



VERDICT & SUMMARY

Glucosamine

(Alateris[®]▼)

For the treatment of osteoarthritis of the knee

Committee's Verdict: **CATEGORY D**

BNF: 4.7.1

Glucosamine (either as the hydrochloride or sulphate salt) is not considered suitable for prescribing. Current clinical evidence for its efficacy is inconsistent, and not convincing, in spite of many randomised clinical trials. The trials showed a clear dichotomy between sponsored trials and independent trials, suggesting bias, or unequal quality of preparation used. Where benefits for glucosamine were found, the size of the effect was small.

Category D: cannot be recommended for prescribing because of inadequate evidence for efficacy and/or safety

MTRAC reviewed glucosamine because a glucosamine hydrochloride product has been recently licensed.

Licensed indication

Glucosamine hydrochloride is indicated for the treatment of osteoarthritis of the knee.¹

Background information

Osteoarthritis (OA) is the most common chronic joint condition in individuals over 65 years² and is a leading cause of impaired mobility in the elderly. The most frequent presenting complaint is pain; other symptoms include morning stiffness and loss of function. One estimate is that up to 8.5 million people in the UK are affected by joint pain that may be attributed to OA.³

Education, weight loss, exercise and physical therapy are first-line treatments in reducing pain and improving function.² The first-line drug of choice is paracetamol. Non-steroidal anti-inflammatory drugs (NSAIDs, including the COX-II-selective inhibitors) and opioids (codeine, dihydrocodeine) may also be used. Glucosamine (as the sulphate or hydrochloride salt) has been used extensively world-wide by patients with OA or joint pain. It has been licensed as a medicinal product in some countries but not in the UK until 2007, with the launch of Alateris, glucosamine hydrochloride.¹

In a Clinical Guideline on OA published in February 2008, the National Institute of Health and Clinical Excellence (NICE) stated that the use of glucosamine products is not recommended for the treatment of osteoarthritis.³

Clinical efficacy

Fourteen published, double-blind, randomised controlled trials (RCTs) using clinical outcomes compared glucosamine with placebo⁴⁻¹⁷ and three compared glucosamine with ibuprofen.¹⁸⁻²⁰ One of the placebo-controlled trials also included a celecoxib arm as an active control,⁵ and another included a paracetamol arm,¹² but the results were not compared with glucosamine. Of the 17 studies, eight appeared to be independent^{4-6,8,10,17,19,20} and nine were supported by manufacturers of glucosamine^{7,9,11-16,18} (the majority by Rotta Pharmaceuticals, Italy). The

number of patients in the independent trials was greater: 2,379 (largely because of one trial of 1,583 patients⁹) compared with 1,282 in the sponsored trials. The range of duration was four weeks to two years in the independent trials and four weeks to three years in the sponsored trials. Two studies used glucosamine hydrochloride,^{5,6} one used both salts,⁸ and the other trials used glucosamine sulphate. The dose of glucosamine salt was 1,500 mg daily in all trials.

Patients in all studies had OA of the knee, except one of OA of the hip,¹⁷ and one in which multiple sites were involved.¹¹ In one study, only previous responders to glucosamine were included.⁴ Patients' mean ages in the studies ranged from 51 to 66 years, and 48 to 91% were female, except in one study, in which 95% of patients were male.¹⁰

In most studies the main outcomes included a measure of pain, such as the pain subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), a pain diary, pain medication use, or visual analogue or unspecified scales. Other commonly used measures were the WOMAC total score (including subscales indicating function and stiffness in addition to pain), the multidimensional Lequesne index, joint tenderness, swelling or stiffness, and global ratings of improvement by physicians or patients. Quality of trial design ranged widely across the studies.

Placebo-controlled studies

None of the six independent trials showed any differences between glucosamine- and placebo-treated groups in primary outcome measures of pain.^{4-6,8,10,17,19,20} One study reported a significant difference between glucosamine hydrochloride and placebo for a secondary outcome, a daily pain diary.⁶

Of the eight manufacturer-supported placebo-controlled studies, all studies except one reported significant differences between glucosamine (all sulphate) and placebo groups in measures of pain, including changes from baseline and absolute values

on the Lequesne questionnaire, WOMAC index, and visual analogue pain scales.^{9,11-16,18} One study showed no effect using a number of different scales including the WOMAC and McGill pain questionnaire.⁷

Few significant differences were reported for the other outcomes in the independent studies, including the incidence of disease flares, analgesic use, stiffness, function, WOMAC total score, and investigator's and patient's global improvement scales. In the sponsored studies, significant differences were reported for most outcomes in most of the studies.

Comparisons with ibuprofen

Glucosamine sulphate was compared with ibuprofen in three RCTs.¹⁸⁻²⁰ The number of patients ranged from 40 to 200 treated for four or eight weeks. Two of the studies (one sponsored and one independent) found that there was no significant difference in the number of responders (Lequesne index) or degree of knee pain (0 to 3 scale) between the two drugs.^{18,19} The third study (independent) found that glucosamine was significantly more effective than ibuprofen as indicated by the score for articular pain.²⁰

Adverse effects

In general, the tolerability of glucosamine was found to be good in the trials, with no reports of differences in the number of reported adverse events or withdrawal rates between glucosamine-treated and placebo-treated groups. Mild gastro-intestinal tract adverse events were the most commonly reported. Glucosamine was found to be better tolerated than ibuprofen, with fewer withdrawals reported due to adverse events in one study (1% vs. 7%, $p < 0.05$)¹⁸ and fewer adverse events reported in another (6% vs. 16%).¹⁹

For additional information on adverse events, see the Summary of Product Characteristics (SPC).¹

Additional information

- The recommended dose for the licensed preparation is 625 mg twice daily.
- At current prices, one year's treatment with glucosamine hydrochloride (Alateris[®]) 1,250 mg per day costs £223.

References

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Launch date: June 2007

Manufacturer: William Ransom & Son plc

PL 25081/0001

WARNING: This sheet should be read in conjunction with the Summary of Product Characteristics

This guidance is based upon the published information available in English at the time the drug was considered. It remains open to review in the event of significant new evidence emerging.

MTRAC can be contacted at the Dept. of Medicines Management, School of Pharmacy, Keele University, Keele, Staffs ST5 5BG
Tel: 01782 584131 Fax: 01782 713586 Email: mtrac@keele.ac.uk Web: www.mtrac.co.uk

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