Formulary decision guide: Alendronic acid 70 mg/100 ml oral solution

Guidelines in practice

Product current status:			
Product proposed status:			
Date of next meeting:			
Decision:	**Yes**		**No**
Restricted use:			

Drug name

Alendronic acid 70 mg/100 ml oral solution (91.35 mg sodium alendronate trihydrate)

Indication

- Alendronic acid 70 mg oral solution is indicated for the treatment of post-menopausal osteoporosis.[1]

Place in treatment

- Alendronic acid oral solution can be used by patients unable/unwilling to swallow alendronic acid tablets
- The patented liquid formulation is designed to overcome difficulties encountered with swallowing traditional bisphosphonate tablets.[2]

Dosage

- Alendronic acid liquid is pleasant and easy to swallow and may aid compliance, avoiding the need to change to more expensive treatments or the cost of hospitalisation following osteoporotic fractures
- Please refer to the SPC,[1] at **www.medicines.org.uk/emc/**, for additional recommendations.

Mode of action

- Alendronic acid (as sodium alendronate trihydrate) is a bisphosphonate that inhibits osteoclastic bone resorption with no direct effect on bone formation[1]
- Preclinical studies have shown preferential localisation of alendronate to sites of active resorption. Activity of osteoclasts is inhibited, but recruitment or attachment of osteoclasts is not affected.[1]

Guideline recommendations

- Generic alendronate, which has a broad spectrum of anti-fracture efficacy, is recommended by NICE and NOGG as first-line treatment for prevention of osteoporotic fractures in women with confirmed osteoporosis[3–5]
- The NICE quality standard recommends that people with hip fracture are offered a bone health assessment to identify future fracture risk and are offered pharmacological intervention as needed before discharge from hospital.[6]

Evidence for use

- Osteoporosis remains a leading cause of morbidity, placing significant burdens on healthcare resources[7]
- It was estimated in 2006 that 3 million people in the UK had osteoporosis and that an osteoporotic fracture would occur every 3 minutes[8]
- In one study, almost 60% of patients aged >60 years experienced some difficulty swallowing solid-dose medication.[9]

Costs of osteoporosis care

- Osteoporotic fractures are estimated to cost the UK around £2 billion per year,[10] and result in over 2 million bed days a year—more than diabetes, ischaemic heart disease, and COPD[11]
- The economic burden of osteoporosis-related fractures includes not only the primary acute hospital costs, but also post-acute social-care costs and additional use of healthcare services:[8]
  - 25%–30% of patients who suffer a hip fracture will die within 12 months
  - 30% will require full-time care
  - 95% will require reparative surgery
- The cost of liquid alendronic acid equates to the branded weekly tablet.[12]

Quality and outcomes framework

- Achievement of the QOF indicators in management of osteoporosis requires that a register of patients includes:[13]
  - the percentage of patients aged between 50 and 74 years, with a fragility fracture, in whom osteoporosis is confirmed on DXA scan, and who are currently treated with an appropriate bone-sparing agent
  - the percentage of patients aged 75 years and over with a fragility fracture, who are currently treated with an appropriate bone-sparing agent.

Contraindications

- Abnormalities of the oesophagus and other factors that delay oesophageal emptying, e.g. stricture or achalasia
- Inability to stand or sit upright for at least 30 minutes
- Hypersensitivity to alendronic acid or to any excipients
- Hypocalcaemia
- Patients who have difficulty swallowing liquids
- Patients at risk of aspiration.

SPC=summary of product characteristics; NICE=National Institute for Health and Clinical Excellence; NOGG=National Osteoporosis Guideline Group; COPD=chronic obstructive pulmonary disease; DXA=dual energy X-ray absorptiometry

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Key points

- Patients who become non-adherent may benefit from liquid alendronic acid
- The most frequently reported side-effects of taking oral bisphosphonate tablets are gastrointestinal disturbances; e.g. abdominal pain, dyspepsia, acid regurgitation, oesophageal ulcer, and dysphagia[1]
- Both mobile and bedridden patients will not obtain the clinical benefits of treatment if they are unable to swallow tablets and so become non-adherent[11]
- Alendronic acid solution reaches the site of absorption quickly.[2]

Precautions and common side-effects

- Please refer to the SPC[1] at **www.medicines.org.uk/emc/**

References

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13. British Medical Association. NHS Employers. *Quality and outcomes framework guidance for GMS contract 2012/13*. London: BMA, NHS Employers, 2012. Available at: www.bma.org.uk/employmentandcontracts/independent_contractors/quality_outcomes_framework/qofchanges2012.jsp#.T3WeP5jrGCF

Alendronic Acid 70 mg/100 ml oral solution

Abbreviated Prescribing Information: Alendronic Acid 70mg/100ml Oral Solution. Consult Summary of Product Characteristics before prescribing. Presentation: Orange coloured opalescent solution containing 70mg alendronic acid (as 91.35mg sodium alendronate trihydrate) in each 100ml bottle. **Therapeutic Indications**: Treatment of post-menopausal osteoporosis. Alendronic acid reduces the risk of vertebral and hip fractures. **Posology:** For oral administration. Adults and Elderly: One 70mg unit-dose (100 ml) once weekly. It must be taken at least 30 minutes before the first food, beverage, or medicinal product of the day followed by at least 30ml of plain water only. Patients should not lie down for 30 minutes after taking Alendronic acid and should not take at bedtime or before arising for the day. Patients should receive supplemental calcium and vitamin D if dietary intake is inadequate. Use in renal impairment: No dosage adjustment is necessary in patients with a glomerular filtration rate (GFR) greater than 35 ml/min. Alendronic acid is not recommended for patients with impaired renal function where GFR is less than 35 ml/min. Use in children: There is insufficient data to support its use in children. **Contra-indications**: Abnormalities of the oesophagus and other factors which delay oesophageal emptying such as stricture or achalasia, inability to stand or sit upright for at least 30 minutes, hypersensitivity to alendronic acid or to any of the excipients, hypocalcaemia, patients who have difficulty swallowing liquids, patients at risk of aspiration. **Precautions:** Alendronic Acid can cause local irritation of the upper gastro-intestinal mucosa. Because there is a potential for worsening of the underlying disease, caution should be used when Alendronic Acid is given to patients with active upper gastro-intestinal problems, such as dysphagia, oesophageal disease, gastritis, duodenitis, ulcers, or with a recent history (within the previous year) of major gastro-intestinal disease. In patients with known Barrett's oesophagus, the benefits and potential risks should be considered on an individual patient basis. Oesophageal reactions have been reported in patients receiving alendronic acid. Patients should be instructed to discontinue alendronic acid and seek medical attention if they develop symptoms of oesophageal irritation such as dysphagia, pain on swallowing or retrosternal pain, new or worsening heartburn. There have been rare reports of gastric and duodenal ulcers, some severe and with complications. Osteonecrosis of the jaw, generally associated with tooth extraction and/or local infection, has been reported in patients with cancer receiving treatment regimens including primarily intravenously administered bisphosphonates. Many of these patients were also receiving chemotherapy and corticosteroids. Osteonecrosis of the jaw has also been reported in patients with osteoporosis receiving oral bisphosphonates. A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors. While on treatment, these patients should avoid invasive dental procedures if possible. Clinical judgement of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment. Bone, joint, and/or muscle pain has been reported in patients taking bisphosphonates. Stress fractures of the proximal femoral shaft have been reported in patients treated long-term with alendronic acid. Poor healing of these fractures was also reported. Discontinuation of bisphosphonate therapy in patients with stress fracture is advisable pending evaluation of the patient, based on individual benefit risk assessment. Patients should be instructed that if they miss a dose of Alendronic Acid 70 mg Oral Solution, they should take one single unit-dose (100 ml) on the morning after they remember. They should not take doses on the same day but should return to taking one unit-dose once a week, as originally scheduled on their chosen day. Hypocalcaemia must be corrected before initiating therapy with alendronic acid. Other disorders affecting mineral metabolism should also be effectively treated. In patients with these conditions, serum calcium and symptoms of hypocalcaemia should be monitored during therapy. There have been rare reports of symptomatic hypocalcaemia, which have occasionally been severe and often occurred in patients with predisposing conditions. Ensuring adequate calcium and vitamin D intake is particularly important in patients receiving glucocorticoids. This medicinal product contains 0.15 % volume ethanol. Harmful for those suffering from alcoholism. To be taken into account in high-risk groups such as patients with liver disease, or epilepsy. Excipient warnings: contains sunset yellow (E110) methyl and propyl parahydroxybenzoates (E218, E216) that may cause allergic reactions. **Interactions**: Patients must wait at least 30 minutes after taking alendronic acid before taking any other oral medicinal product. No other interactions with medicinal products of clinical significance are anticipated. Since NSAID use is associated with gastrointestinal irritation, caution should be used during concomitant use with alendronate. In clinical studies alendronic acid was used concomitantly with a wide range of commonly prescribed medicinal products without evidence of clinical adverse interactions. **Pregnancy and Lactation**: Alendronic acid should not be used during pregnancy. It is not known whether alendronate is excreted into human breast milk so alendronic acid should not be used by breast-feeding women. **Effects on Ability to Drive and Use Machines**: Certain adverse reactions that have been reported with alendronic acid may affect some patients' ability to drive or operate machinery. **Undesirable Effects**: Hypersensitivity reactions, symptomatic hypocalcaemia, headache, dysgeusia, uveitis, scleritis, episcleritis, abdominal pain, dyspepsia, constipation, diarrhoea, flatulence, oesophageal ulcer, dysphagia, abdominal distension, acid regurgitation, nausea, vomiting, gastritis, oesophagitis, oesophageal erosions, melena, oesophageal stricture, oropharyngeal ulceration, upper gastrointestinal PUBs (perforation, ulcers, bleeding,) rash, pruritus, erythema, alopecia, rash with photosensitivity, severe skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis, musculoskeletal pain, osteonecrosis of the jaw has been reported, transient symptoms as in an acute-phase response (myalgia, malaise and rarely, fever), typically in association with initiation of treatment, dizziness, vertigo, joint swelling, stress fractures, asthenia, peripheral oedema, asymptomatic, mild and transient decreases in serum calcium and phosphate. **Overdose**: No specific information is available on the treatment of overdosage with alendronic acid. Milk or antacids should be given to bind alendronic acid. Owing to the risk of oesophageal irritation, vomiting should not be induced and the patient should remain fully upright. Shelf Life and Storage: **2 years, store below 25°C**. Legal Category: POM. Pack size and Price: **4x100mls - £22.80**. Marketing Authorisation Holder: **Xeolas Pharmaceuticals Ltd., 97 Furry Park Road, Dublin 5, Ireland**. Date of Preparation: **November 2010**. **Further information is available on request from Rosemont Pharmaceuticals Ltd., Rosemont Pharmaceuticals Ltd., Rosemont House, Yorkdale Industrial Park, Braithwaite Street, Leeds LS11 9XE on Tel 0113 244 1999**.

Adverse events should be reported.
Reporting forms and information can be found at yellowcard.mhra.gov.uk. Adverse events should also be reported to Rosemont Pharmaceuticals Ltd on 0113 244 1400.