

DRUG UPDATE

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GLUCOSAMINE

Glucosamine, a component of cartilage, is a food supplement claimed to modify the progression of osteoarthritis (OA). Short-term use reduces pain by as much as a NSAID and improves joint function in patients with OA. There is limited evidence that long-term use in patients with OA of the knee is associated with a reduction in pain, improvement in joint function and less joint space narrowing compared with placebo. Glucosamine appears to be well tolerated but its long-term safety is uncertain. It can be prescribed on the NHS but it is not a licensed medicine and the quality and consistency of different products may vary.

What is it?

Glucosamine, a component of glycosaminoglycans in articular cartilage, is claimed to modify the progression of osteoarthritis (OA). In the UK it is sold as a food supplement and can be obtained from high street stores and via the internet. It is usually formulated as the sulphate and is derived from the shells of shellfish or produced as a synthetic compound.¹ Glucosamine is not a licensed medicine and the quality and content of the available products may therefore vary. However, prescriptions written generically or for non-blacklisted products are reimbursed at NHS expense.

How effective is it?

Three meta-analyses (search dates 1999, 1999 and 2002) have reviewed a total of 17 randomised placebo-controlled trials evaluating the efficacy and safety of glucosamine.^{2,4} Trial duration ranged from 4 weeks to 3 years; the usual oral dose of glucosamine was 1500 mg/day.

A meta-analysis of trials of short-term use has suggested improvements in pain and joint function with glucosamine.² A second meta-analysis (n=911) included six trials lasting at least four weeks with oral or parenteral glucosamine. Important methodological failings were identified by the author but they concluded that the moderate effects of glucosamine observed on pain and functional outcomes were worthwhile.³

The most recent meta-analysis⁴ included 7 trials of oral glucosamine and 8 trials of chondroitin, another component of cartilage; separate results for glucosamine were reported only for two 3-year trials and these are discussed below.

Both trials were randomised double-blind comparisons of oral glucosamine 1500 mg/day with placebo in middle-aged to elderly patients with mild to moderate knee OA. The primary outcome was the change in mean joint width in the medial tibiofemoral joint compared with baseline. Approximately 200 patients were randomised in each trial but 34 - 43%

withdrew prematurely, with no inter-group differences. Intention to treat analysis showed little change in mean joint space after 3 years of glucosamine treatment (-0.06⁵ and +0.04⁶ mm) but there was a decrease with placebo (-0.31⁵ and -0.19⁶ mm). However, change in joint space may not be a valid marker of OA progression.¹

Both trials also used the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) to assess OA symptoms. In the first trial,⁵ the WOMAC score improved by 11.7% in patients taking glucosamine but worsened by 9.8% in those on placebo. The difference between the groups was significant and due largely to reduced pain and improved joint function; stiffness did not change significantly. There was no correlation between the changes in joint space and symptom score and no significant differences in the consumption of rescue analgesics (paracetamol, diclofenac or piroxicam).

In the second trial,⁶ glucosamine was associated with significantly greater reductions than placebo in total WOMAC score and its subscales for pain, function and stiffness. There were no differences in the consumption of rescue analgesia (paracetamol).

One more trial has since been published: this 3-month trial in 205 patients with knee OA found that oral glucosamine did not significantly reduce self-assessed pain compared with placebo.⁷ No comparison with paracetamol has been published.

The combination of glucosamine and chondroitin may be effective but it is currently unknown how it compares with glucosamine alone.¹ The results from the NIH/NCCAM sponsored trial, comparing these treatments should be available later this year.⁸

How safe is it?

The first meta-analysis concluded that glucosamine was well tolerated in short-term trials.² The two 3-year trials reported

no difference between glucosamine and placebo in the frequency, nature or severity of adverse effects.^{5,6} People who are allergic to shellfish may react to naturally sourced glucosamine; this risk has not been clarified in published trials but allergic reactions were not more common than with placebo. Large doses of glucosamine may affect glucose homeostasis⁹ but no relevant adverse effects were identified in the 3-year trials^{5,6} and none were reported in patients with type 2 diabetes who were taking glucosamine plus chondroitin.¹⁰

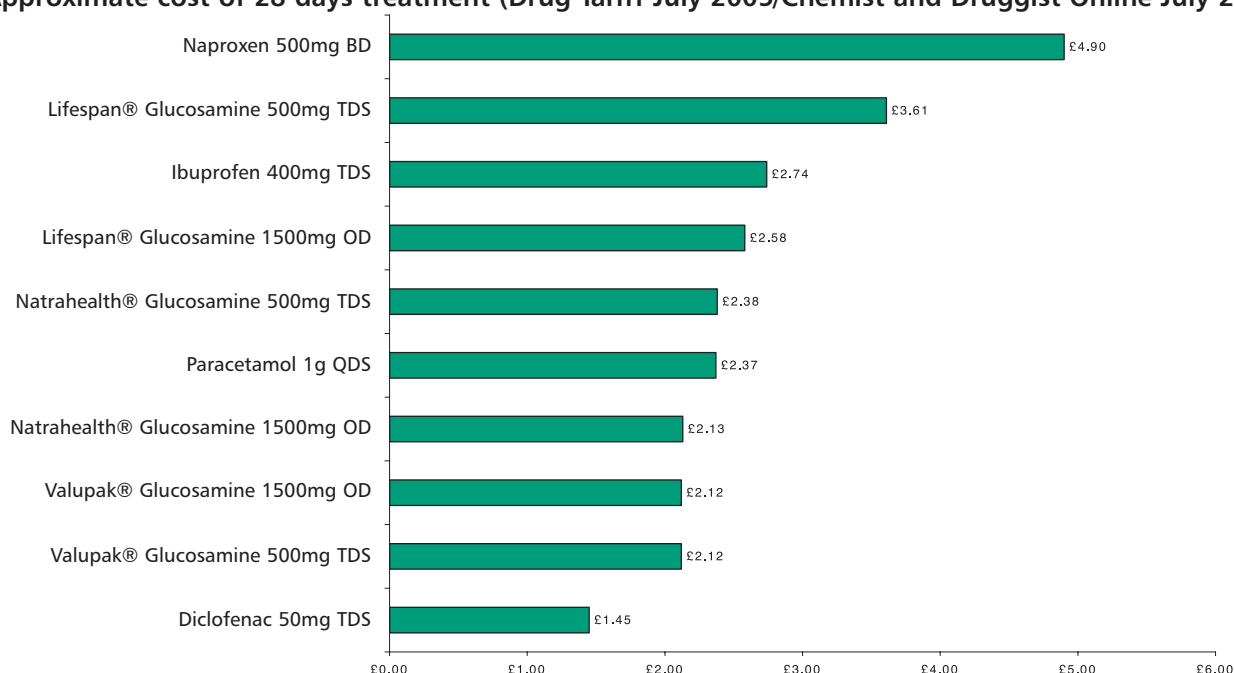
When should it be used?

Although there is evidence of modest efficacy and safety for up to 3 months, most patients with OA are likely to seek long-term treatment. Evidence suggests the modest benefits of

acute treatment are sustained but this data is derived from the relatively few patients who have completed 3-year trials. The use of Glucosamine has increased since the decision to allow prescribing on NHS FP10 prescriptions in November 2002. In the last financial year (2004/05) 18,364 items at a cost of £150,603 were dispensed in the former Northern and Yorkshire Region and 7,817 items at a cost of £62,008 were dispensed in the Greater Manchester strategic health authority. The use of glucosamine may be justifiable for some patients who wish to avoid NSAIDs or other licensed treatments. However prescribers should be aware that these are unlicensed preparations and pharmaceutical quality may not be assured and, while there is some evidence of efficacy and safety, this is currently limited.

How much do they cost?

Approximate cost of 28 days treatment (Drug Tariff July 2005/Chemist and Druggist Online July 2005)



N.B. Doses shown are for general comparison only and do not imply therapeutic equivalence.

Brands included in this chart are examples of those, which can be prescribed on NHS FP10 prescription. See current Drug Tariff for full details.

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KEY RCT - randomised controlled trial, MA-meta analysis, R-review

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