Chapter 6: ENDOCRINE SYSTEM
Updated: May 2020

The following prescribing guidelines are relevant to the endocrine chapter and can be found here

- Blood Glucose monitoring meter formulary
- Diabetes (type 2- management in adults)
- FreeStyle Libre- JAPC briefing
- Hyperprolactinaemia (cabergoline & quinagolide)
- Liothyronine- position statement
- Menopause- local management guideline
- Osteoporosis- bisphosphonate holiday
- Osteoporosis- diagnosis & management
- Pioglitazone- prescribing statement

Detailing aids: CKD
Relevant resources:

- Think Kidneys Resources for Primary Care
- Transgender and Non-Binary Adults - Primary Care guidance
- Trans healthcare - Advice based on GMC guidance
- Gender incongruence in primary care - Advice from BMA

6.1 Drugs used in diabetes

6.1.1 Insulins

Insulins should be **prescribed by brand** as they are not interchangeable.

Adult patients on insulin should receive an insulin passport (http://pcse.england.nhs.uk/ for supply) to provide accurate identification of their current insulin therapy across healthcare sectors. Errors in the administration of insulin are common and consequence may be severe and can cause death. All insulin doses should be measured and administered using an insulin syringe or commercial insulin pen device, and the term 'units' should always be used in full without abbreviating. Do NOT use insulin needle and syringe to administer insulin withdrawn directly from a pen device or replacement cartridge due to risk of severe harm and death (NHS PSA November 2016).

Patients should be trained on how to use their insulin device, and for patients using high strength preparations, particularly on how to check the dose displayed on the prefilled pen (MHRA April 2013). Care should be taken when prescribing high strength, fixed combination and biosimilar products- prescriber and patients must understand the insulin strength of products and how to use them correctly to minimise the risk of medication errors (MHRA April 2015).

Where a biosimilar exists the most cost effective preparation should be used in new patients and considered in patients with unstable glucose control who are under close supervision.

MHRA Sept 2020 Injection of insulin (all types) can lead to deposits of amyloid protein under the skin (cutaneous amyloidosis) at the injection site which interferes with insulin absorption thus it is important to rotate injection site. There is a risk of hypoglycaemia in patients that suddenly change injection site from an area with cutaneous amyloidosis to an unaffected area (for example, changing the injection site from the torso to the leg). Patients should therefore carefully monitor blood glucose after changing injection site and consider adjusting the dose of insulin or antidiabetic medication to avoid hypoglycaemia, as needed.

GlucoRx Carepoint pen needles (4mm/31g, 5mm/31g, 6mm/31g, 8mm/31g) and **GlucoRx Carepoint Ultra** (4mm/32g) are the formulary choice of insulin pen needles. If this is unsuitable consider other brands costing less than £5 per 100 needles.

Safety needles should NOT be used by patients who self-administer insulin. If safety needles are indicated GlucoRx Safety Pen Needle (5mm/30g, 8mm/30g) – **GREEN** 1st line option (preferred brand).
Safety needles with acquisition cost <£20 per 100 are classified as **GREEN** alternative 2nd line option.
All other safety needles with acquisition cost > £20 per 100 are classified as **Do Not Prescribe (DNP).**

	Insulin (all preparations are 100units/ml unless stated)	Timing of injection	Onset of action	Peak	Duration of action
Mealtime insulins	**Short acting human insulins**				
	Soluble insulin (e.g. **Actrapid, Humulin S, Insuman rapid**)	Within 30 mins before meal	Within 30 mins	1.5-3.5 hrs	7-8 hrs
	Rapid-acting analogues				
	Insulin aspart (**Fiasp**) (After specialist recommendation) *-an option for type 1 diabetes (NG17) in new adult patients*	Within 0-15 mins of meal	4 mins	1-3 hrs	3-5 hrs
	Insulin aspart (**Novo Rapid**) *-an option for children and type 1 diabetes in patients already on treatment (NG17)*	Immediately before meal	10-20 mins	1-3 hrs	3-5 hrs
	Insulin lispro (**Humalog**) *-an option for type 1 diabetes (NG17)*	Within 0-15 mins of meal	About 15 mins	30-70 mins	2-5 hrs
	Insulin lispro (**Lyumjev**) *Slightly different releasing profile to Humalog – used in adults in whom a more rapid acting mealtime insulin is desirable*	Up to 2min before or 20min after starting meal	Within 20min	1-3 hrs	5 hrs
	Insulin glulisine (Apidra)	Within 0-15 mins of meal	10-20 mins	About 1 hr	1.5-4 hrs
Basal insulins	**Intermediate (NPH) human insulin**				
	Isophane (NPH) insulin (**Insulatard, Humulin I, Insuman Basal**) *- first line for most patients with type 2 diabetes*	At bedtime/12 hrly	Within 1.5 hrs	4 -12 hrs	About 24 hrs
	Long-acting analogues				
	Insulin detemir (**Levemir**) *- preferred choice for adult type 1 diabetes (NG17)*	Once/twice daily	0.5-1 hr	3-14 hrs	Up to 24 hrs
	Insulin glargine biosimilar (**Semglee**) - positioned ahead of insulin glargine (Lantus), when a long-acting insulin analogue is indicated in new patients or patients who are having a review of treatment due to suboptimal control	Once daily	0.5-1 hr	No peak	Up to 24 hrs
	Insulin glargine biosimilar (**Abasaglar**) - when a long-acting insulin analogue is indicated. Patients already initiated on Abasaglar should remain on this	Once daily	0.5-1 hr	No peak	Up to 24 hrs
	Insulin glargine (**Lantus**) *- an option to continue for existing stable patients*	Once daily	0.5-1 hr	No peak	Up to 24 hrs
	Insulin glargine **300 units/ml** (Toujeo) **GREY**	Once daily	0.5-1 hr	No peak	24-36 hrs
	Insulin degludec (Tresiba) **100units/ml** **GREY**	Once daily	0.5 –1.5 hrs	No peak	>42 hrs
	Insulin degludec (Tresiba) **200units/ml** **GREY**	Once daily	0.5 –1.5 hrs	No peak	>42 hrs
Biphasic insulins	**Pre-mixed human insulin** *(commonly used in twice daily regimens in type 2 diabetes)*				
	Biphasic isophane insulin (soluble insulin 30%+isophane insulin 70%; **Humulin M3**; Insuman Comb **25** (25%soluble/75% Isophane); Insuman Comb **50** (50% soluble/50% Isophane))	Within 30 mins before meal	Within 30 mins	2 and 8hrs	Up to 24hrs
	Pre-mixed analogues *(an option in type 2 diabetes if a person prefers to inject insulin immediately before a meal)*				
	Biphasic aspart (insulin aspart 30%+ insulin aspart protamine 70%; **novomix 30**)	Within 0-10 mins of meal	Within 10-20 mins	1-4 hrs	up to 24hrs
	Biphasic insulin lispro (insulin lispro 25%+ insulin lispro protamine 75%; **Humalog Mix 25**)	Within 0-15 mins of meal	About 15 mins	About 2 hrs	up to 24hrs
	Biphasic insulin lispro (insulin lispro 50%+insulin lispro protamine 50%; **Humalog Mix 50**)	Within 0-15 mins	About 15 mins	About 2 hrs	up to 24hrs

Traffic light classification for high strength insulins and insulin degludec

Insulin/strength	Traffic light status
Insulin glargine **300**units/ml (Toujeo)	**GREY** after consultant/specialist initiation: • for patients on insulin Degludec or • for patients being considered for insulin pump therapy or • for patients currently on high dose of insulin (>150units/day) who would otherwise have been started with Humulin R U-500 or degludec.
Insulin degludec **200**units/ml (Tresiba)	**GREY** after consultant/specialist initiation for patients currently on high dose of insulin (>150units/day) after consideration of Toujeo.
Insulin degludec **100**units/ml (Tresiba)	**GREY** after consultant/specialist initiation- restricted to those with documented nocturnal hypoglycaemia or loss of hypoglycaemia awareness despite using long acting insulin analogue, who would otherwise have been started on an insulin pump in type 1 diabetes.
Humulin R U500 **500**units/ml	**GREY** after consultant/specialist initiation for patients unable to use Toujeo or Insulin Degludec. (Only KwikPens currently available)

1. In a meta-analysis, short-acting insulin analogues for type 2 diabetes did not improve HbA1c, hypoglycaemia, or quality of life, compared with conventional human insulin. JAPC has agreed that insulin analogues in type 2 diabetes are overused, and should be considered after conventional human insulin.
2. Human NPH insulin is preferred, however, long acting analogues can be considered as an alternative in type 2 diabetes if:
   - the person needs assistance from a carer or healthcare professional to inject insulin and use of detemir or glargine (ensure glargine prescribed as brand name) would reduce the frequency of injections from twice to once daily or
   - the person's lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes or
   - the person would otherwise need twice-daily NPH insulin injections in combination with oral glucose-lowering drugs.
3. NICE NG17 recommends patients with type 1 diabetes should usually be offered two insulins that act in different ways:
   - a background (also known as a 'basal' or 'long-acting') insulin ideally injected twice a day **AND**
   - a 'quick-acting' (also known as a 'bolus' or 'rapid-acting') insulin injected before each meal to deal with the rise in blood glucose from eating.

Insujet the needle free insulin device classified as **Do Not Prescribe (DNP).**

NPH and insulin analogue products and cost comparisons

Active substance	Brand name	Strength	Insulin type	Cartridge cost	Pre-filled inj/pen cost	Vial cost	Cost per 100 unit
Isophane (NPH) insulin	Insuman Basal	100units/ml	Intermediate (NPH) human insulin	£17.50 (5 x 3ml)	£19.80 (5 x 3ml injection)	£5.61 (5ml)	£1.12 - £1.32
	Humulin I	100units/ml	Intermediate (NPH) human insulin	£19.08 (5 x 3ml)	£21.70 (5 x 3ml pen)	£15.68 (10ml)	£1.27 - £1.57
	Insulatard	100units/ml	Intermediate (NPH) human insulin	£22.90 (5 x 3ml)	£20.40 (5 x 3ml pen)	£7.48 (10ml)	£0.75 - £1.53
Insulin glargine (and biosimilar)	Semglee	100units/ml	Long-acting analogues	--	£29.99 (5 x 3ml pen)	--	£1.99
	Lantus	100units/ml	Long-acting analogues	£37.77 (5 x 3ml)	£37.77 (5 x 3ml pen)	£27.92 (10ml)	£2.52 - £2.79
	Abasaglar	100units/ml	Long-acting analogues	£35.28 (5 x 3ml)	£35.28 (5 x 3ml pen)	--	£2.35
Insulin detemir	Levemir	100units/ml	Long-acting analogues	£42.00 (5 x 3ml)	£42.00 (5 x 3ml pen) £44.85 (InnoLet 5 x 3ml)	--	£2.80 - £2.99
Insulin degludec	Tresiba	100units/ml	Long-acting analogues	£46.60 (5 x 3ml)	£46.60 (5 x 3ml pen)	--	£3.10
		200units/ml		--	£55.92 (3 x 3ml pen)	--	£3.10
Insulin glargine	Toujeo	300units/ml	Long-acting analogues	--	£33.14 (3 x 1.5ml pen)	--	£2.45
					£64.27 (3x 3ml pen)		£2.38

Price as per MIMs May 2020

Insulin pen price comparisons

Name	Cartridge size	Price (£)
Autopen 24	3ml	16.71
Autopen classic	3ml	16.96
JuniorSTAR	3ml	26.00
AllStar Pro	3ml	25.00
HumaPen Luxura HD	3ml	26.82
HumaPen Savvio	3ml	26.82
NovoPen 5	3ml	26.86
NovoPen Echo	3ml	26.86

Price as per MIMs May 2020

6.1.2 Antidiabetic drugs

A HbA1c reduction of at least 5 mmol/mol (0.5%) is considered clinically significant. At each review re-assess the person's needs and circumstances and think about stopping any medicines that are not effective at 6 months. **See local diabetes guideline.**

Metformin tabs 500mg, 850mg
Metformin SR tabs 500mg*, 750mg, 1000mg* (*Sukkarto SR preferred, cost-effective choice)
Gliclazide tabs 80mg

1. Metformin is the first-line oral hypoglycaemic for all people with type 2 diabetes (unless contraindicated). Start low and go slow. To be taken with meals for example, start metformin at 500mg od with main meal. After 1 week, increase to 500mg bd. Then increase in 500mg steps at weekly intervals to highest dose tolerated or maximum dose reached. Maximum dose in BNF is 2 g/day, but doses up to 3 g/day are commonly used in clinical practice.
   There is additional glucose lowering benefit by increasing doses from 2 to 3 g/day, although the UKPDS used a dose of metformin of 1700mg in the morning and 850mg in the evening (target dose).
2. Metformin SR should be restricted for use in those patients who are intolerant of standard release metformin, even after slow dose titration. Try metformin SR before switching to an alternative hypoglycaemic agent.
3. The risk of lactic acidosis with metformin, especially until creatinine clearance is below 30ml/min, is very minimal. NICE advises to review the dose of metformin if the serum creatinine exceeds 130 micromol/litre or the estimated glomerular filtration rate (eGFR) is below 45 ml/minute/1.73-m^2, and to **stop the metformin if the serum creatinine exceeds 150 micromol/litre or the eGFR is below 30 ml/minute/1.73-m^2**. A recent Cochrane systematic review (April 2014) compared over 70,000 patient years of metformin exposure with a matched group receiving other hypoglycaemic agents and found no evidence of excess lactic acidosis.
4. Gliclazide is the most cost-effective option if metformin cannot be used and the first-line option for add-on therapy to metformin. Gliclazide MR is **GREY** for patients with compliance problems requiring once daily dosing.
5. NICE PH38 – type 2 diabetes-prevention in people at high risk, recommends clinicians use their judgement on whether (and when) to offer metformin to support lifestyle change for people whose HbA1c or fasting plasma glucose blood test results have deteriorated if
   - This has happened despite their participation in intensive lifestyle-change programmes or they are unable to participate in an intensive lifestyle-change programme, particularly if they have a BMI greater than 35.
   - High risk patients are defined as HbA1c of 42-47mmol/mol (6.0-6.4%) or fasting plasma glucose of 5.5-6.9mmol/l
   - Dosage recommendation: Start with a low dose (for example, 500 mg once daily) and then increase gradually as tolerated, to 1500–2000 mg daily. If the person is intolerant of standard metformin consider using modified-release metformin. (Off-licence prescribing, only Glucophage SR is licenced to delay the onset of diabetes)
   - Metformin should be prescribed for 6–12 months initially. Monitor the person's fasting plasma glucose or HbA1c levels at 3-month intervals and stop the drug if no effect is seen.

DPP-4 inhibitors (gliptins)

Alogliptin tabs 6.25mg, 12.5mg, 25mg	*preferred 1st line DPP-4 inhibitor*
Linagliptin tabs 5mg	*if alogliptin is restricted by renal/hepatic impairment*

1. A review by MTRAC concluded that no significant differences were reported between the DPP-4 inhibitors with respect to blood-glucose lowering efficacy against other oral diabetic treatments.
2. Sitagliptin, saxagliptin, and vildagliptin have been classified as **GREY** by exceptionality defined as intolerance to the preferred choices or restricted by their licensing.
3. Patients treated with DPP-4 inhibitors should report any persistent, severe abdominal pain (sometimes radiating to the back). Discontinue DPP-4 inhibitor if pancreatitis is suspected (MHRA Sept 2012). DPP-4 inhibitors may also cause joint pain that can be severe and disabling, discontinuation of therapy with this class of drugs if severe and persistent joint pain occurs (FDA Aug 2015).

Glucagon-like Peptide 1 (GLP-1) agonists

Lixisenatide prefilled pen 10microg, 20microg

1. Liraglutide and exenatide have been classified as **GREY** by exceptionality defined as intolerance to the preferred first line choice or restricted by its license. For patients who require a once weekly GLP1 preparations exenatide MR is classified as **GREY** alongside exenatide MR weekly preparation
   - If compliance is an issue or
   - If the patient requires regular visits from a nursing team to administer the drug.
2. Review after 6 months of initiation to ensure continuation is in line with NICE (HBA1c reduction of 1.0% and 3% weight loss if initial BMI above 35 (criteria has also been adopted locally for lixisenatide)).
3. Liraglutide (Saxenda) is **Do Not Prescribe (DNP)** as an adjunct to diet and exercise for weight loss management.
4. Diabetic ketoacidosis has been reported in patients with type 2 diabetes on a combination of a GLP-1 receptor agonist and insulin who had doses of concomitant insulin rapidly reduced or discontinued. GLP-1 receptor agonists are not substitutes for insulin, and any reduction of insulin should be done in a stepwise manner with careful glucose self-monitoring. See MHRA June 2019.
5. Suliqua (insulin glargine + lixisenatide) has been classified as **GREY** specialist initiation and stabilisation of dosage, restricted for those patients struggling to manage multiple injections. Ongoing specialist support should be maintained for patients on this treatment. Prescriber must ensure the correct strength and number of dose steps are stated on the prescription.

Thiazolidinedione (glitazones)

Pioglitazone tabs 15mg, 30mg, 45mg

1. Use of pioglitazone is associated with a small increased risk of bladder cancer. Healthcare professionals should be aware of new warnings and precautions for use in at-risk patients (MHRA Aug 2011)
2. Other known side effects and safety concerns include eye disorders, heart failure, oedema and increased risk of fractures. **See pioglitazone prescribing statement**.

Sodium glucose co-transporter 2 (SGLT2) inhibitors

Empagliflozin tabs 10mg, 20mg *as per NICE TA336 & TA390 as monotherapy or in combination with other glucose-lowering agents*

1. Dapagliflozin, Canagliflozin, and Ertugliflozin have been designated as **GREY** by exceptionality defined as intolerance to the preferred 1st line choice or restricted by their licensing. Indicated for use as per their NICE TA288 and NICE TA315 respectively, in combination with other glucose-lowering agents and for use as monotherapy. See local guidance.
2. Dapagliflozin with insulin for treating type 1 diabetes is **RED** as per NICE TA597.
3. The combination products dapagliflozin and metformin (Xigduo), canagliflozin and metformin (Vokanamet) and empagliflozin and metformin (Synjardy) have been classified as **GREY**. The combination products are cheaper than the separate components and may aid compliance; however they are limited by the inability to increase to the target metformin dose.
4. SGLT2 inhibitors used in type 2 diabetes may lead to ketoacidosis. Inform patients to seek immediate medical advice if they have signs and symptoms of DKA eg. rapid weight loss, feeling sick or being sick, stomach pain, fast and deep breathing, sleepiness, a sweet smell to the breath, a sweet or metallic taste in the mouth, or a different odour to urine or sweat. Test for raised ketones in patients with signs and symptoms of DKA and stop SGLT2 inhibitor treatment immediately if DKA suspected or diagnosed (MHRA April 2016).
5. SGLT2 inhibitor treatment should be interrupted in patients who are hospitalised for major surgical procedures or acute serious medical illnesses and ketone levels measured. MHRA March 2020
6. SGLT2 inhibitors: reports of Fournier's gangrene (necrotising fasciitis of the genitalia or perineum). Rare but potentially life-threatening infection that requires urgent medical attention. MHRA February 2019.
7. Canagliflozin may increase the risk of lower-limb amputation in patients with type 2 diabetes (MHRA June 2016). Evidence does not show an increased risk for dapagliflozin and empagliflozin, but the risk may be a class effect.

6.1.4 Treatment of hypoglycaemia

Refer to the BNF

6.1.5 Treatment of diabetic nephropathy and neuropathy

Refer to the neuropathic pain guideline

6.1.6 Diagnostic and monitoring agents for diabetes mellitus

See Blood Glucose monitoring meter formulary

	Meter	Blood Glucose Test Strips	Lancets	Ketone test strips
Category A : Patients with type 2 diabetes or gestational diabetes	Tee2+	**Tee2**	CareSens	N/A
	WaveSense Jazz	**WaveSense Jazz**	AgaMatrix ultra-thin	
	Wavesense Jazz Wireless	**WaveSense Jazz**	AgaMatrix ultra-thin la	
Category B: Patients with type 1 diabetes (T1DM) - All of which require access to ketone testing (not carb counting/insulin pumps)	CareSens Dual	**CareSens PRO**	CareSens	KetoSens
	Fora Advanced pro GD40	**Fora Advanced Pro GD40**	Omnican	Advanced pro GD40
	GlucoMen Areo 2k	**GlucoMen Areo Sensor**	Glucoject plus	GlucoMen Areo Ketone Sensor
Category C: Patients with T1DM who have been taught carbohydrate counting and require the inbuilt bolus calculator feature	Accu-Chek Aviva Expert System	**Aviva (separate ketone meter needed)**	FastClix	N/A

If none of the above meters are suitable use any meter with blood glucose test strips costing less than £9 for 50 for patients in Category A; costing less than £10 for 50 blood glucose and less than £10 for 10 ketone strips for patients in Category B.

In patients where the above lancets are unsuitable consider any lancets under £3 per 100 lancets.
Safety lancets are designed so that the sharp retracts after use. These are primarily for the benefit of healthcare workers to avoid needle stick injury, **NOT** to be used by patients self-monitoring blood glucose. Unistik Touch is the recommended cost effective safety lancet.

1. NICE NG28 recommends do NOT routinely offer self-blood glucose monitoring (SBGM) for adults with type 2 diabetes. For details see local diabetes guidance.
2. NICE NG17 recommends type 1 diabetics should test their blood glucose at least 4 times a day and up to 10 times a day if any of the following apply:
   - Desired target HbA1c level is not achieved,
   - Frequency of hypoglycaemic episodes increases,
   - There is a legal requirement to do so (e.g. such as before driving , in line with DVLA guidance)
   - During periods of illness
   - Before, during and after sport
   - When planning pregnancy, during pregnancy and while breastfeeding
   - If there is a need to know blood glucose levels >4 times a day for other reasons (e.g. impaired awareness of hypoglycaemia, high-risk activities).

   Newly diagnosed patients with (or are suspected to have) type 1 diabetes may need to test for both ketones and glucose.
3. Blood glucose testing for people with diabetes who drive - see chapter 3 of "assessing fitness to drive – guide for medical professionals for the latest information.
4. Freestyle Libre is **GREY** after diabetic consultant/specialist initiation within a Derbyshire Diabetes service - see JAPC briefing

6.2.1 Thyroid Hormones

See also shared care pathology guideline

Levothyroxine (thyroxine) tabs 25, 50, 75, 100 microgram (taken preferably 30 minutes before breakfast)

1. In the elderly, and in patients with significant ischaemic heart disease or long-standing profound hypothyroidism, thyroid hormones should be commenced at a low dose and increased very cautiously, since angina and arrhythmias can be precipitated on starting treatment. If the patient is very unstable, contact an endocrinologist for advice.
2. Local endocrinologists advise to use lower doses and taper up according to bio markers and QoL markers with an informed decision with the patient. They also recognise that NICE NG145 (2019) recommends *consider* starting dose for primary hypothyroidism in adults:
   - Age under 65 and *no* history of CVD: 1.6 micrograms/kg/day (rounded to nearest 25 micrograms)

- Age 65 and over and adults with a history of CVD: 25-50 micrograms/day/with titration.

3. TSH level can take up to 6 months to normalise for people who had a very high TSH level before starting levothyroxine or a prolonged period of untreated hypothyroidism.
4. As levothyroxine (thyroxine) has a long half-life (about 7 days), full effects may not be seen for several weeks, and dosage adjustments should be made at 2-3 monthly intervals. Repeating thyroid function tests with a view to adjustment of replacement dosage any more frequently is inappropriate.
5. Follow up & monitoring for adults age 16 and over:
   - Primary hypothyroidism: TSH every 3 months until level stabilised within reference range then once a year; Consider FT4 if symptoms persist after starting levothyroxine
   - Subclinical hypothyroidism (untreated or stopped levothyroxine treatment): consider measuring TSH and FT4 once a year if they have features suggesting underlying thyroid disease e.g. thyroid surgery or raised level of autoantibodies; otherwise every 2-3 years.
6. The effects of warfarin may be potentiated when thyroid hormones are started.
7. If pregnancy is being considered, a target TSH of the bottom end of the normal range, 0.4 to 2.0, is recommended. Refer to the endocrine antenatal service if further advice needed or if patient become pregnant (urgent thyroid testing required).
8. Liothyronine in combination with levothyroxine is **AMBER** - for existing patients following review of benefit by an NHS endocrinologist and the treatment dose stabilised for 3 months. See shared care guideline. Liothyronine is classified as **Do Not Prescribe (DNP)** for new patients; **RED** when used as monotherapy for resistant depression and in doses which exceed 60 microgram per day. See local position statement.
9. Desiccated thyroid products are classified as **Do Not Prescribe (DNP)** e.g. Armour/ERFA/Nature thyroid. These are unlicensed products in the UK, derived from pig thyroid, and contain an excessive amount of L-T3 in relation to LT-4. For further information see the Liothyronine position statement.
10. Remember that a normal TSH may be found in patients with secondary hypothyroidism from pituitary disease – if clinically suspicious ask for FT4 as well.

6.2.2 Antithyroid Drugs

See also shared care pathology guideline

Carbimazole 5mg, 20mg tabs

1. Hyperthyroid patients should be referred. Carbimazole may be initiated in primary care pending a patient referred to the specialist. Check FBC and LFT before starting but not again during treatment unless there is a clinical suspicion of agranulocytosis or liver dysfunction. See UKMI drug monitoring.
2. Carbimazole: increased risk of congenital malformation, particularly when used in the first trimester and at doses above 15mg/day. Women of childbearing potential should use effective contraception during treatment with carbimazole. (MHRA Feb 2019)
3. Carbimazole: risk of acute pancreatitis. If acute pancreatitis occurs during treatment with carbimazole, immediately and permanently stop treatment. Re-exposure to carbimazole may result in life-threatening acute pancreatitis with a decreased time to onset. (MHRA Feb 2019)
4. Counsel patient to report signs and symptoms suggestive of infection, especially sore throat due to risk of neutropenia and agranulocytosis.
5. See UKMI drug monitoring in adults in primary care for baseline and on-going monitoring.
6. Hyperthyroid patients are generally more sensitive to oral anticoagulants; increased dosage of anticoagulant may be necessary as the hyperthyroidism becomes controlled. Frequent review of INR is therefore recommended.
7. Specialist review of women on thyroid medication is recommended as early as possible in pregnancy.

6.3 Corticosteroids

6.3.1 Replacement Therapy

Fludrocortisone tabs 100 microgram

6.3.2 Glucocorticoid therapy

Prednisolone tabs 1mg, 5mg
Dexamethasone tabs 2mg
Hydrocortisone tabs 10mg, 20mg

1. Corticosteroids should preferably be taken in the morning after breakfast.
2. Plain prednisolone tablets can be crushed and dispersed in water for patient with swallowing difficulties. Prednisolone soluble tablets (5mg) are classified **GREY** restricted for use in patients with fine-bore tubes only. They are considerably more expensive than the plain tablets.

3. Hydrocortisone replacement therapy – doses are usually taken with the 3 main meals of the day to mimic the normal diurnal rhythm and to avoid insomnia because of late administration of hydrocortisone.
4. MHRA Dec 2018 Hydrocortisone muco-adhesive buccal tablets: should not be used off-label for adrenal insufficiency in children due to serious risks of insufficient cortisol absorption and life-threatening adrenal crisis.
5. Steroid warning cards should be carried by those on long term treatment, both replacement and therapeutic.
   Patients on replacement therapy should be fully educated about the need to increase dosage during intercurrent illness. Abrupt withdrawal of steroids following long term therapy (> 3 weeks) should be avoided.
6. Patients on or commencing high dose oral corticosteroid long-term (15mg or more per day prednisolone or its equivalent for 3 months or more) should be offered bone protection with bisphosphonate. See local osteoporosis guideline.
7. Prolonged courses of corticosteroids can increase susceptibility to infection and serious infections can go unrecognised. Unless already immune, patients are at risk of severe chickenpox and should avoid close contact with people who have chickenpox or shingles. Precautions should also be taken against contracting measles.
8. See BNF for information on initiating corticosteroids and equivalent doses.
9. Betamethasone 500microgram soluble tablet is a cost-effective option for treating oral lichen planus (OLP) compared to soluble prednisolone.
10. Advice patients to report any blurred vision or other visual disturbances due to rare risk of central serous chorioretinopathy with corticosteroids (MHRA Aug 2017).

6.4 Sex Hormones
6.4.1 Female Sex Hormones
6.4.1.1 Oestrogens and HRT
See local menopause guideline.

6.4.1.2 Progestogens and progesterone receptor modulators

Norethisterone tabs 5mg

1. Ulipristal acetate (Esmya) 5mg tablets is classified as **Do Not Prescribe (DNP)** following suspension of the licence due to risk of serious liver injury. See MHRA March 2020. Contact patients currently taking Esmya for uterine fibroids as soon as possible and advise them to stop their treatment. Advise recent users to seek immediate medical attention if they develop signs and symptoms of liver injury and perform LFTs 2-4 weeks after stopping Esmya.

6.4.2 Male Sex Hormones and Antagonists

Testosterone preparations for androgen deficiency *follow consultant advice*
Finasteride tabs 5mg

1. Alpha blockers remain the drug of first choice for the medical management of benign prostatic hypertrophy (BPH). See section 7.4.1.
2. Choice of testosterone preparation should be based on cost-effectiveness and patient preference.
3. Dutasteride designated as **GREY** second line option to finasteride. Exceptional criteria being finasteride is not tolerated or patient does not respond to it after an adequate trial.
4. Combodart is classified as **Do Not Prescribe (DNP)** as is significantly more expensive that the individual components of dutasteride and tamsulosin.
5. Finasteride 1mg is classified as **Do Not Prescribe (DNP)** for male baldness.

6.4.3 Anabolic Steroids
No drug is recommended for this section.

6.5 Hypothalamic and pituitary hormones and anti-oestrogens
6.5.1 Hypothalamic and anterior pituitary hormones and anti-oestrogens
For growth hormones (Somatropin) follow shared care guideline
All other drugs in this section are for specialist use only.

6.5.2 Posterior pituitary hormones and antagonists
To be initiated after specialist advice

Desmopressin nasal spray 10 microgram/metered spray
Desmopressin tabs 100, 200 microgram

1. **GREEN** for nocturnal enuresis and **GREEN after specialist recommendation** for diabetes insipidus.
2. Desmopressin tablets are expensive and should be reserved for those patients who have problems with nasal preparations. The exception is primary nocturnal enuresis where only tablets are licensed. For prescribing advice see NICE CG 111 on the management of bedwetting in children and young people.
3. See BNF for CSM warning regarding hyponatraemic convulsions:
   Patients being treated for primary nocturnal enuresis should be warned to avoid fluid overload (limit fluid intake from 1 hour before until 8 hours after administration and avoid ingesting during swimming) and to stop taking desmopressin during an episode of vomiting and diarrhoea (until fluid balance normal). The risk of hyponatraemic convulsions can also be minimised by keeping the recommended starting doses and by avoiding concomitant use of drugs which increase secretion of vasopression (e.g. tricyclics)

6.6 Drugs affecting bone metabolism

6.6.1 Calcitonin and parathyroid hormone

No drug is recommended for this section.

6.6.2 Bisphosphonates and other drugs affecting bone metabolism

See local osteoporosis and bisphosphonate treatment length guideline for further detail. Calcium + Vitamin D preparations are listed in formulary chapter 9.

Alendronic acid once-weekly tabs 70mg — *1st line*
Risedronate once-weekly tabs 35mg — *2nd line*

1. Patients should be made aware of the adverse reactions associated with oral bisphosphonates (MHRA Dec 2014, Dec 2015):
   - Serious oesophageal reactions- ensure administration direction adhered to
   - Osteonecrosis of the jaw- ensure good oral hygiene & regular dental check up
   - Atypical fractures- report any thigh, hip, or groin pain
   - Osteonecrosis of external auditory canal (rare)- report any ear pain, discharge from ear or ear infection
2. Alendronic acid and risedronate should be taken whole on arising, on the same day each week on an empty stomach (at least 30 minutes before the first food, beverage or medicinal product of the day) with a full glass (not less than 200ml) of plain water only (not mineral water). Patients should be advised to stay fully upright for at least 30 minutes after swallowing the tablet.
3. Alendronic acid 70mg effervescent tablet (Binosto) is **GREY** for use in patients with dysphagia/long-term swallowing difficulties only. Patients with short-term swallowing difficulties should omit this treatment. Binosto should be fully dissolved in no less than 120ml of plain water and taken as per administration direction above. Patient should take 30ml of plain water after taking the dose.
4. Ibandronate 150mg monthly for osteoporosis is **GREY** due to lack of data on safety and effectiveness.
5. Ibandronate 50mg has been designated as **RED** for reduction of bone damage in bone metastases in breast cancer; **GREEN after consultant/specialist initiation-** use in post-menopausal women with breast cancer as per NICE NG101. Cost effective to prescribe generically. Denosumab is **AMBER** for the prevention of osteoporotic fractures in post-menopausal women and men. SCG can be found here.
6. Other drug treatments for osteoporosis include raloxifene (specialist initiation); teriparatide and zolendronic acid which are classified **RED**.

6.7 Other endocrine drugs

6.7.1 Bromocriptine and other dopaminergic drugs

Follow consultant advice. See local guideline for cabergoline and quinagolide.

6.7.2 Drugs affecting gonadotrophins

Follow consultant/specialist advice

6.7.3 Metyrapone

Follow consultant/specialist advice

6.7.4 Somatomedins

Follow consultant/specialist advice