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NHS Foundation Trust

Guidelines For Prescribing And Administering Teriparatide (Forsteo ®) For The Treatment of Osteoporosis

CATEGORY:	Guidelines
CLASSIFICATION:	Clinical
PURPOSE	This guideline outlines the responsibilities for prescribing and administering Teriparatide (Forsteo ®) for the treatment of osteoporosis in postmenopausal women at increased risk of fractures.
Controlled Document Number:	**CG260**
Version Number:	2
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Approved By:	Clinical Guidelines Group
On:	December 2016
Review Date:	December 2019
Distribution: • **Essential Reading for:** • **Information for:**	• Essential reading for: All clinicians in metabolic bone clinic. • Information for: clinicians in rheumatology and elderly care.

Quick Guide: Guidelines For Prescribing And Administering Teriparatide

Patient Pathway

Patient Requiring Teriparatide (Forsteo ®) Injection

Patient requiring teriparatide (Forsteo ®) Treatment (Parathyroid Hormone Daily Subcutaneous Injection)

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Apply for Funding

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Funding Approved by CCG

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Refer to Endocrine CNS

- Contact patient to discuss the treatment (if not covered during the consultation) and discuss the process of commencing the treatment.
- Ensure that baseline bloods including bone turnover markers are done.
- Register patient to Home Service Provider within 5 working days of funding approval.
- Give patient all the relevant contact details.

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Home Service Provider

- To contact patient within 5 working days of receiving referral from UHB to arrange delivery of supplies.
- To arrange home visit and patient training on self-administration of Teriparatide injection within 10 working days of receiving the referral from UHB.
- To inform Endocrine Nurse, by email, of patient's treatment start date within 3 working days of commencement. This should include a copy of the Clinical Evaluation Report.
- To conduct telephone follow-up to check patient's concordance within 7 working days of patient commencing treatment.

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Follow-up Clinic Appointment (Nurse-Led Clinic)

- **2-4 weeks**
  - Telephone follow-up to check concordance.
  - Refer to Home Service Provider if patient requires further home visit/training.
- **2-3 months**
  - Nurse-Led clinic follow-up (BV9Q Clinic).
  - To check bone turn over markers, LTFs and bone profile.
  - Arrange follow-up review as below.

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Follow-up Clinic Appointments

- 12 months following commencement (NJ7Q or BV9Q Clinic)
- 22 months (NJ7Q Clinic only)

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1 INTRODUCTION

1.a) This guideline outlines the roles and responsibilities for managing the prescribing and administration of Teriparatide for the treatment of osteoporosis in postmenopausal women at increased risk of fractures.

1.b) This guideline relates only to treatment for secondary prevention of fragility fractures in postmenopausal women who have osteoporosis and have sustained a clinically apparent osteoporotic fragility fracture.

1.c) Osteoporosis is defined by a T-score of $\leq$ 2.5 standard deviations (SD) or below on dual-energy X-ray absorptiometry (DXA) scanning. It is a progressive, systemic skeletal disorder characterised by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture (NICE TA 161).

2 PHARMACEUTICAL FORM

2.a) Teriparatide (Forsteo ®) comes in a pre-filled pen of 2.4 ml containing 600 micrograms of teriparatide (corresponding to 250 micrograms per ml).

3 THERAPEUTIC INDICATION

The NICE technology appraisal (TA 161) states:

3.a) Teriparatide (Forsteo; Eli Lilly & Company) is a recombinant fragment of human parathyroid hormone and, as an anabolic agent it stimulates new formation of bone and increases resistance to fracture.

3.b) Teriparatide is recommended as an alternative treatment option for the secondary prevention of osteoporotic fragility fractures in postmenopausal women:

- who are unable to take alendronate and either risedronate or etidronate, or have a contraindication to or are intolerant of alendronate and either risedronate or etidronate, **or** who have a contraindication to, or are intolerant to strontium ranelate, **or** who have had an unsatisfactory response to treatment with alendronate, risedronate or etidronate **and;**
- who are 65 years or older and have a T-score of **-4.0 SD** or below, or a T-score of **-3.5 SD** or below plus more than two fractures, **or** who are aged 55-64 years and have a T-score of **-4.0 SD** or below plus more than two fractures.

4 POSOLOGY, DOSAGE AND METHOD OF ADMINISTRATION

4.a) The recommended dose of Teriparatide is 20 micrograms administered once daily by subcutaneous injection in the thigh or abdomen.

4.b) Patients must be trained to use the proper injection techniques (see section 6.6). A User Manual is also available to instruct patients on the correct use of the pen.

4.c) The maximum total duration of treatment with Teriparatide should be 24 months (see section 4.4). The 24-month course of Teriparatide should not be repeated over a patient's lifetime.
4.d) Patients should receive supplemental calcium and vitamin D supplements if dietary intake is inadequate.
4.e) Following cessation of Teriparatide therapy, patients may be continued on other osteoporosis therapies.
4.f) Use in renal impairment: Teriparatide should not be used in patients with severe renal impairment (see section 4.3). In patients with moderate renal impairment, Teriparatide should be used with caution.
4.g) Use in hepatic impairment: No data are available in patients with impaired hepatic function (see section 5.3).
4.h) Paediatric population and young adults with open epiphyses: There is no experience in paediatric patients (less than 18 years). Teriparatide should not be used in paediatric patients (less than 18 years), or young adults with open epiphyses. Elderly patients: Dosage adjustment based on age is not required.

5 **CONTRAINDICATIONS (**as per the 'Summary of Product Characteristic') http://www.medicines.org.uk/emc/medicine/12561/SPC/Forsteo+20+micrograms+80+microlitres+solution+for+injection+in+pre-filled+pen/

5.a) Hypersensitivity to the active substance or to any of the excipients.
5.b) Pregnancy and lactation.
5.c) Pre-existing hypercalcaemia (below the agreed local reference range).
5.d) Severe renal impairment.
5.e) Metabolic bone diseases (including hyperparathyroidism and Paget's disease of the bone) other than primary osteoporosis or glucocorticoid-induced osteoporosis.
5.f) Unexplained elevations of alkaline phosphatase.
5.g) Prior external beam or implant radiation therapy to the skeleton.
5.h) Patients with skeletal malignancies or bone metastases should be excluded from treatment with teriparatide.

6 SPECIAL WARNINGS AND PRECAUTION FOR USE
(as per the 'Summary of Product Characteristic') http://www.medicines.org.uk/emc/medicine/12561/SPC/Forsteo+20+micrograms+80+microlitres+solution+for+injection+in+pre-filled+pen/

6.a) In normocalcaemic patients, slight and transient elevations of serum calcium concentrations have been observed following teriparatide injection. Serum calcium concentrations reach a maximum between 4 and 6 hours and return to baseline by 16 to 24 hours after each dose of teriparatide. **Routine calcium monitoring during therapy is not required.**
6.b) If any blood samples are taken from a patient, this should be done at least 16 hours after the most recent Teriparatide injection.

6.c) Teriparatide may cause small increases in urinary calcium excretion, but the incidence of hypercalciuria did not differ from that in the placebo-treated patients in clinical trials.

6.d) Teriparatide has not been studied in patients with active urolithiasis. Teriparatide should be used with caution in patients with active or recent urolithiasis because of the potential to exacerbate this condition.

6.e) In short-term clinical studies with Teriparatide, isolated episodes of transient orthostatic hypotension were observed. Typically, an event began within 4 hours of dosing and spontaneously resolved within a few minutes to a few hours. When transient orthostatic hypotension occurred, it happened within the first several doses, was relieved by placing subjects in a reclining position, and did not preclude continued treatment.

6.f) Caution should be exercised in patients with moderate renal impairment.

6.g) Experience in the younger adult population, including premenopausal women, is limited. Treatment should only be initiated if the benefit clearly outweighs risks in this population.

7 UNDESIRABLE EFFECTS

7.a) The most commonly reported adverse reactions in patients treated with Teriparatide are nausea, pain in limb, headache and dizziness.

7.b) The undesirable reactions associated with the use of teriparatide in osteoporosis clinical trials and post-marketing exposure are summarised in the table below. The following convention has been used for the classification of the adverse reactions: very common (≥ 1/10), common (≥ 1/100 to <1/10), uncommon (≥ 1/1,000 to <1/100), rare (≥ 1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

7.c) Below are the detailed side effects as per the 'Summary of Product Characteristic' http://www.medicines.org.uk/emc/medicine/12561/SPC/Forsteo+20+micrograms+80+microlitres+solution+for+injection+in+pre-filled+pen/

Blood and lymphatic system disorders *Common*: Anaemia
Cardiac disorders *Common*: Palpitations *Uncommon*: Tachycardia
Ear and labyrinth disorders *Common*: Vertigo
Gastrointestinal disorders *Common*: Nausea, Vomiting, Hiatus hernia, Gastro-oesophageal reflux disease *Uncommon*: Haemorrhoids
General disorders and administration site conditions

Common: Fatigue, Chest pain, Asthenia, Mild and transient injection site events, including pain, swelling, erythema, localised bruising, pruritus and minor bleeding at injection site *Uncommon*: Injection site erythema, Injection site reaction *Rare*: Possible allergic events soon after injection: acute dyspnoea, oro/facial oedema, generalised urticaria, chest pain, oedema (mainly peripheral)
Investigations *Uncommon*: Weight increased, Cardiac murmur, Alkaline phosphatase increase
Metabolism and nutrition disorders *Common*: Hypercholesterolaemia *Uncommon*: Hypercalcaemia greater than 2.76 mmol/L, Hyperuricaemia *Rare*: Hypercalcaemia greater than 3.25 mmol/L
Musculoskeletal and connective tissue disorders *Very common*: Pain in limb *Common*: Muscle cramps *Uncommon*: Myalgia, Arthralgia, Back cramp/pain*
Nervous system disorders *Common*: Dizziness, Headache, Sciatica, Syncope
Psychiatric disorders *Common*: Depression
Renal and urinary disorders *Uncommon*: Urinary incontinence, Polyuria, Micturition urgency, Nephrolithiasis *Rare:* Renal failure/impairment
Respiratory, thoracic and mediastinal disorders *Common*: Dyspnoea *Uncommon:* Emphysema
Skin and subcutaneous tissue disorders *Common*: Sweating increased
Vascular disorders *Common*: Hypotension

8 STORAGE

8.a) Store in a refrigerator (2°C-8°C) at all times. The pen should be returned to the refrigerator immediately after use. Do not freeze.

8.b) Do not store the injection device with the needle attached. The needle should be removed immediately after use and discard appropriately in the sharp bin provided. The pen should be stored in the fridge with the pen cover immediately after use.

9 DISPOSAL AND HANDLING

9.a) Teriparatide is supplied in a pre-filled pen. Each pen should be used by only one patient. A new, sterile needle must be used for every injection. Each Teriparatide pack is provided with a User Manual that fully describes the use of the pen. No needles are supplied with the product. The device can be used with insulin pen injection needles. After each injection, the Teriparatide pen should be returned to the refrigerator.

9.b) Teriparatide should not be used if the solution is cloudy, coloured or contains particles.

9.c) Please also refer to the User Manual for instructions on how to use the pen.

10 RESPONSIBILITIES AND ROLES

10.a UHB Doctors/Specialist (Endocrinologists/Rheumatologists)

- To assess the suitability of the patient for Teriparatide (Forsteo ®) treatment following the current NICE Guidelines (NICE TA 161).
- To discuss with the patient the indication, mode of action, benefits and possible side effects of Teriparatide.
- To apply for funding from the respective CCG for Teriparatide Treatment (or advise the Clinical Nurse Specialist [CNS] to apply for funding).
- To prescribe Teriparatide on a 3-monthly basis to be delivered and supplied by a Home Service Provider (or advice the CNS to organise prescription on a 3-monthly basis).
- To ensure that baseline bloods (U/E, serum Calcium, serum Vitamin D and bone turn over makers) are done and reviewed prior to commencing the patient on Teriparatide treatment.
- To ensure that patient is supplemented with Calcium and/or Vitamin D if required.
- To advise patient to stop other osteoporosis treatment except Calcium and/or Vitamin D supplement if still required.
- To review the patient and the treatment at 12 and 22 months.
- To review patient at 22 months of treatment and assess the need for patient to have anti-resorptive agent immediately after completing the 2-year course of teriparatide.

10.b UHB Clinical Nurse Specialist- Endocrinology

- To apply for funding for Teriparatide treatment from respective CCG following a request from the consultant.
- To follow up funding application made for patient regarding Teriparatide treatment.
- Once funding is approved, to call patient and explain the process of initiating treatment. This telephone clinic should include discussion regarding the treatment ensuring that patient understand the indication, mode of action, benefits and possible side effects and method of administration of Teriparatide. If patient prefers a clinic consultation to discuss the treatment in detail, patient can be seen in the Nurse-Led clinic.
- Once funding is approved, to register patient to a Home Service Provider (BUPA) within 7 working days of funding approval. This should include sending all the relevant paperwork including valid prescription.
- To give patient relevant contact details of main key worker at UHB.
- To conduct telephone follow-up to check concordance and patient's response to treatment within 2-4 weeks of commencing treatment.
- To liaise closely with Home Service Provider ensuring that prescriptions are issued regularly and supplies are delivered to the patient efficiently.
- To request additional home visit from Home Service Provider as required by patient.
- To follow-up patient in the Nurse-Led clinic 2-3 months after commencing the treatment. This should include taking blood samples for bone turn over makers, U/E and LFTs.
- To arrange clinic follow-up appointment for review at 12 months following commencement of treatment (either in the nurse-led or consultant clinic) and at 22 months in the consultant's clinic.
- To immediately report any adverse events to the Consultant and arrange clinic review as soon as practical.
- To discuss with the Consultant any concerns pertaining to the treatment and/or patient's response to treatment.
- Following instruction from the consultant, discuss and arrange anti-resorptive treatment required following completion of patient's 2-year course of teriparatide. If anti-resorptive treatment is required, this should be arranged within 2 weeks of completing teriparatide treatment.

10.c Patient's role (or that of carer)

- Patient to immediately report any adverse events to the doctor or key worker at UHB.

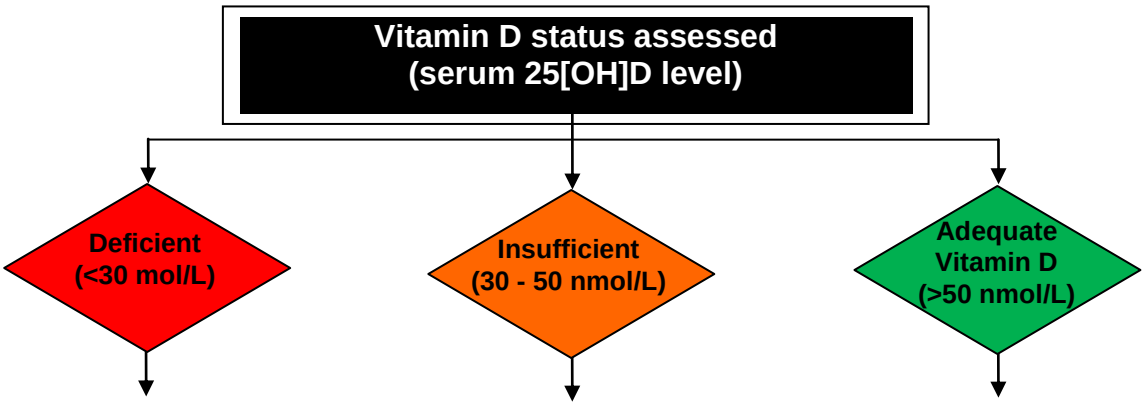
- Patient to immediately report any problem with the pen device and delivery of supplies to the home service provider and/or UHB specialist.
- Patient to consult the GP or secondary care specialist should their condition significantly worsen or they experience any adverse reactions.
- Patient to attend clinic follow-up appointment for review and blood test.
- Patient to keep a record of treatment (i.e. diary) ensuring that injection is administered regularly on a daily basis.

10.d Home Service Provider (BUPA)

- To acknowledge promptly the receipt of referral from UHB specialist to commence patient on Teriparatide. Acknowledgment should be made by email within 2 working days of receiving referral.
- To contact patient within 5 working days of receiving referral from UHB specialist to arrange delivery of supplies.
- To arrange home visit and patient training on self-administration of Teriparatide injection within 10 working days of receiving the referral from UHB specialist.
- To inform the Clinical Nurse Specialist (Endocrinology) at UHB of patient's treatment start date by email within 3 working days of commencement. This should include a copy of the Clinical Evaluation Report.
- To conduct telephone follow-up to check patient's concordance within 3 working days of patient commencing Teriparatide treatment.
- To send request of prescription at least 2 weeks before the patient is due for next delivery.
- To inform UHB specialist of any issue concerning patient, treatment, prescription, concordance and supplies as soon as possible.

11 Vitamin D Supplementation

- Below is the recommended regimes for correction of Vitamin D deficiency with colecalciferol in patients commencing or receiving active bone metabolism drug



- Commence patient on pharmacological strength vitamin D.
  a. **<u>Loading dose:</u> Colecalciferol 40000 - 50000IU weekly for 6 - 7 weeks followed by**
  b. **<u>Maintenance dose:</u> Colecalciferol 800IU – 2000IU daily.**
- Check serum vitamin D level after the loading regime.
- Advise patient on appropriate sun exposure and dietary source of Vitamin D.

- Commence patient on pharmacological strength vitamin D.
  a. **Loading dose: Colecalciferol 3200IU daily for 6 weeks, followed by**
  b. **Maintenance dose: Colecalciferol 800IU – 2000IU daily.**
- Check serum vitamin D level after the loading regime.
- Advise patient on appropriate sun exposure and dietary source of Vitamin D.

- Adequate Vitamin D level.
- If patient is already on vitamin D supplementation, continue as normal.
- Patients who are not on daily supplementation does not require any treatment.
- Advise patient on appropriate sun exposure and dietary source of Vitamin D.

11.A Fixed Loading Dose Regime Loading regimen should provide a total of approximately 300,000 IU. Below are the recommended loading dose regimes.		
Example Preparation	**Dose**	**Duration of Treatment**
Fultium-D3 capsules (colecalciferol)	3200 IU one daily	10-12 weeks (224,000-268,800IU in total)
Fultium-D3 capsules (colecalciferol)	20,000 IU two weekly	7 weeks (280,000 IU in total)
InVita-D3 oral solution (colecalciferol)	50,000 IU one weekly	6 weeks (300,000 IU in total)
Ergocalciferol (intramuscular injection) ***only to be used in patients with malabsorption problem.**	300000 IU single dose	May be repeated every 3-6 months if needed.

11.B Maintenance Dose Regime Typical maintenance dose is 800IU – 2000IU tailored to individual needs and condition.	
Example Preparation	**Dose**
Fultium-D3 capsules (colecalciferol)	800 IU (1-2 capsules daily)
Densunin tablets (colecalciferol)	800 IU (1-2 tablets daily)
Stexerol-D3 caplets (colecalciferol)	1000 IU (1-2 caplets daily)

12 USEFUL CONTACT NUMBERS

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