): 657-66.
18. Data on file.
19. Adcal-D₃ Caplet SmPC.
20. Data on file.
21. Halal Authority Board. Adcal-D₃ Caplet Halal Certificate.
22. Kosher Certificate.
23. Barber N, et al. BMJ Quality & Safety 2004;13:172-175.
24. Grant AM, et al. Lancet 2005; 7-13; 365(9471): 1621-8.
25. Ashish A, et al. MedGenMed. 2005; 7(1): 4.
26. Gold D T, et al. The American Journal of Medicine 2006; 119: 32S-37S.
27. Salovaara K et al. J Bone Miner Res 2010; 25(7): 1487-95.
28. Porthouse J, et al. BMJ 2005; 330 1003-1006.
29. NHS England: <https://www.england.nhs.uk/five-year-forward-view/next-steps-on-the-nhs-five-year-forward-view/funding-and-efficiency/> Last accessed May 2021.
30. National Hip Fracture Database. Annual Report September 2018.
31. Kyowa Kirin Ltd. Data on file 001.
32. Golombick T, Diamond T. Clin Interv Aging 2008; 3(1): 183-186.
33. Protecting fragile bones. A strategy to reduce the impact of osteoporosis and fragility fractures in England. Royal Osteoporosis Society, May 2009.

Prescribing information

PRESCRIBING INFORMATION Please refer to the full Summary of Product Characteristics before prescribing.

Name, Active Ingredients, Marketing Authorisation number and NHS cost: *Adcal-D3 Caplets*; 750mg calcium carbonate and 200 IU colecalciferol, PL 16508/0039, 112 tablets: £2.95. *Adcal-D3 Chewable Tablets*; 1500mg calcium carbonate and 400 IU colecalciferol, PL 16508/0001, 56 tablets: £3.65, 112 tablets: £7.49. *Adcal-D3 Lemon Chewable Tablets*; 1500mg calcium carbonate and 400 IU colecalciferol, PL 16508/0028, 56 tablets: £3.65, 112 tablets: £7.49. *Adcal-D3 Dissolve Effervescent Tablets*; 1500mg calcium carbonate and 400 IU colecalciferol, PL 16508/0026, 56 tablets: £5.99. **Indication:** As an adjunct to therapy for osteoporosis and for therapeutic supplementation of malnutrition, e.g. in pregnancy and established vitamin D dependent osteomalacia. Prevention and treatment of calcium deficiency/vitamin D deficiency, especially in the housebound and institutionalised elderly. Deficiency is indicated by raised levels of PTH, lowered 25-hydroxy-vitamin D and raised alkaline phosphatase levels associated with increased bone loss. **Dosage and administration:** *Not recommended for children under the age of 12 years.* Doses for adults and the elderly as follows. *Adcal-D3 Caplets*; Two tablets twice daily, preferably two in the morning and two in the evening. *Adcal-D3 Chewable Tablets, Adcal-D3 Lemon Chewable Tablets*; Two tablets daily, preferably one in the morning and one in the evening. *Adcal-D3 Dissolve Effervescent Tablets*; Two tablets daily, preferably one in the morning and one in the evening, dissolved in approximately 200ml of water. **Adverse effects:** Hypersensitivity reactions, mild gastrointestinal disturbances, skin rash, hypercalciuria. Rarely, hypercalcaemia, with long-term use at high dosages. Prescribers should consult the summary of product characteristics for further details of side effects. **Precautions:** Mild to moderate renal failure or mild hypercalciuria, history of renal stones, immobilised patients with osteoporosis. Monitor serum and urinary calcium levels and kidney function during long-term treatment. Caution is required in patients receiving treatment for cardiovascular disease, and those suffering from sarcoidosis or malignancies. Patients taking digitalis and other cardiac glycosides require strict medical supervision. Thiazide diuretics can reduce urinary calcium excretion. Concomitant use of glucocorticoids, phenytoin or barbiturates can decrease the effect of vitamin D. Calcium salts may reduce the absorption of thyroxine, bisphosphonates, sodium fluoride, quinolone or tetracycline antibiotics and iron, so allow a minimum of four hours before taking the calcium. Allow for other sources of calcium and vitamin D supplementation. Certain foods may reduce the absorption of calcium. Not for patients with fructose intolerance. Normal requirements for calcium and vitamin D are increased during pregnancy – therapy should be under medical supervision. Vitamin D and its metabolites pass into breast milk. *Adcal-D3 Dissolve Effervescent Tablets* contain 1.672mg sugar per tablet, which may be harmful to teeth if used for a prolonged period and should be taken into account by patients with diabetes mellitus or who require a low-sugar diet. **Contraindications:** Hypercalcaemia (resulting for example from myeloma, bone metastases or other malignant bone disease, sarcoidosis, primary hyperparathyroidism and vitamin D overdose), severe renal failure, hypersensitivity to any of the tablet ingredients, osteoporosis due to prolonged immobilisation, renal stones, severe hypercalciuria. *Adcal-D3 Chewable Tablets, Adcal-D3 Lemon Chewable Tablets and Adcal-D3 Dissolve Effervescent Tablets* contain a small quantity of soya oil and are contraindicated in patients allergic to peanuts or soya. **Marketing Authorisation Holder:** Kyowa Kirin Ltd., Galabank Business Park, Galashiels TD1 1QH, UK. **Legal classification:** P. **Date of prescribing information:** April 2017.

Adverse events should be reported. Reporting forms and information can be found at <https://yellowcard.mhra.gov.uk>. Adverse events should also be reported to Kyowa Kirin Ltd on +44 (0)1896 664000, email medinfo@kyowakirin.com