

**South East London Integrated Medicines Optimisation Committee
Formulary recommendation**

Reference	165
Intervention:	Zoledronic acid 4 mg/100 ml solution for infusion for the primary and secondary prevention of fragility fractures and for osteoporosis in men and postmenopausal women with impaired renal function (off-label use) (Zoledronic acid is a third-generation bisphosphonate)
Date of Decision	January 2026
Date of Issue:	February 2026
Recommendation:	RED – suitable for prescribing, supply and administration by hospital only
Further Information	<ul style="list-style-type: none"> • Zoledronic acid 4 mg/100 ml solution for infusion is accepted for use in South East London (SEL) in patients with a creatinine clearance (CrCl) 30-35ml/min or in some cases eGFR >30ml/min, in the following settings in adults: <ul style="list-style-type: none"> (i) As an 18 monthly infusion in patients, for the following indications: <ul style="list-style-type: none"> ○ Primary and secondary prevention of fragility fracture, OR ○ First line treatment for secondary prevention of a fragility fracture (ii) As a single dose for osteoporosis in men aged 50 years or older and postmenopausal women post fracture, with a limited life expectancy of 6 -12 months. In selected patients in this cohort, a single dose may be given if the CrCl is under 30ml/min and the estimated glomerular filtration rate (eGFR) is over 30ml/min/1.73m². This will be determined by the specialist on a case-by-case basis. • Zoledronic acid is available in two strengths: 4 mg and 5 mg, each with distinct indications and dosing schedules. It is only the 4 mg strength that has been accepted for use in this setting. • The use of zoledronic acid 4mg/100 mL solution for infusion in this setting is off-label*. The off-label nature should be explained to the patient/carer and informed consent gained. • The infusion should be administered in line with local Trust guidelines and protocols, incorporating management of risks in this patient cohort including appropriate hydration. • The Medicines and Healthcare products Regulatory Agency (MHRA) have outlined precautions that should be taken into account to minimise the risk of renal adverse reactions with zoledronic acid, see the Drug Safety Update for further information. • An update to the current SEL osteoporosis treatment pathway is underway to reflect this formulary approval. <p style="font-size: small; margin-top: 10px;">*Zoledronic acid 4 mg/100 ml solution for infusion is licensed for the prevention of skeletal related events in adult patients with advanced malignancies involving bone and the treatment of adult patients with tumour-induced hypercalcaemia</p>
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	<ul style="list-style-type: none"> • The application estimates that approximately 155 patients per annum in SEL will be eligible for treatment with zoledronic acid in this setting. • The total estimated cost for SEL is ~ £90,000 per annum (or ~£4,300 per 100,000 population). This cost is inclusive of service delivery costs. The drug cost impact is expected to be negligible.
Usage Monitoring & Impact Assessment	<p>Acute Trusts:</p> <ul style="list-style-type: none"> • Monitor and audit usage as agreed and report back to the Committee (against this recommendation) upon request of the Committee <hr/> <p>SEL Borough Medicines Teams:</p> <ul style="list-style-type: none"> • Monitor exception reports from GPs if inappropriate prescribing requests are made to primary care

Evidence reviewed	References (from evidence review)
	<ol style="list-style-type: none"> 1. Boonen S, Eastell R, Su G et al. Time to onset of antifracture efficacy and year-by-year persistence of effect of zoledronic acid in women with osteoporosis. <i>J Bone Miner Research</i> 2012; 27: 1487–93. [PMC free article] [PubMed] [Google Scholar] 2. Lyles KW, Colón-Emeric CS, Magaziner JS et al. Zoledronic acid and clinical fractures and mortality after hip fracture. <i>N Engl J Med</i> 2007; 357: 1799–1809 [PMC free article] [PubMed] [Google Scholar] 3. Cipriani C, Pepe J, Clementelli C et al. Effect of a single intravenous zoledronic acid administration on biomarkers of acute kidney injury (AKI) in patients with osteoporosis: a pilot study. <i>Br J Clin Pharmacol</i> 0217 83: 2266–73. [PMC free article] [PubMed] [Google Scholar] 4. Fixen CW, Fixen DR R. Renal safety of zoledronic acid for osteoporosis in adults 75 years and older. <i>Osteoporos Int</i> 2022; 33: 2417–22. [PubMed] [Google Scholar] 5. Johansen A, Sahota O, Dockery F, Black AJ, MacLulich AMJ, Javaid MK, Ahern E, Gregson CL. Call to action: a five nations consensus on the use of intravenous zoledronate after hip fracture. <i>Age Ageing</i>. 2023 Sep 1;52(9):afad172. Doi: 10.1093/ageing/afad172. Erratum in: <i>Age Ageing</i>. 2024 Jan 2;53(1): PMID: 37776543; PMCID: PMC10542103 6. Sahota A, Barbary R, Cameron M, Stewart AM, Sahota O. Safety of zoledronate in older patients at high risk of fracture with reduced renal function. <i>Osteoporos Int</i> 2022; 33: 1823–4. [PubMed] [Google Scholar] 7. Rosen LS, Gordon D, Kaminski M et al. Zoledronic acid versus pamidronate in the treatment of skeletal metastases in patients with breast cancer or osteolytic lesions of multiple myeloma: a phase III, double-blind, comparative trial. <i>Cancer J</i> 2001; 7: 377–87. [PubMed] [Google Scholar] 8. Saad F, Gleason DM, Murray R et al. A randomized, placebo-controlled trial of zoledronic acid in patients with hormone-refractory metastatic prostate carcinoma. <i>J Natl Cancer Inst</i> 2002; 94: 1458–68. [PubMed] [Google Scholar] 9. Osteoporosis Treatment Pathway. South East London. December 2023. Available at: https://www.selondonics.org/wp-content/uploads/dlm_uploads/SEL-OSTEOPOROSIS-PATHWAY-Final-December-2023.pdf 10. Management of osteoporosis and the prevention of fragility fractures. SIGN national clinical guidance 142. Revised January 2021. Available at: https://www.sign.ac.uk/media/1812/sign-142-osteoporosis-v3.pdf 11. Wang, Huan & Liu, Qi & Jiang, Muhan & Song, Chun-Li & Liu, Dongyang. (2023). Optimization of the dosage regimen of zoledronic acid with a kinetic-pharmacodynamic model and exposure-response analysis. <i>Frontiers in Pharmacology</i>. 14. 10.3389/fphar.2023.1089774. 12. Durgia H, Kamalanathan S, Ramkumar G, Sarkar S, Reddy SVB, Sahoo J, Palui R, Raj H. Effect of 2 mg Versus 4 mg of Intravenous Zoledronic Acid on Bone Mineral Density at the Lumbar Spine in Indian Postmenopausal Women with Osteoporosis: A Double-blind Parallel-arm Randomized Controlled Trial. <i>J Res Pharm Pract</i>. 2021 Aug 3;10(2):71-77. doi: 10.4103/jrpp.JRPP_20_130. PMID: 34527611; PMCID: PMC8420937. 13. Schini M, Peel N, Toronjo-Urquiza L, Thomas E, Salam S, Khwaja A, Eastell R, Walsh JS. Evaluation of estimated glomerular function (eGFR) versus creatinine clearance (CrCl) to predict acute kidney injury when using zoledronate for the treatment of osteoporosis. <i>Osteoporos Int</i>. 2022 Mar;33(3):737-744. doi: 10.1007/s00198-021-06160-6. Epub 2021 Oct 15. PMID: 34654939. 14. Paul D. Miller, The kidney and bisphosphonates, <i>Bone</i>, Volume 49, Issue 1, 2011, Pages 77-81, ISSN 8756-3282, https://doi.org/10.1016/j.bone.2010.12.024. (https://www.sciencedirect.com/science/article/pii/S8756328210021381)

NOTES:

- a) SEL IMOC recommendations and minutes are available publicly via the [website](#).
- b) This SEL IMOC recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.
- c) **Not to be used for commercial or marketing purposes. Strictly for use within the NHS**