

## BNF CHAPTER 6: ENDOCRINE SYSTEM

### 6.1 DRUGS USED IN DIABETES

#### 6.1.1 INSULINS

Insulin should be prescribed by brand name to reduce the risk of prescribing errors.

##### Type of Insulin

Insulin profile	Insulin (brand name)
<p><b>Rapid-acting human insulin analogues</b> Immediate onset of action – injected immediately before, with or immediately after food; Peak action 60 minutes; Duration up to 4 hours</p>	<p>Apidra Humalog NovoRapid</p>
<p><b>Short-acting soluble insulin</b> 30-60 minute onset of action therefore needs to be injected 30 minutes before food; Peak action 2-4 hours; Duration up to 8 hours</p>	<p>Humulin S Actrapid Hypurin Bovine Neutral* Hypurin Porcine Neutral*</p>
<p><b>Intermediate-acting isophane insulin (NPH)</b> Onset of 1-2 hours; Peak action 4-12 hours; Duration 16-35 hours.</p>	<p>Humulin I Insuman Basal Insulatard Hypurin Bovine Isophane* Hypurin Porcine Isophane*</p>
<p><b>Long-acting insulin</b> Onset of 4 hours; Duration &gt; 24 hours</p>	<p>Hypurin Bovine Protamine Zinc* Hypurin Bovine Lente*</p>
<p><b>Long-acting insulin analogues</b> Duration up to 24 hours  See <a href="#">Long acting insulins guidance</a></p>	<p>Insulin glargine (products not directly interchangeable): Lantus 100units/ml Abasaglar 100units/ml (<a href="#">see policy</a>) Toujeo 300units/ml</p> <hr/> <p>Levemir (insulin detemir)</p> <hr/> <p><b>Tresiba (insulin degludec) 100units/ml and 200units/ml</b> <b>AMBER initiated in adults and paediatrics</b></p>
<p><b>Mixed preparations</b></p>	<p>Humulin M3</p>

	<p>Insuman Comb 15, 25 and 50  Humalog Mix 50 and Humalog Mix 25  NovoMix 30  Hypurin Porcine 30/70 Mix*</p>
<b>GLP-1 receptor agonist and insulin combination</b>	<p>Insulin degludec 100u/ml and liraglutide 3.6mg/ml (Xultophy®▼)  <u>AMBER shared care – consultant only</u></p>

\*Insulins rarely used

## **Insulin Initiation**

The choice of insulin and insulin regimen should be a joint decision between the patient and healthcare professional taking in to account the patient's lifestyle and occupation. The patients preferred insulin delivery device usually determines the type of insulin they are prescribed.

### **Once daily regimen**

Insulin as add on therapy should be considered for patients with type 2 diabetes that are inadequately controlled on oral therapy HbA<sub>1c</sub> ≥59mmol/mol. Once daily regimens are not suitable for patients with type 1 diabetes.

Once daily intermediate acting isophane insulin (NPH) is the basal insulin of choice.

As per NICE guidelines, when insulin is required for patients with type 2 diabetes as add on therapy insulin detemir or insulin glargine should only be considered for those:

- Who require assistance with injecting insulin
- Whose lifestyle is significantly restricted by recurrent symptomatic hypoglycemia
- Who would otherwise require twice daily basal injections in combination with oral antidiabetic drugs
- Who cannot use the device needed to inject isophane insulin

Insulin degludec is a long-acting human insulin analogue for once daily subcutaneous administration. It is the first long-acting insulin available at a higher strength formulation, 200 units/mL.

### **Twice daily regimen**

This regimen is suitable for patients whom are unwilling to have multiple injections.

Human isophane insulin (NPH) is the insulin of choice for a twice daily regimen.

Consider pre-mixed preparations that include short-acting insulin analogues, rather than pre-mixed preparations that include short-acting human insulin preparations when:

- A person prefers to inject immediately before a meal
- Hypoglycemia is a problem
- Blood glucose rises markedly after meals

## Multiple injection regimen

The most commonly used regimen in type 1 diabetes. Also sometimes used in patients with type 2 diabetes. Usually 4 injections are given daily, known as basal bolus regimen. Rapid-acting insulin analogue or soluble insulin is injected before meals (bolus) and intermediate or long-acting insulin is injected once daily (bolus) to provide background cover. The basal bolus regimen has the advantage of increased flexibility with exercise, meal timings and meal size.

## Continuous subcutaneous insulin infusion (Insulin Pump therapy)

NICE recommends continuous subcutaneous insulin infusion for the treatment of type 1 diabetes as an option in adults and children over 12 years when:

- Patients suffer repeated or unpredictable hypoglycemia, whilst attempting to achieve optimal glycaemic control with multiple-injection regimens
- Patients whose glycaemic control is inadequate ( $HbA_{1c} > 69 \text{ mmol/mol}$ ) despite multiple-injection regimens (including use of long-acting analogues where appropriate)

Refer to Countess of Chester guidelines (on hospital intranet). Also refer to NICE guidance: [NG17 Type 1 Diabetes in Adults: diagnosis and management](#)  
[NG28 Type 2 Diabetes in Adults: management](#)

## Insulin safety

Refer to NRLS/ NPSA safe administration of Insulin

- All regular and single insulin doses are measured and administered using an insulin syringe or commercial insulin pen device. Intravenous syringes must never be used for insulin administration.
- An insulin syringe must always be used to measure and prepare insulin for intravenous infusions.
- Insulin should always be written in units and NEVER abbreviated i.e. "U" or "IU" must NOT be used.
- All healthcare professionals who prescribe, prepare and administer insulin should have adequate training.
- Adult patients on insulin therapy receive a patient information booklet and an Insulin Passport to help provide accurate identification of their current insulin products and provide essential information across healthcare sectors. Further information is available at <http://www.nrls.npsa.nhs.uk/resources/type/alerts/?entryid45=130397&q=0%c2%acinsulin+passport%c2%ac>

### 6.1.1.3 Hypodermic equipment

#### Needles for pre-filled and re-usable pen injectors (insulin and GLP-1 agonists)

- **GlucorX Finepoint**  
Compatible with all existing pens
- |              |
|--------------|
| 4mm/31gauge  |
| 5mm/31 gauge |
| 6mm/31 gauge |

All needles are for single use only.

**N.B.** there are a small number of patients who may require covered needles (e.g. Mylife Clickfine AutoProtect, NovoFine Autocover, BD AutoShield Duo), due to needle phobia. The necessity for these needles should be explained in secondary care clinic letters.

#### **Insulin administration**

**Adults:** there is no clinical reason for recommending needles longer than 8mm.

4, 5 and 6mm needles are suitable for all adults regardless of BMI; they no longer require a lifted skin fold and can be given at 90 degrees to the skin.

**Children and adolescents:** there is no clinical reason for using needles longer than 6mm.

#### [Blood glucose monitoring guidelines](#)

## 6.1.2 ANTIDIABETIC DRUGS

For the management of Type 2 Diabetes please refer to local guidelines on the [Medicines Management website](#), and NICE Clinical Guideline [NG28 Type 2 Diabetes in Adults: management](#)

### 6.1.2.1 Sulfonylureas

- **Gliclazide** 40mg, 80mg tablets  
30mg m/r tablets (restricted to patients with poor compliance)
- **Glimepiride** 1mg, 2mg, 3mg, 4mg tablets

### 6.1.2.2 Biguanides

- **Metformin** 500mg, 850mg tablets  
500mg, 1g m/r tablets - restricted use for patients with GI intolerance to standard release metformin  
Metformin oral solution sugar-free 500mg/5ml – for patients unable to swallow tablets or administration via feeding tube

### 6.1.2.3 Other Antidiabetic drugs

- **Glitazones**
- **Pioglitazone** 15mg, 30mg, 45mg tablets

- **DPP-4 inhibitors**

- **Alogliptin** 6.25mg, 12.5mg, 25mg tablets\*

- **Linagliptin** 5mg tablets

Linagliptin should be used 1<sup>st</sup> line when eGFR is < 60ml/min, alogliptin should be used 1<sup>st</sup> line for other patients.

- **Sitagliptin** 25mg, 50mg, 100mg tablets\* (existing patients)

- **Saxagliptin** 2.5mg, 5mg tablets\* (existing patients)

\* Monitor eGFR every 6 months to ensure no dose reduction is necessary

**Dose reductions in renal impairment**

Drug	Standard Dose	eGFR 30-50 ml/min/1.73m <sup>2</sup>	eGFR 15-29 ml/min/1.73m <sup>2</sup>	eGFR < 15 ml/min/1.73m <sup>2</sup>
Alogliptin	25mg	Reduce dose to 12.5mg	Reduce dose to 6.25mg	Reduce dose to 6.25mg
Linagliptin	5mg	No dose change	No dose change	No dose change
Saxagliptin	5mg	Reduce dose to 2.5mg	Reduce dose to 2.5mg	Not recommended
Sitagliptin	100mg	Reduce dose to 50mg	Reduce dose to 25mg	Reduce dose to 25mg

Vildagliptin is not recommended due to the requirement to regularly monitor liver function tests.

- **SGLT2 inhibitor**

- **Dapagliflozin**▼ 5mg, 10mg tablets

In accordance with [NICE TA 288](#) as combination therapy

- **Canagliflozin**▼ 100mg, 300mg tablets

In accordance with [NICE TA 315](#) as combination therapy

- **Empagliflozin**▼ 10mg, 25mg tablets

In accordance with [NICE TA 336](#) as combination therapy

Also [NICE TA 390](#) – canagliflozin, dapagliflozin and empagliflozin as monotherapy

- **GLP-1 receptor agonists**

See [GLP-1 guidelines](#).

**For initiation by COCH diabetes specialist or Primary Care clinicians undertaking Diabetes LES Level 2.**

If initiated by COCH for LES Level 1 Practice, patient will be monitored for 6 months by clinic.

**1<sup>st</sup> choice: Lixisenatide**▼

50microgram/mL, 3ml pre-filled pens for 10microgram/dose

100microgram/mL, 3mL pre-filled pens for 20microgram/dose

**2<sup>nd</sup> choice: Exenatide MR /  
Liraglutide /  
Dulaglutide**

Exenatide MR 2mg vial

Exenatide MR 2mg dual chamber pen

Liraglutide 6mg/mL, 3mL pre-filled pens. Maximum dose 1.2mg daily ([NICE TA 203](#))

Dulaglutide 0.75 mg solution for injection (pre-filled pen or pre-filled syringe)

Dulaglutide 1.5 mg solution for injection (pre-filled pen or pre-filled syringe)

**Existing patients only:  
Exenatide**

250micrograms/mL injection – supplied as:

5micrograms/dose pre-filled pen

10micrograms/dose pre-filled pen

**GLP-1 receptor agonist and insulin combination**

**Insulin degludec / Liraglutide (Xultophy<sup>®</sup>)**▼

Insulin degludec 100u/ml and liraglutide 3.6mg/ml  
**AMBER shared care – consultant only**

- **Others**

- **Repaglinide**

500microgram, 1mg, 2mg tablets

## TREATMENT OF HYPOGLYCAEMIA

- **Glucagon** 1mg (1 unit) vial
- **Glucogel<sup>®</sup>** 9.2g glucose/23g oral ampoule

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## GUIDELINES FOR THE TREATMENT OF HYPOGLYCAEMIA

See "HYPOGLYCAEMIA" - PROTOCOL FOR HOSPITAL MANAGEMENT (on Hospital Intranet)

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## XRAY CONTRAST MEDIA AND METFORMIN

See DIABETIC PATIENTS TAKING METFORMIN, WHO REQUIRE INTRAVENOUS RADIOGRAPHIC CONTRAST MEDIUM. RECOMMENDATIONS FOR MANAGEMENT OF (on Hospital Intranet)

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## DIABETIC KETOACIDOSIS (DKA) IN ADULTS (JUMP)

See DIABETIC KETOACIDOSIS – Guidelines for the Management of (on Hospital Intranet)

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## DIABETES AND SURGERY IN ADULTS (JUMP)

See DIABETES AND SURGERY – Guidelines for the Management of (on Hospital Intranet)

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## SUBCUTANEOUS INSULIN PUMPS

These pumps administer short acting insulin continuously to control diabetes and the patient with such a pump will be skilled in managing these pumps.

The patient should be allowed to continue to manage their diabetes using their pump unless:

- They have DKA or more than a trace of ketones
- They have impaired ability to do so (unconscious, surgery, confused, distressed etc.)

Please contact the Diabetes Specialist Nurses if a patient with a subcutaneous insulin pump is admitted.

Do not stop the pump until an IV infusion is started or bolus subcutaneous insulin has been given.

When converting from IV to pump insulin allow a 30 minute overlap.

## **6.2 THYROID AND ANTITHYROID DRUGS**

### **6.2.1 THYROID HORMONES**

- **Levothyroxine sodium** 25, 50, 100microgram tablets

### **6.2.2 ANTITHYROID DRUGS**

#### **First choice**

- **Carbimazole** 5mg, 20mg tablets

Patients receiving carbimazole are advised to stop their tablets immediately and see their GP urgently (same day) if they develop signs and symptoms suggestive of infection, especially sore throat and/or mouth ulcers.

A white blood cell count should be taken and a neutrophil count below  $1.5 \times 10^9/L$  reported to the endocrinology team

#### **Second choice**

- **Propylthiouracil** 50mg tablets

#### **Preparations for thyroidectomy:**

- **Aqueous iodine solution** (Lugol's solution)

## **6.3 CORTICOSTEROIDS**

### **6.3.1 Replacement Therapy**

- **Hydrocortisone** 10mg, 20mg tablets  
(glucocorticoid)

- **Fludrocortisone** 100microgram tablets  
(mineralocorticoid)

### 6.3.2 Glucocorticoid therapy

- **Prednisolone** 1mg, 5mg, 25mg tablets

Soluble prednisolone is no longer included on formulary.

Adults: disperse or crush / mix standard tablets with water (unlicensed)

Children: disperse or crush / mix standard tablets with water / cordial or give with jam / fruit purée (unlicensed).

For patients with swallowing difficulties consider Prednisolone Dompe 1.0 mg/ml oral solution unit dose vials.

Note: Corticosteroid therapy is only weakly linked with peptic ulceration. The use of enteric-coated preparations to reduce the risk is speculative only.

Prophylaxis against osteoporosis should be considered in patients who currently, or who are expected to take corticosteroid treatment at doses  $\geq 7.5$ mg prednisolone/day, or equivalent, for 3 months or more.

- **Dexamethasone** 500microgram, 2mg tablets  
2mg/5mL, 500microgram/mL oral solution
- **Dexamethasone (base)** 3.3mg/1mL injection
- **Hydrocortisone** 100mg injection  
(sodium succinate)
- **Methylprednisolone** 40mg, 500mg, 1g vial
- **Triamcinolone** 40mg/mL injection (1mL and 2mL)

### Anti-inflammatory dose equivalents of corticosteroids

Prednisolone 5mg	≡	Hydrocortisone 20mg
	≡	Cortisone acetate 25mg

- ≡ Methylprednisolone 4mg
- ≡ Triamcinolone 4mg
- ≡ Dexamethasone  
750microgram
- ≡ Betamethasone  
750microgram

## **6.4 SEX HORMONES**

### **6.4.1 FEMALE SEX HORMONES**

Tablets are the preferred first line treatment. Patches may be prescribed for those patients who decline oral therapy.

#### **Unopposed oestrogen**

Unopposed oestrogen, for HRT, should only be given to women who have had a hysterectomy. No single preparation is recommended. Choice will depend on indication, patient preference (tablets, patches) and price. Please contact pharmacy re current availability.

Below are the preparations that are routinely stocked in COCH pharmacy

#### **Tablets**

- **Estradiol hemihydrate** 1mg, 2mg tablets (Elleste-Solo)  
(oestradiol)

#### **Patches**

- **Estradiol** 25, 50 micrograms/24 hours patches  
(oestradiol)  
*(eg. Estraderm MX, Evorel)*  
  
Change after 3 to 4 days
- **Estradiol** 50, 100 micrograms/24 hours patches  
(oestradiol)  
*(eg. Progynova TS, FemSeven)*  
  
Change once a week

#### **Other Oestrogen Preparations**

*For topical (vaginal) preparations see TREATMENT OF VAGINAL AND VULVAL CONDITIONS*

- **Estradiol implant** 50mg, 100mg implants  
(oestradiol)

#### **Combined oestrogen/progestogen preparations**

##### **Monthly bleed preparations**

There are many HRT preparations that are taken cyclically that result in a monthly bleed for the woman. No single preparation is recommended. Choice will depend on indication, patient preference (tablets, patches) and price. Please contact pharmacy re current availability.

## Tablets - No bleed

- **Premique** conjugated oestrogens 625micrograms/  
medroxyprogesterone acetate 5mg
  - **Tibolone** 2.5mg tablets
  - **Raloxifene** 60mg tablets
- Does not prevent vasomotor symptoms, it is licensed for the treatment and prevention of postmenopausal osteoporosis only.  
To be prescribed according to NICE technology appraisals [TA160](#) and [TA161](#)
- See also section 6.6

## Progestogens

- **Medroxyprogesterone acetate** 5mg, 10mg tablets
- **Norethisterone** 5mg tablets
- **Ulipristal acetate (Esmya®)** 5mg tablets

## 6.4.2 MALE SEX HORMONES AND ANTAGONISTS

- **Testosterone** Various preparations and formulations - consult pharmacy on availability  
Implants would generally remain hospital only

## Anti-androgens

- **Cyproterone acetate** 50mg tablets
- **Finasteride** 5mg tablets  
For use, please refer to [management of benign prostatic hyperplasia](#) on the guidelines section of the Medicines Management website.

## **6.5 HYPOTHALAMIC AND PITUITARY HORMONES AND ANTI-OESTROGENS**

### **6.5.1 HYPOTHALAMIC AND ANTERIOR PITUITARY HORMONES AND ANTI-OESTROGENS**

#### **Anti-oestrogens**

- **Clomifene** 50mg tablets

#### **Corticotrophins**

- **Tetracosactide** (Synacthen<sup>®</sup>)  
250 micrograms/mL injection - for short (30 min) diagnostic test of adrenal function  
1mg/1mL depot injection - for long (5 hour) test of adrenal function.

#### **Gonadotrophins**

- **Chorionic gonadotrophin** 5000unit s/c injection (Pregnyl<sup>®</sup>)
- **Choriogonadotropin alfa** 6500unit (250microgram)/0.5mL s/c injection (Ovitrelle<sup>®</sup>)
- **Follitropin**  
alfa - 75unit injection (Gonal-F<sup>®</sup>)  
beta - 50unit injection (Puregon<sup>®</sup>)
- **Human menopausal gonadotrophins**  
Menogon<sup>®</sup> 75/75unit im injection  
Menopur<sup>®</sup> 75/75unit s/c injection

#### **Growth hormone**

- **Somatropin** Various strengths and devices - consult pharmacy

Refer to NICE guidance for treatment of [adults](#) and [children](#)

#### **Hypothalamic hormones**

- **Gonadorelin (LH-RH, GnRH, gonadotrophin-releasing hormone)** 100microgram injection
- **Protirelin (TRH)** 200 micrograms/2mL injection

## 6.5.2 POSTERIOR PITUITARY HORMONES AND ANTAGONISTS

- **Desmopressin** 200microgram tablets  
120microgram oral lyphilisate  
10 micrograms/metered nasal spray  
100microgram/mL nasal drop  
(NB - limited licensed indications for nasal preparations)  
4 micrograms/ mL injection
- **Vasopressin** (argipressin) 20 units/ mL , 1mL injection
- **Terlipressin** 1mg (+ 5mL diluent) injection  
For management of bleeding oesophageal varices - see Chapter 1

### Antidiuretic hormone antagonists

Used for treatment of hyponatraemia associated with inappropriate secretion of anti-diuretic hormone

- **Demeclocycline** 150mg capsules

### V2-receptor antagonist

- **Tolvaptan** (Jinarc<sup>®</sup>) For treating autosomal dominant polycystic kidney disease as per [NICE TA358](#).

## **6.6 DRUGS AFFECTING BONE METABOLISM**

### **OSTEOPOROSIS**

Osteoporosis is characterised by microarchitectural deterioration of bone tissue and low bone mass leading to increased bone fragility and risk of fracture.

- Predisposing factors:**
- Family history (especially maternal hip fracture). Rheumatoid arthritis.
  - Low body weight and secondary thinness.
  - Height loss.
  - Cigarette smoking.
  - Excessive alcohol use.
  - Physical inactivity.
  - Hyperthyroidism.
  - Hyperparathyroidism.
  - Osteomalacia.
- Major risk factors:**
- Low trauma fractures or fractures of hip or forearm at < 65 years.
  - Early natural or surgical menopause at < 45 years.
  - Secondary amenorrhoea > 6 months.
  - Hypogonadism in men.
  - Patients over 65 years of age.
  - Corticosteroid therapy
- Aim of treatment:** To reduce occurrence vertebral and non-vertebral fractures.

**Calcium and vitamin D supplementation:**

Those at risk of osteoporosis should maintain an adequate intake of calcium and vitamin D either by dietary means or by taking supplements of calcium and vitamin D.

Frail, elderly, housebound (or in a care home) males and females should receive oral supplements of calcium (1000 - 1200mg/day) and vitamin D (800units/day)

Preparations providing the required amounts include:

**Calcichew D3 Forte** - 1 tablet twice daily

**Adcal D3** - 1 tablet twice daily (chewable or effervescent tablets)

Choice of preparation usually depends on palatability, local purchasing agreements and current cost. However, as long as the daily dose of the preparation provides the right amounts and proportions of both calcium and vitamin D, then the preparations are interchangeable.

Calcium and vitamin D supplementation (as above) should also be prescribed whenever bisphosphonates (or alternatives) are initiated for the prevention or treatment of osteoporosis.

## **6.6.2 BISPHOSPHONATES AND OTHER DRUGS AFFECTING BONE METABOLISM**

See [NICE guidance TA 161](#) on alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women

**AND** [NICE guidance TA 160](#) Primary prevention of osteoporotic fragility fractures in postmenopausal women.

### **Bisphosphonates**

Indicated for:

- Treatment of established osteoporosis in men and women > 45 years.
- Treatment AND prevention of osteoporosis in postmenopausal women.
- Treatment and prevention of corticosteroid induced osteoporosis.

### **First line**

- **Alendronic acid**
  - 10mg tablets – daily dose
  - 70mg tablets – weekly dose
  - 70mg/100ml oral solution – weekly dose

## Second line

- **Risedronate sodium** 5mg tablets – daily dose  
35mg tablets – weekly dose

It is recognised that once weekly preparations of bisphosphonates are often used outside of their licensed indications to promote patient compliance which may be poor because of the various restrictions on administration times in relation to food (see below).

## Third line

- **Ibandronic acid** 150mg tablets – monthly dose

### Counselling points for bisphosphonates

- Oral preparations should be taken with plenty of water while sitting upright or standing. Tablets should be whole, not chewed or allowed to dissolve in the mouth.
- Take on an empty stomach at least 30 minutes before breakfast or other oral medications. Risedronate may be taken at other times of the day but must avoid food and drink for at least 2 hours before or after, particularly calcium containing products (milk, supplements, antacids).
- Patients should stand or sit upright for at least 30 minutes after taking oral bisphosphonates.
- Severe oesophageal reactions have been reported with **alendronic acid**. Patients should be warned to stop taking it and seek medical attention if they develop symptoms of oesophageal irritation (dysphagia, new or worsening heartburn, pain on swallowing or retrosternal pain)
- Bisphosphonates should not be prescribed in pregnancy or for women who are trying to conceive. Premenopausal women should be advised to use adequate contraception while taking bisphosphonates and should ensure that they are not pregnant when starting treatment. Patients should be counselled about the potential risks of bisphosphonate treatment in case of future wish to become pregnant as even if the drug has been discontinued prior to conception, there is a theoretical risk that it may be released from bone during pregnancy. Risedronate may have a shorter half-life in bone than alendronic acid and so may be a more appropriate choice for use in premenopausal women.

### Bisphosphonates in renal impairment\*:

Alendronate: not recommended if GFR <35ml/min. There are anecdotal reports of renal units using 70mg weekly in CKD 3, 4 and 5, but this prescribing should only be undertaken on the advice of the renal team on an individual patient basis.

Risedronate: GFR >20ml/min, dose as in normal renal function. SPC states contraindicated if creatinine clearance <30ml/min, and Renal Handbook states renal clearance decreased by 70% in these patients. Prescribing should only be undertaken on the advice of the renal team on an individual patient basis.

\*From Summary of Product Characteristics accessed 17/10/2013 and The Renal Drug Handbook 3rd edition, 2009.

## **Bisphosphonate holidays:**

Consider a 2 year bisphosphonate holiday for patients who have completed 5 years of oral bisphosphonate treatment, following an up to date DEXA scan (see below).

### **UNLESS**

- aged  $\geq 75$  years
- previously sustained a hip or vertebral fracture
- taking continuous oral glucocorticoids in a dose of  $\geq 7.5$  mg / day prednisolone or equivalent
- sustain one or more low trauma fractures during treatment. After exclusion of poor adherence to treatment (e.g., less than 80% of treatment taken), and after causes of secondary osteoporosis have been excluded, the treatment option should be re-evaluated and patients referred to the endocrine/metabolic bone clinic at the Countess of Chester Hospital NHS Foundation Trust.
- total hip or femoral neck BMD T-score is  $\leq -2.5$  SD (continuation of treatment advised)

In the above individuals in whom treatment is continued, treatment review should be performed every 5 years, including assessment of renal function.

If treatment is discontinued, fracture risk should be reassessed:

- after a new fracture regardless of when this occurs
- after two years.

**A DEXA scan** should be performed before starting a bisphosphonate holiday, to check baseline BMD, and again after 2 years to assess for a significant decline in BMD and to consider restarting treatment if there is a significant decline or if clinically indicated.

## OTHER TREATMENTS FOR OSTEOPOROSIS

- **Strontium ranelate** 2g sachet once daily

For treatment of severe osteoporosis in postmenopausal women at high risk of fracture, or in men at increased risk of fracture only where bisphosphonates are not tolerated (severe GI symptoms) or contraindicated.

### MHRA Drug Safety advice:

Strontium ranelate (Protelos): risk of serious cardiac disorders—restricted indications, new contraindications, and warnings

See [here](#) for full advice

- **Denosumab** 60mg injection

For primary and secondary prevention osteoporotic fractures according to [NICE TA204](#)

Hospital initiation then GP prescribing according to the [local shared care agreement](#)

### MHRA Drug safety advice

Atypical femoral fractures have been reported rarely in patients with postmenopausal osteoporosis receiving long-term ( $\geq 2.5$  years) treatment with denosumab 60 mg (Prolia ▼) in a clinical trial.

During denosumab treatment, patients presenting with new or unusual thigh, hip or groin pain should be evaluated for an incomplete femoral fracture. Discontinuation of denosumab therapy should be considered if an atypical femur fracture is suspected, while the patient is evaluated.

Further information can be found [here](#)

- **Raloxifene**  
60mg once daily

Raloxifene can be used for prevention and treatment of vertebral fractures in postmenopausal women. However, it is not as effective as the bisphosphonates for treatment and not as cost effective as the bisphosphonates for the prevention of osteoporosis. Reserved for secondary prevention where bisphosphonates not tolerated or contraindicated. Not recommended for primary prevention.

- Hormone Replacement Therapy (HRT)**

1<sup>st</sup> line for prevention of osteoporosis in those with early natural or surgical menopause (before the age of 45). HRT should be continued until an age that would be considered appropriate for natural menopause (i.e., 50 years of age)

For postmenopausal women who are at an increased risk of fracture and are aged over 50 years, HRT should be used to prevent osteoporosis **only** in those who are intolerant of, or contraindicated for, other osteoporosis therapies. (CSM recommendation.)

See “Drugs used in Obstetrics and Gynaecology” for a list of recommended preparations.
- Teriparatide**

Specialist use only, according to the criteria outlined by [NICE guidance TA 161](#)
- Zoledronic acid**

5mg (100ml infusion bottle) As per [NICE TA464](#)
- Ibandronic acid**

3mg (3mg/3ml) As per [NICE TA464](#)
- Zoledronic acid**

5mg (4mg in 5mL vial)

For patients taking cytokine modulators where bisphosphonates are not tolerated and denosumab is contra-indicated.
- Calcitonin salmon (salcatonin)**

400 unit injection

May be useful for pain relief for up to 3 months after vertebral fracture if other analgesics are ineffective. (unlicensed indication)

## CORTICOSTEROID INDUCED OSTEOPOROSIS

- Prevention**
- Use smallest effective dose of corticosteroid for shortest possible time to minimise risk of associated osteoporosis.
  - Reduce high doses of inhaled steroids used during exacerbations to a minimum maintenance dose as soon as possible.
- Preventative treatment**
- Prophylaxis for osteoporosis is dependent on the following factors: age, duration of corticosteroid therapy, fracture risk, bone mineral density and T-score
  - Prophylaxis should be initiated if: current or planned corticosteroid treatment  $\geq$  7.5mg prednisolone/day, or equivalent, based on age and fracture probability: those aged over 65y are at the greatest risk. However, some sources say that preventative treatment should be given for steroid treatment for 3 months or longer regardless of dose.
  - More than three or four courses of corticosteroids taken in the previous 12 months may be considered to be equivalent to more than 3 months of continuous treatment.
  - Patients taking oral corticosteroids who have sustained a low trauma fracture should be started on treatment for osteoporosis.
  - High dose inhaled steroids – patients taking high doses of fluticasone (1000mcg per day or more) need protection. 1000mcg inhaled fluticasone is approximately equivalent to 8mg oral prednisolone. However, there is no general consensus on the use of preventative treatment with high dose inhaled steroids.
- Preventative treatment should be initiated at the same time as corticosteroids as greatest rate of bone loss occurs in the first 6-12 months. Bisphosphonate treatment may be stopped at the same time that corticosteroids are withdrawn, providing there are no other major risk factors for osteoporosis or fragility fractures.
- Preparations used**
- 1<sup>st</sup> line - **alendronate** (see above for dose and preparations)  
**N.B.** commence calcium and vitamin D at the same time

## **PAGET'S DISEASE OF BONE**

- **Risedronate** 30mg tablets  
(NB this is a different preparation to that used for osteoporosis)  
Dose: 30mg daily for 2 months: may be repeated if necessary after at least 2 months.
- **Zoledronic acid** 5mg (4mg in 5mL vial)
- **Calcitonin salmon** 200unit/mL, 2mL multidose vial  
(Salcatonin)  
50 units 3 times weekly - 100 units daily, adjusted according to response.

## **METASTATIC BONE DISEASE**

Osteonecrosis of the jaw has been reported in patients, predominantly those with cancer, receiving treatment with intravenous bisphosphonates

### **First line**

- **Disodium pamidronate** 15mg, 30mg, 60mg, 90mg injection

Bone pain: 90mg every 4 weeks

Hypercalcaemia of malignancy: see Hypercalcaemia – [guidelines for management](#)

See [Pamidronate IV protocol preparation & administration](#) for administration instructions

### **Other preparations**

- **Sodium clodronate** 400mg cap  
800mg tab  
(Restricted use: haem-oncology patients only)
- **Zoledronic acid** 4mg in 5mL vial  
(Restricted use: haematology only)
- **Denosumab** 120mg injection  
Prevention of skeletal related events in adults with bone metastases from solid tumours (not including prostate cancer). Refer to [NICE guidance TA 265](#).

## **6.7 OTHER ENDOCRINE DRUGS**

### **6.7.1 BROMOCRIPTINE AND OTHER DOPAMINE-RECEPTOR STIMULANTS**

- **Bromocriptine** 2.5mg tablets
- **Cabergoline** 500microgram tablets

### **6.7.2 DRUGS AFFECTING GONADOTROPHINS**

- **Cetrorelix** 250microgram, 3mg injection
- **Danazol** 100mg, 200mg capsules

#### **Gonadorelin analogues**

- **Buserelin** 1mg/mL (5.5mL) injection
- **Triptorelin** As Decapeptyl® SR  
3mg injection (monthly)  
11.25mg injection (3 monthly)
- **Nafarelin** 200 micrograms/metered nasal spray