Guideline for the use of intravenous zoledronate following hip fracture within trauma and orthopaedic unit	University Hospitals of Leicester NHS NHS Trust Trust Reference C61/2024

1.Introduction and Who Guideline applies to

This guidelines applies to patients admitted to the trauma and orthopaedic unit who have sustained a fragility (low trauma) hip fracture. All fragility fracture patients require a bone health assessment and a management plan to reduce future fracture risk.

Zoledronate is established as an effective treatment for post menopausal osteoporosis in women and men at increased risk of fracture, including those with a recent low-trauma hip fracture . Zoledronic acid has been shown to reduce the incidence of vertebral, non-vertebral and hip fractures in postmenopausal women with osteoporosis (Black *et al* 2007) and to reduce the risk of clinical fracture and attendant mortality when given to patients shortly after their first hip fracture (Lyles et al 2007). Approval for its use in men with osteoporosis and postmenopausal women and men taking glucocorticoids was granted on the basis of BMD bridging studies (Boonen *et al* 2012, Reid *et al* 2009). The National Osteoporosis Group Guidelines (NOGG) have now recommended it be considered as a first line option following hip fracture (Ref1).

Zoledronate (also known as Zoledronic acid) belongs to the class of nitrogen-containing bisphosphonates and acts primarily on bone. It is an inhibitor of osteoclast-mediated bone resorption.

2. Guideline Standards and Procedures

This section may include or comprise a flow chart but in any event should be set out in a logical order.

This protocol will provide clinical staff with guidelines which will enable the safe and appropriate administration of IV Zoledronate. Doctors experienced in the management of osteoporosis will consider the appropriateness of use and trained nurses will administer this drug.

Patients in hospital with a hip fracture who have this treatment prescribed:

1. Will have been reviewed by the orthogeriatric team to assess its suitability.
2. Have received verbal and written information (ROS leaflet and A4 Blue Apr 2019 (leicestershospitals.nhs.uk))
3. Bloods tests reviewed (Renal function, calcium, phosphate, alkaline phosphate, 25-OH Vitamin D levels and Creatinine Clearance using Cockcroft Gault equation)
4. Dental assessment including any dental pain or planned dental extractions/implants. Advise on good dental hygiene.

This treatment can be given as an annual (or 18-monthly) infusion for osteoporosis. Many patients with hip fracture are frail and have significant co morbidity with limited life expectancy. In this group a single dose of 5mg IV zoledronate may be an appropriate treatment for osteoporosis management.

Preadministration checks

1. Serum adjusted calcium and correction of hypocalcaemia prior to administration http://insitetogether.xuhl-tr.nhs.uk/pag/pagdocuments/Hypocalcaemia%20UHL%20Guideline.pdf

2. Vitamin D status and replacement of deficiency via a rapid loading regime

If **Vitamin D** is < 50 nmol/l then this should be replaced **before** administration of IV zoledronate in patients who have sustained a fragility hip fracture

- Load with colecalciferol 40 000 units orally daily for 7 days (use 20 000unit oral capsules)

If swallowing difficulties/unable to tolerate:

- Load with colecalciferol 50 000 units orally daily for 6 days (use 25 000unit oral ampoules)

3. Renal function and calculation of creatinine clearance. A creatinine clearance of > 35ml/min is safe for the administration of IV zoledronate.
4. If the patient has a **creatinine clearance 30 - 35ml/min** (using the Cockcroft-Gault Equation) it can be considered after discussion with patient and/or family about risks and benefits. If decision to proceed consider giving the infusion at a slower rate, omitting diuretics on the day of infusion and additiona fluids pre infusion.
5. Intravenous zoledronate can cause an acute phase reaction and should not be given in an patient with intercurrent illness/active infection.

Contraindications

IV zoledronate is contraindicated for patients with:

- Hypersensitivity to the active substance or to any of the excipients or to any bisphosphonates
- Hypocalcaemia: requires correction
- Vitamin D deficiency: requires replacement regime
- Creatinine clearance < 30ml/min calculated using cockroft equation and careful consideration in those with a creatinine clearance between 30-35 ml/min.
- During pregnancy and in breast-feeding women
- Osteonecrosis of the jaw
- Awaiting dental work

Side effects

Common side effects may include: Flu-like symptoms, headache, nausea, vomiting, diarrhoea, joint, bone, or muscle pain.

Precautions and considerations

- Ensure patients are well hydrated. Consider omitting diuretic on day of administration. Additional intravenous fluid Nsaline 250mls IV to be prescribed prior to infusion following a review of fluid balance by prescribing doctor.
- Do not give if signs of acute or ongoing infection
- Ensure paracetamol 500 mg -1000 mg is prescribed to reduce flu like side effect profile/effects of acute phase reaction.

Administration

- Aseptic techniques must be followed during the preparation of the infusion
- 5mg IV zoledronate in 100mls Normal Saline is administered via a vented infusion line at a rate no faster than 15 minutes
- After the infusion the line must be flushed with 10mls of sodium chloride 0.9%.

Monitoring

- The patient must be observed for any adverse reactions during the infusion

- Record baseline blood pressure, pulse, and temperature and oxygen saturation prior to the infusion and if the patient becomes unwell or experiences an adverse reaction

Follow up

Maintenance treatment

All inpatients with a Fractured Neck of Femur resulting from a fall from standing height or less should be prescribed combined Calcium and Vitamin D (Evacal D3® or Theical-D3®) unless osteoporosis has been excluded or some other cause for fragility fracture has been identified. Exception: patients with hypercalcaemia or hypocalcaemia. Theical D3 1 tablet od is a first line choice in LLR.

Routine monitoring of plasma 25(OH) D is unnecessary but may be appropriate in patients with symptomatic vitamin D deficiency or in situations where malabsorption or poor compliance with medication is suspected or in patients taking antiresorptive therapy who have extremely low levels at baseline assessment

- Document administration of iv zoledronate on the patients discharge letter
- Recommend calcium to be rechecked one month after treatment for unmasked primary hyperparathyroidism
- Send letter to patient and GP confirming indication given, follow up plans and routine advice whilst on treatment

3. Education and Training

None required

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements

5. Supporting References (maximum of 3)

1. Gregson CL, Compston JE. New national osteoporosis guidance—implications for geriatricians. Age Ageing 2022; 51:1– 6. https://doi.org/10.1093/ageing/afac044.

2.The National Osteoporosis Guideline Group. NOGG. Clini cal guideline for the prevention and treatment of osteoporosis. 2021; 24–8. www.nogg.org.uk

3. 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. Osteoporos Int 2022; 33: 1823–4. 24.

6. Key Words

Fragility Hip fracture

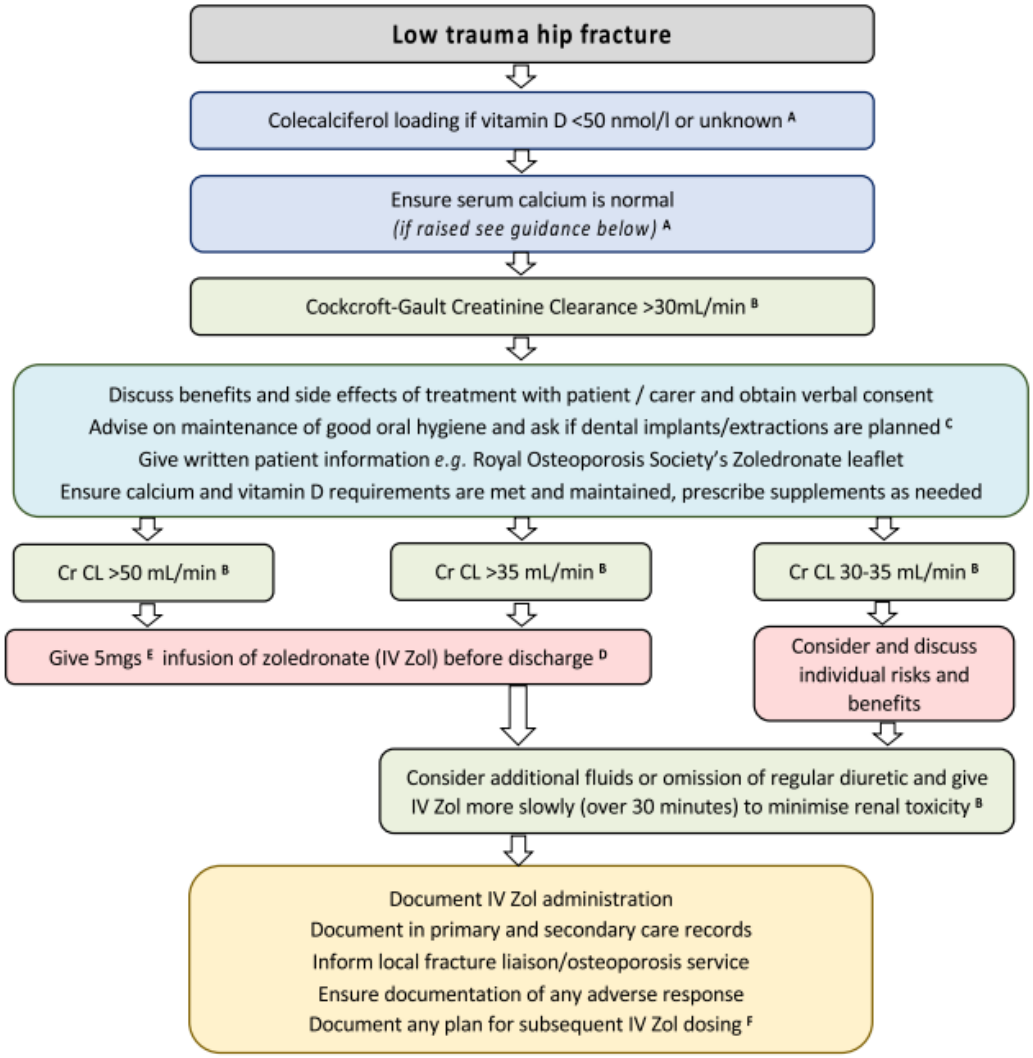
Osteoporosis

Zoledronate

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) **N Morgan/I Musa /C Atkin**	**Executive Lead**
Details of Changes made during review:	

Appendix 1 from consensus document see references

A. Johansen *et al.*



Appendix 2

Flow chart for use quick guide

Administration of IV Zoledronate quick guide

University Hospitals of Leicester NHS