Glucosamine for osteoarthritis

Background
Glucosamine is an amino monosaccharide. The rationale for its use in osteoarthritis (OA) is that it is a precursor for glycosaminoglycans, and glycoproteins which are a major component of joint cartilage and synovial fluid. Commonly sold forms of glucosamine are glucosamine sulfate and glucosamine hydrochloride. It is available in the UK in over 50 different preparations (in strengths of 500mg, 750mg and 1500mg, as tablets, capsules and liquid formulations, and with or without chondroitin).

Prescription Status
The first prescription only glucosamine product to receive a marketing authorisation in the UK (launched October 2007) is a 625mg tablet of glucosamine hydrochloride branded Alateris™. Alateris is indicated for the relief of symptoms in mild to moderate OA of the knee. All other glucosamine preparations are unlicensed.

Although glucosamine (as Alateris™) is now available as a UK licensed preparation Alateris™ is non-formulary in Gwent and is not recommended by NICE.

NICE Guideline CG59 (February 2008)
Osteoarthritis the care and management of osteoarthritis in adults
http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11926
1.3.6.1 The use of glucosamine or chondroitin products is not recommended for the treatment of osteoarthritis.

The Gwent Partnership Medicines & Therapeutics Committee therefore advise -

- Practitioners in Gwent should not prescribe any glucosamine (or chondroitin) preparation.
- Patients currently being prescribed glucosamine (or chondroitin) should be reviewed in the light of NICE guidance.
- Those patients expressing a desire to try (or continue taking) glucosamine should be advised:
  - To buy it over the counter using a brand of glucosamine sulfate manufactured in accordance with current UK Good Manufacturing Practice (GMP) standards.
  - To use it in OA of the knee only (see From evidence to recommendations overleaf).
  - That a single daily dose of 1500mg has the most favourable evidence.
  - How to perform their own trial of therapy, that is, to evaluate their pain before starting glucosamine and ensure they review the benefits of glucosamine after three months.
Cost
The dose of Alateris™ is 2 tablets once a day and the cost of 60 tablets is £18.40. This is more costly than the Valupak brand of glucosamine sulfate tablets 500mg (currently the most widely dispensed glucosamine preparation in Gwent):

<table>
<thead>
<tr>
<th>Qty. x strength</th>
<th>Retail</th>
<th>Annual retail cost of 1500mg daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 x 1500mg</td>
<td>£4.99</td>
<td>£61</td>
</tr>
<tr>
<td>30 x 500mg</td>
<td>£1.49</td>
<td>£54</td>
</tr>
<tr>
<td>90 x 500mg</td>
<td>£3.99</td>
<td>£49</td>
</tr>
</tbody>
</table>

(Chemist & Druggist list price January 2007)

Evidence

6.6.6 From evidence to recommendations

“The evidence from these studies is often difficult to compare due to differences between the products employed (and their bioavailability), between the study populations, patient BMI, and the use of analgesia at the time of pain and function assessment in the trials. Overall, those trials which used glucosamine sulfate as a single dose of 1500 mg, rather than hydrochloride 500 mg tds, showed a small benefit over placebo for treatment of knee OA. However, at the time of writing, the hydrochloride preparation has been granted a European Medicines Evaluatory Agency licence, while the sulfate has not. The evidence for efficacy of chondroitin was less convincing.

Evidence to support the efficacy of glucosamine hydrochloride as a symptom modifier is poor. For the non-licensed product (glucosamine sulfate), the evidence is not strong enough to warrant recommending that it should be prescribed on the NHS. Notwithstanding some evidence of benefit and very little evidence of harm in clinical practice, and despite the extra scrutiny these agents have received, the economic cost-consequence table (see Appendix C, online at http://www.rcplondon.ac.uk/pubs/brochure.aspx?e=242) shows that only glucosamine sulphate is potentially cost effective out of the interventions considered in this section. There are a wide range of incremental cost-effectiveness ratios (ICERs) reported and the poorest estimates of efficacy would take it beyond the threshold of affordability in the NHS. Because only one glucosamine hydrochloride product is licensed, it would not be cost effective to prescribe glucosamine on the NHS.

In assessing the outcomes given in the evidence base, the GDG regarded measurement of joint space narrowing as of questionable value in assessing any potential beneficial structural modification, and convincing evidence of improvement in patient-centred outcomes consequent on any structural modification is still lacking. There is therefore no positive recommendation regarding structure modification.

Many people with osteoarthritis take over-the-counter nutriceutical products and may benefit from clear, evidence-based information. This is reinforced in the recommendation in section 5.1. In particular, the GDG felt that it would be beneficial to advise people who wanted to trial over-the-counter glucosamine that the only potential benefits identified in early research are purely related to a reduction of pain (to some people, and to only mild or modest degree) with glucosamine sulfate 1500 mg daily. They could also benefit from advice on how to perform their own trial of therapy, that is, to evaluate their pain before starting glucosamine and ensure they review the benefits of glucosamine after three months.”

section 5.1 (page 35-46):
RECOMMENDATION
R7 Healthcare professionals should offer accurate verbal and written information to all people with osteoarthritis to enhance understanding of the condition and its management, and to counter misconceptions, such as that it inevitably progresses and cannot be treated. Information sharing should be an ongoing, integral part of the management plan rather than a single event at time of presentation.

† The Rottapharm brand of glucosamine sulphate (Dona™ - http://www.donausa.com) has the most favourable evidence base but is currently not marketed in the UK.