NI Medicines Management Formulary (Adult)
BNF Chapter 6 –Endocrine System

Version Control Record

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Health and Social Care in Northern Ireland

NI Medicines Management Formulary

BNF Chapter 6 – Endocrine

(Adult)

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6.0 Endocrine

6.1 Diabetes

6.1.1 Insulins

General advice

- Refer to NICE Guideline 17 for information on the management of type 1 diabetes, NICE Guideline NG3 for information on diabetes in pregnancy, and NICE Guideline 28 for information on the management of type 2 diabetes
- Type of insulin, device and needle gauge and length should be specified. Care should be taken to **write the brand name in full** to avoid errors such as, for example, administration of Humalog® in place of Humalog® Mix25 or Humalog® Mix50
- Choice of insulin prescribed is guided by the duration of action and regimen choice, and patient choice regarding device types. The table below indicates preferred choices where all things are equal regarding device choice
- Several new high strength, fixed combination and biosimilar insulin products are now on the market. Healthcare professionals and patients need to understand the insulin strength of these products and how to use them correctly, to minimise the risk of medication errors such as the wrong insulin strength being prescribed or supplied. Insulin should only be initiated and managed by healthcare professionals with the relevant expertise and training. For further information on minimising the risk of medication error with insulin, see MHRA Drug Safety Update April 2015

	Rapid (analogue) Immediate with food	Short 15 to 30 mins before food	Intermediate (isophane)* Same time every day	Long (analogue) Same time every day	Biphasic Up to 15 mins before food	Biphasic Isophane* Up to 30 mins before food
Formulary Choices	Apidra® Humalog® 100 Humalog® 200 Novorapid® Fiasp ®	Actrapid® Humulin S®	Humulin I® Insulatard®	Abasaglar® Lantus® Levemir® Toujeo® Tresiba®100 Tresiba®200	Humalog® Mix 25 Humalog® Mix 50 Novomix® 30	Humulin® M3
***Human NPH (isophane and biphasic isophane) insulin is the preferred first-choice insulin recommended by NICE for type 2 diabetes** Insulin is available as different branded products, some of which are biosimilars. It is important they are prescribed by brand name to ensure the patient receives the intended product.						

Prescribing notes

- For most people with type 2 diabetes, long-acting insulin analogues offer no significant advantage over NPH insulin
- Consider, as an alternative to NPH insulin, using insulin detemir or insulin glargine if:
    - the person needs assistance from a carer or healthcare professional to inject insulin, and use of insulin detemir or insulin glargine 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

Insulin Pump Therapy

- Continuous subcutaneous insulin infusion (CSII) is an option for people with type 1 diabetes meeting NICE TA151 recommendations (http://www.nice.org.uk/TA151)
- CSII therapy should be initiated by a trained specialist team

6.1.2 Antidiabetic drugs

General advice

- Refer to NICE NG28 Type 2 diabetes in adults: management. A NICE visual summary and patient decision aid to discuss options with the patient can be found here
- Integrate dietary advice with a personalised diabetes management plan, including other aspects of lifestyle modification such as increasing physical activity and losing weight
- Standard-release metformin is the first-line drug treatment for adults with type 2 diabetes. Second line and add on therapies are dependent on cardiovascular status and as such an assessment should be completed to guide treatment. See NG28 on type 2 diabetes for full advice.
- Patients commencing blood glucose lowering agents may need to inform the DVLA and their vehicle insurance company. Advise patients to check with their insurer and the GOV.UK website.
- Patients with type 2 diabetes who become pregnant whilst taking antidiabetic medication should be referred urgently for specialist advice. It is safe to use metformin and insulin but all other blood glucose-lowering agents should be stopped before pregnancy. See NICE NG3 on diabetes in pregnancy.
- Visit the Think Kidneys website to find help and advice for people with Chronic Kidney Disease (CKD).

Cautions

Oral hypoglycaemics in elderly patients

- Certain aspects of type 2 diabetes in elderly patients require special consideration. Drug-induced hypoglycaemia is one of the most serious potential complications
- Risk of hypoglycaemia is increased when combination therapy is used

- Risk of hypoglycaemia is increased with renal impairment. Decreased renal function in elderly subjects is frequent and asymptomatic. Special caution should be exercised in situations where renal function may become impaired, for example when initiating antihypertensive therapy or diuretic therapy and when starting therapy with a non-steroidal anti-inflammatory drug (NSAID)

6.1.2.1Biguanides

Choice	Drug
Formulary choice	Metformin tablets 500mg (immediate release)

Prescribing Notes

- Prescribe as per NICE Guideline NG28 recommendations. See also NICE visual summary for blood glucose lowering therapy in adults with type 2 diabetes
- Metformin is the first choice oral antidiabetic drug. It is the only oral antidiabetic drug which has a proven survival advantage. It does not need to be limited to overweight patients
- Metformin may cause gastro-intestinal adverse effects; it should be started at low dose and taken with or after meals. A slow increase in dose may improve gastrointestinal tolerability.
- Hypoglycaemia is not a problem with metformin monotherapy
- Metformin prolonged release tablets are more expensive than immediate release tablets, but less expensive than other newer oral agents.
    - Metformin prolonged release tablets should be reserved for patients:
        - **unable to tolerate** immediate release metformin, or
        - with **demonstrable compliance problems** (once daily dosing)
- For patients with difficulties swallowing tablets, ‘metformin 500mg powder sachets for oral solution’ are a cost-effective

option and should be used where possible. Metformin oral solution is very expensive.

Cautions

- Metformin is a useful drug and can be safely used in mild/moderate stable CKD. It is associated with lactic acidosis, however this is rare and the risk may be overstated. It is reasonable for GPs to use metformin in people with Stage 3 CKD (eGFR >30mL/min). However, dose reduction and specialist involvement should be considered as renal function declines towards this level.

- Continuing metformin during periods of dehydration or acute illness (such as diarrhoea and vomiting) can increase the risk of lactic acidosis. This is compounded if the patient is also taking diuretics, ACE inhibitors, ARBs, NSAIDs and/or SGLT2 inhibitors in combination with metformin. Unlike acute illnesses in type 1 diabetes (where insulin treatment must be continued), stopping the drugs for a day or two will not cause any immediate problem for the patient and will protect renal function until the patient improves. See the sick day rules page for further information.

- See the June 2022 Drug Safety Update, 'Metformin and reduced vitamin b12 levels: new advice for monitoring patients at risk.'

6.1.2.2Sulfonlyureas

Choice	Drug
1st choice	Gliclazide tablets 40mg, 80mg
2nd choice	Glimepiride 1mg,2mg,3mg,4mg

Prescribing Notes

- Prescribe as per NICE Guideline NG28 recommendations. See also NICE visual summary for blood glucose lowering therapy in adults with type 2 diabetes

- Gliclazide modified release tablets should be reserved for patients with **demonstrable compliance problems**
- Patients should be informed that sulfonylureas can cause hypoglycaemia. The risk of hypoglycaemia increases with age
- Driving requirements and advice for monitoring of blood glucose in people with type 2 diabetes differ depending on medication and license group. Information may be accessed on the GOV.UK website
- Counsel patients on 'sick day guidance' with sulphonylureas – click here for further information [*add jump to 'Sick Day Rules' box below which will be hidden unless clicked on]*

6.1.2.3 Dipeptidyl peptidase-4 inhibitors (DPP-4 inhibitors)

Choice	Drug
1st choice	Sitagliptin tablets 25mg, 50mg, 100mg
2nd choice	Linagliptin tablets 5mg

Prescribing Notes

- Prescribe as per NICE Guideline NG28 recommendations. See also NICE visual summary for blood glucose lowering therapy in adults with type 2 diabetes
- DPP-4 inhibitors have been shown to have a modest impact on HbA1c with mean reduction of 0.6-0.8%**,** but there is no data on morbidity, mortality or long-term adverse effects. Review after 6 months to assess benefit
- The DPP-4 inhibitors differ in terms of their licensed indications / combinations
- Sitagliptin has the greatest clinical experience and widest range of licensed indications and has demonstrated cardiovascular safety in outcome trials.
- A small increased risk of acute pancreatitis has been identified for all licensed DPP-4 inhibitors. Patients should be informed of the characteristic symptoms of acute pancreatitis – persistent,

severe abdominal pain (sometimes radiating to the back) – and encouraged to tell their healthcare provider if they have such symptoms. Refer to MHRA advice for full details

6.1.2.4 Glitazones (thiazolidinediones)

Choice	Drug
Formulary choice	Pioglitazone tablets 15mg, 30mg, 45mg

Prescribing Notes

- Prescribe as per NICE Guideline NG28 recommendations. See also NICE visual summary for blood glucose lowering therapy in adults with type 2 diabetes
- Do not commence or continue pioglitazone in people who have heart failure, or who are at higher risk of fracture, or who have bladder cancer (or a history of)
- Liver function should be checked before initiating pioglitazone and periodically thereafter based on clinical judgement. It should not be initiated in anyone with ALT > 2.5 times the upper limit of normal or with other evidence of liver disease
- The balance of risks and benefits should be considered both before initiating and during treatment. Prescribers should review patients after three to six months (and regularly thereafter) to ensure only patients who are benefiting from treatment continue
- Competact® (pioglitazone and metformin) should be reserved for patients with **demonstrable compliance problems.** It is significantly more expensive than prescribing pioglitazone and metformin separately

Cautions

- Pioglitazone can cause significant weight gain and fluid retention. It must not be used in patients with heart failure or history of heart failure

- Macular oedema has been associated with use of pioglitazone
- Pioglitazone should not be used in patients with current or a history of bladder cancer or in patients with uninvestigated macroscopic haematuria. See EMA advice
- Do not commence/continue in people with a high risk of fracture (refer to FRAX or QFracture to assess risk)

6.1.2.5 Sodium-glucose co-transporter 2 (SGLT-2) inhibitors

Choice	Drug
Formulary choices	Canagliflozin ▼100mg, 300mg tablets Or Dapagliflozin10mg tablets Or Empagliflozin▼ 10mg, 25mg tablets

Prescribing Notes

- Prescribe as per NICE Guideline NG28 recommendations. See also NICE visual summary for blood glucose lowering therapy in adults with type 2 diabetes. Differences in licensed indications between the SGLT2 inhibitors should be considered when selecting an appropriate drug
- Glycaemic lowering efficacy of SGLT-2 inhibitors is dependent on renal function and is reduced in patients who have moderate renal impairment and likely absent in patients with severe renal impairment. Please refer to BNF for specific advice on the use of Canagliflozin, Dapagliflozin, or Empagliflozin in renal impairment
- Counsel patients on the signs and symptoms of DKA and advise them to seek immediate medical advice if they develop any of these
- Counsel patients on 'sick day guidance' with SGLT-2 inhibitors – click here for further information. [*add jump to 'Sick Day Rules' box below which will be hidden unless clicked on]*

- Dapagliflozin and empagliflozin are accepted for use as options for treating symptomatic chronic heart failure with reduced ejection fraction in adults, only if used as an add-on to optimised standard care. Treatment should only be started on the advice of a heart failure specialist. For further information see NICE TA679 and NICE TA773.
- Dapagliflozin is accepted for use as an option for treating chronic kidney disease (CKD) in adults, only if used as an add on to optimised standard care as specified in NICE TA775

Hide box below:

Sick Day Rules

- Acute kidney injury (AKI) is a sudden and recent reduction in a person's kidney function.
- Renal function is vulnerable to modest reductions in blood pressure or blood volume, including dehydration arising from diarrhoea or vomiting.
- 1 in 5 people admitted to hospital each year as an emergency has acute kidney injury.
- Patients and carers should be educated to **temporarily discontinue selected medications if they develop vomiting, diarrhoea or infections associated with increased fluid losses.** These medicines include:

  ◊ Metformin
  ◊ ACE inhibitors and angiotensin II antagonists
  ◊ Diuretics
  ◊ NSAIDs
  ◊ SGLT-2 inhibitors
  ◊ GLP-1 agonists
  ◊ Some sulfonylureas
  ◊ Trimethoprim

- See NICE CKS and Managing Multiple Medicines websites for further guidance

Cautions

- Glycosuria, osmotic symptoms and a slightly higher rate of problems due to volume depletion effects (dehydration, hypovolaemia and hypotension) are seen with SGLT-2 inhibitors. Use with caution in those on loop diuretics and frail elderly patients

- Serious cases of diabetic ketoacidosis (DKA) have been reported in patients taking an SGLT-2 inhibitor. A number of factors may predispose patients to DKA e.g. a history of pancreatitis, alcohol abuse, conditions leading to restricted food intake or severe dehydration see MHRA Drug Safety Update April 2016 for full details. Address modifiable risks for DKA before starting an SGLT2 inhibitor. For example, people who are following a very low carbohydrate or ketogenic diet may need to delay treatment until they have changed their diet.
- SGLT-2 inhibitors should be permanently discontinued post DKA
- SGT2- inhibitors should not be prescribed in type 1 diabetes
- Canagliflozin may increase the risk of lower-limb amputation (mainly toes) in patients with type 2 diabetes. Evidence does not show an increased risk for dapagliflozin and empagliflozin, but the risk may be a class effect. Preventive foot care is important for all patients with diabetes. See MHRA advice for healthcare professionals
- There have been reports of Fournier's gangrene (necrotising fasciitis of the genitalia or perineum) with SGLT2 inhibitors. If Fournier's gangrene is suspected, stop the SGLT2 inhibitor and start treatment urgently (including antibiotics and surgical debridement). Fournier's gangrene is a rare but potentially life-threatening infection that requires urgent medical attention. See MHRA for further details.

6.1.2.6 GLP-1 mimetic (injectable)

Note – there is currently a supply issue affecting Trulicity® and Ozempic®. No new patients should be initiated on these products at this time. Further information available here.

Choice	Drug
Daily Injection	Liraglutide (Victoza®) injection 6mg/ml **Prescribe by Brand Name**
Weekly Injection	Dulaglutide (Trulicity®) 0.75mg/0.5ml, 1.5mg/0.5ml, 3mg/0.5ml, 4.5mg/0.5ml solution for injection **Prescribe by Brand Name**
	OR
	Semaglutide (Ozempic) 0.25mg/0.16ml, 0.5mg/0.37ml, 1mg/0.75ml soluition for injection **Prescribe by Brand Name**
Oral tablets	Semaglutide (Rybelsus) 3mg, 7mg 14mg

Prescribing Notes

- Prescribe as per NICE Guideline NG28 recommendations. See also NICE visual summary for blood glucose lowering therapy in adults with type 2 diabetes
- Stop DPP-4 inhibitor if initiating GLP-1 agonist (the combination is unlikely to provide synergistic effects beyond monotherapy with either agent)
- The formulary covers the use of GLP-1 mimetics in **type 2 diabetes only**. GLP-1 mimetics **should not be prescribed** for managing overweight and obesity until a specialist weight management service (tier 3) has been established. See correspondence for further details
- To prevent waste, please avoid prescribing large quantities. GLP-1 mimetics require refrigeration and are expensive. One month's supply should be adequate for most patients – refer to GLP-1 agonists supplement for further details on appropriate quantities

- **Stopping rules with GLP-1 mimetics:** NICE state only continue GLP‑1 mimetic therapy if the person with type 2 diabetes has had a beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA1c and a weight loss of at least 3% of initial body weight in 6 months)
- Gastric emptying may be delayed. Therefore the rate and extent of absorption of other oral drugs administered at the same time may be affected
- Doses of concomitant sulfonylurea may need to be reduced when a GLP-1 mimetic is started
- Upper gastrointestinal side effects such as nausea are common with GLP-1 mimetic therapy
- There are rare reports of acute pancreatitis in patients using these drugs. GLP-1 mimetics should be avoided in patients considered to be at high risk of pancreatitis. Patients and their carers should be told how to recognise signs and symptoms of pancreatitis
- Thyroid adverse events, including increased blood calcitonin, goitre and thyroid neoplasm, have been rarely reported in clinical trials with liraglutide, particularly in patients with pre-existing thyroid disease

Cautions

- Diabetic ketoacidosis has been reported in patients with type 2 diabetes on a combination of a GLP-1 receptor antagonist and insulin who had doses of concomitant insulin rapidly reduced or discontinued. See MHRA for further details

6.1.4 Treatment of hypoglycaemia

Choice	Drug	Dosage
Formulary choices	Glucose (oral) Or Glucagon 1mg vial (GlucaGen® HypoKit) Or Glucose intravenous infusion	See information below Dose:See BNF As per local trust policy

Prescribing Notes

Prevention and management of hypoglycaemia

Acute management:

- Hypoglycaemia is defined as blood glucose of less than 4mmol/L (if not < 4mmol/L but the patient is symptomatic, give a small carbohydrate snack for symptom relief)
- If the patient is conscious, capable and co-operative, give 15-20g quick acting carbohydrate of the patient's choice where possible. Examples are given in on the Diabetes UK website under 'treating and managing a hypo'
- If the patient is conscious but not capable and/or co-operative, give 2 tubes of oral glucose gel (squeezed into mouth between teeth and gums) OR glucagon 1mg IM
- Once capillary blood glucose (CBG) is above 4mmol/L, give 20g of long acting carbohydrate, e.g. 2 digestive biscuits or a slice of bread or next meal if due. If IM glucagon has been used, give 40g of long acting carbohydrate in order to replenish glycogen stores
- Adults with decreased level of consciousness due to hypoglycaemia who are unable to take oral treatment safely should be:
  - given intramuscular glucagon by a trained user (intravenous glucose may be used by professionals skilled in obtaining intravenous access)

- monitored for response at 10 minutes, and then given intravenous glucose if the level of consciousness is not improving significantly
- then be given oral carbohydrate when it is safe to administer it, and placed under continued observation by a third party who has been warned of the risk of relapse

6.1.6 Diagnostic and monitoring agents for diabetes mellitus

ADD LINK TO POLICIES

6.2 Thyroid and antithyroid drugs and parathyroid disease

6.2.1 Hypothyroidism

Choice	Drug
Formulary choice	Levothyroxine tablets 25micrograms, 50micrograms, 100 micrograms

Prescribing Notes

- Refer to NICE guideline Thyroid disease: assessment and management
- Prior to treatment, it is important to establish that thyroid stimulating hormone (TSH) is elevated, thus confirming primary hypothyroidism. A normal or low TSH may suggest pituitary or hypothalamic disease for which specialist referral is necessary

Levothyroxine monitoring (see SPS for full details):

- After started or dose changed:
  - TSH from 6 weeks; repeated every 3 months
  - Consider (where symptoms are ongoing) – Free T4 from 6 weeks; repeated every 3 months
- Ongoing once stable (2 similar measurements within the reference range, 3 months apart); TSH annually
- Alteration in levothyroxine absorption may occur with introduction of other medication such as iron and calcium preparations or drugs altering gastric acid, such as proton pump inhibitors. Thyroid function should be checked 6 weeks after starting such treatment

- Pregnant patients with hypothyroidism should be referred to a specialist for titration of levothyroxine regimens, although it is recommended that upon confirmation of pregnancy, due to the early increase in levothyroxine requirements, levothyroxine dosage is doubled on Saturdays and Sundays until early review by a specialist
- Although generic prescribing remains appropriate for the majority of patients, a small proportion report re-emergence of symptoms

after switching between levothyroxine products and hence may benefit from consistent prescribing of a specific brand. See MHRA for further information.

- Liothyronine should only be used on the recommendation of a Health Service endocrine specialist in secondary care; prescribers in primary care should not initiate liothyronine. For further information please see Shared Care Guideline
- Where prescribing of liothyronine is appropriate, the initiating specialist in secondary care should recommend prescribing of liothyronine capsules instead of tablets. For further information refer to SPPG letter

6.2.2 Hyperthyroidism

General advice

- Refer to NICE guideline Thyroid disease: assessment and management
- Radioactive iodine is increasingly used as first choice for thyrotoxicosis. Treatment should be under specialist care

6.2.2.1Antithyroid drugs

Choice	Drug
Formulary choice	Carbimazole tablets 5mg, 20mg **To be initiated on specialist advice**

Prescribing Notes

- Carbimazole tablets 10mg and 15mg are very high cost (£81.32 for 10mg and £239.66 for 15mg – June 23 Drug Tariff)
- Refer to NICE guideline Thyroid disease: assessment and management

- Carbimazole should be initiated under specialist advice to ensure the correct diagnosis is made and that treatment is appropriate. Carbimazole can be given by titration method or in a block and replacement regimen
- Carbimazole is a finite treatment and guidance should be given to patients on the proposed treatment duration
- Carbimazole has rarely been associated with bone marrow suppression and treatment should be stopped promptly if there is clinical or laboratory evidence of neutropenia. Patients should be asked to report symptoms and signs suggestive of infection, especially sore throat. A white blood cell count should be performed if there is any clinical evidence of infection
- Propylthiouracil may be an alternative for patients who suffer sensitivity reactions to carbimazole and similar advice regarding neutropenia should be given when using this drug. Prescribe 50mg tablets where appropriate (propylthiouracil 25mg and 100mg tablets are very high cost)
- Severe hepatic reactions have been reported with propylthiouracil, including fatal cases and cases requiring liver transplant. Liver function should be monitored and propylthiouracil discontinued if significant liver-enzyme abnormalities develop
- Patients with hyperthyroidism planning a pregnancy should be referred to a specialist endocrine team. Propylthiouracil is the drug of choice during early pregnancy and breastfeeding. Patients maintained on carbimazole should be switched to propylthiouracil under specialist guidance

Cautions

- Carbimazole is associated with an increased risk of congenital malformations, especially when administered in the first trimester of pregnancy and at high doses. Women of childbearing potential should use effective contraception during treatment with carbimazole. See MHRA for further details https://www.gov.uk/drug-safety-update/carbimazole-increased-

risk-of-congenital-malformations-strengthened-advice-on-contraception

- Cases of acute pancreatitis have been reported very infrequently during treatment with carbimazole. 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. See MHRA for further details https://www.gov.uk/drug-safety-update/carbimazole-risk-of-acute-pancreatitis

6.2.2.2 Beta-blockers

Choice	Drug
Formulary choice	Propranolol tablets 10mg, 40mg Or Propranolol MR capsules 80mg, 160mg

Prescribing Notes

- Refer to NICE guideline Thyroid disease: assessment and management
- Beta blockade can be withdrawn once hyperthyroidism is controlled (2-6 weeks), and the patient maintained on carbimazole
- Diltiazem may be considered as an alternative if a beta-blocker is contraindicated (under specialist advice)

6.2.3 Parathyroid disease

6.2.3.1 Hyperparathyroidism

Prescribing Notes

- Primary hyperparathyroidism: parathyroid surgery is the treatment of choice in most symptomatic patients. Medical management is used for those for whom surgery is not suitable. Cinacalcet is occasionally used, under specialist supervision only. Refer to NICE guideline NG132
- Secondary hyperparathyroidism: medical management is the mainstay of treatment and the underlying condition needs to be treated
- A shared care guideline for cinacalcet is available here
- All patients with severe hypercalcaemia (>3mmol/l) should be referred for urgent specialist input

6.3 Corticosteroids

6.3.1 Replacement therapy

Choice	Drug
Formulary choices	**Replacement therapy (Mineralocorticoid) –** Fludrocortisone tablets 100 micrograms **(Glucocorticoid**) – Hydrocortisone tablets 10mg

Prescribing Notes

- In Addison's disease (primary adrenal failure), hydrocortisone (glucocorticoid) and fludrocortisone (mineralocorticoid) are given in combination
- Addison's Disease Self-help group supply patient leaflets with clear instructions and pictures on how to administer intramuscular hydrocortisone in an emergency
- In secondary adrenal failure (hypopituitarism), hydrocortisone is given alone, as a mineralocorticoid is not usually required
- Patients deficient in glucocorticoids do not respond adequately to stress and should be advised to double the replacement dose of hydrocortisone for several days if significantly unwell. They should all be encouraged to wear a Medi-Alert bracelet. More serious illnesses or gastro-intestinal disturbances necessitate prompt parenteral hydrocortisone
- A Steroid Emergency Card for Northern Ireland has been developed in response to the National Patient Safety Alert that was issued in August 2020. The alert highlights the dangers associated with adrenal insufficiency for patients taking corticosteroid medication, and recommends that all eligible patients prescribed (or initiated on) steroids are assessed and where necessary issued with a Steroid Emergency Card. Community pharmacies and GP practices can order these from pharmacystationeryorders@hscni.net

6.3.2 Glucocorticoid therapy

Choice	Drug
Formulary choices	Prednisolone tablets 1mg, 5mg; **Note: Soluble tablets are high cost** Or Dexamethasone tablets 500micrograms, 2mg; injection 3.8mg/mL, 3.3mg/mL Or Hydrocortisone sodium succinate 100mg powder and solvent for solution for injection vials Or Methylprednisolone tablets 2mg, 4mg, 16mg, 100mg; Methylprednisolone sodium succinate (Solu-Medrone®) vials 40mg, 125mg, 500mg, 1g, 2g; Intramuscular depot: Methylprednisolone acetate (Depo-Medrone®) vials 40mg/mL, 80mg/2mL, 120mg/3mL

Prescribing Notes

- Corticosteroids are used in the treatment of a wide range of conditions. Doses of corticosteroids used vary widely in different diseases and in different patients. Refer to relevant section of BNF
- Steroid cards should be given when appropriate. Community pharmacies and GP practices can order these from pharmacystationeryorders@hscni.net
- An additional Steroid Emergency Card for Northern Ireland has been developed in response to the National Patient Safety Alert that was issued in August 2020. The alert highlights the dangers associated with adrenal insufficiency for patients taking corticosteroid medication, and recommends that all eligible patients prescribed (or initiated on) steroids are assessed and

where necessary issued with a Steroid Emergency Card. Community pharmacies and GP practices can order these from pharmacystationeryorders@hscni.net

- Consider osteoporosis prophylaxis for patients receiving 7.5mg or more of prednisolone daily (or equivalent) for longer than 3 months. For further details refer to NOGG guideline. No osteoporosis prophylaxis is indicated when corticosteroids are used as physiological replacement therapy for the management of adrenal insufficiency, unless replacement doses exceed hydrocortisone 30mg per day, prednisolone 7.5mg per day or equivalent. See BNF chapter 6
- Care should be taken in reducing pharmacological doses of glucocorticoids if the patient has been treated for longer than 3 weeks, to avoid cortisol insufficiency due to prolonged suppression of the hypothalamic-pituitary-adrenal (HPA) axis
- In terms of their anti-inflammatory properties, approximately 20mg hydrocortisone is equivalent to 5mg prednisolone or 750 micrograms dexamethasone. See BNF chapter 6

Equivalent anti-inflammatory doses of oral corticosteroids – see table

6.4 Sex hormones

6.4.1.1 Hormone replacement therapy (HRT) for menopausal symptoms

General advice

- See NICE NG23 Menopause: diagnosis and management
- See CKS Menopause for practical guidance on best practice
- **In most women with troublesome symptoms the benefits of HRT outweigh the risks.** Discuss risks and benefits prior to starting (refer to links above)
- Women with a premature menopause (<40 years of age) should be referred to a specialist HRT clinic. HRT is normally recommended until the average age of the natural menopause (52 years of age)
- Specialist advice on HRT regimen is required for women who have had a subtotal hysterectomy or who have a history of endometriosis
- HRT preparations should be **brand prescribed** to aid product identification
- For use of HRT in osteoporosis prophylaxis refer to *(ADD JUMP to 6.6 (c))*
- Tibolone is a synthetic steroidal compound with oestrogenic, progestogenic, and androgenic activity. It is licensed for the treatment of oestrogen deficiency symptoms in postmenopausal women, more than one year after menopause

For PDF click here *[add link- see accompanying document for consultation purposes]*

6.4.1.1 a) Women who have not had a hysterectomy

HRT shortages – if products are unavailable see SPS and BMS websites for current availability and alternative products

Sequential combined (oral)

Choice	Drug
1st choice	Elleste-Duet® 1mg, 2mg tablets (estradiol and norethisterone) Or Femoston® 1/10, 2/10 tablets (estradiol and dydrogesterone)

Sequential combined (transdermal)

Choice	Drug
1st choice	Evorel® Sequi patches: combination pack of 4 Evorel® 50 patches (estradiol 50micrograms/24hours) and 4 Evorel® Conti patches (estradiol 50micrograms/24hours) and norethisterone acetate 170micrograms/24hours

Continuous combined (oral)

Choice	Drug
1st choice	Femoston® - conti 0.5mg/2.5mg tablets; 1mg/5mg tablets (estradiol and dydrogesterone)
	or
	Kliovance® tablets (estradiol 1mg and norethisterone 500micrograms)
	or
	Kliofem® tablets (estradiol 2mg and norethisterone 1mg)
	or
	Bijuve® 1mg/100mg capsules (estradiol 1 mg and progesterone 100mg)
	or
	Indivina® 1mg/2.5mg tablets;1mg/5mg tablets; 2mg/5mg tablets (estradiol and medroxyprogesterone acetate)

Continuous combined (transdermal)

Choice	Drug
1st choice	Evorel® Conti patches (estradiol 50micrograms/24hours and norethisterone 170micrograms/24hours (matrix patch))

Prescribing Notes

- HRT preparations should be **brand prescribed** to aid product identification
- It is recommended that the lowest dose of HRT based on relieving menopausal symptoms should be prescribed
- Women with an early menopause (<45 years), especially if surgically induced, require the higher dose of oestrogen to control their vasomotor symptoms and for bone protection
- Women who commence sequential combined HRT should expect a monthly bleed, although a small percentage of women won't have any bleeding. Women who commence continuous combined HRT may experience some irregular light bleeding for 4-6 months
- Refer to a gynaecology or menopause service if:
    - Heavy, prolonged bleeds with HRT, or
    - Lighter bleeding which continues for >6 months after commencing continuous combined HRT
- Amenorrhoea with HRT is not a risk for endometrial cancer and does not require investigation
- Progestogenic side effects (women typically describe symptoms similar to 'PMS') may resolve within a few months. For persistent or troublesome symptoms consider:
    - Changing the progestogen type, e.g. to a less androgenic one such as dydrogesterone
    - Changing the route of delivery e.g. oral to transdermal
    - 3 monthly bleed preparation (Tridestra®)
    - Using a Mirena® IUS as the progestogen component of HRT
- In Northern Ireland, micronised progesterone (Utrogestran 100mg oral capsules) is accepted for adjunctive use with oestrogen as HRT in line with SMC2529. It provides an additional treatment choice for women requiring combined HRT but unsuitable for or intolerant of standard combination preparations listed in the NI Formulary choices.

- The licensed dose is 200mg at night for 12 days (Day 15-26 of cycle) or 100mg at bedtime from Day 1-25 of cycle.
- Alternatively, women may be advised to take Utrogestan 200mg at night for the first 12 days of each calendar month (if irregular/infrequent cycles) or 100mg on a continuous basis. This dosing regimen differs slightly from licensed doses but is endorsed by the BMS as it may be more straightforward to take in this way

6.4.1.1 b) Women who have had a hysterectomy or who have a Mirena® Intra Uterine System (ISU) in situ for < 5 years

HRT shortages – if products are unavailable see SPS and BMS websites for current availability and alternative products Unopposed oestrogens (oral)

Choice	Drug
1st choice	Elleste-Solo® 1mg, 2mg (estradiol) tablets
	Or
	Zumenon 1mg, 2mg (estradiol) tablets

Unopposed oestrogens (transdermal)

Choice	Drug
1st choice	Evorel® patches 50micrograms (or 25micrograms, 75micrograms, 100micrograms/24 hours) (estradiol)

Unopposed oestrogens (gel)

Choice	Drug
1st choice	Oestrogel® 0.06% gel
	Or
	Sandrena gel sachets 500mcg, 1mg

Unopposed oestrogens (spray)

Choice	Drug
1st choice	Lenzetto 1.53mg/dose transdermal spray

Prescribing Notes

- HRT preparations should be brand prescribed to aid product identification
- It is recommended that the lowest dose of HRT based on relieving menopausal symptoms should be prescribed
- For Women with an early menopause (<45 years), consider the higher dose of oestrogen for bone protection
- Mirena® is licensed for 4 years for endometrial protection during oestrogen replacement therapy (i.e. Mirena® provides the progestogen component of HRT). In practice, it is used for up to 5 years, providing the woman is not experiencing bleeding

Preparations for vaginal atrophy

See section 7.2.1

6.4.2 Male sex hormones

Prescribing Notes

- Testosterone is an amber drug. A shared care guideline is available here
- Testosterone supplementation can be considered for post-menopausal women with low sexual desire if oestrogen (+/- progestogen) HRT alone is not effective (note off-label use). See BMS and NICE CKS for further information on initiation and ongoing monitoring

6.6 Drugs affecting bone metabolism

General Notes

- Refer to NICE Pathway – Osteoporosis and the NOGG clinical guideline
- Consider risk assessment using FRAX or QFracture
- Consider falls prevention measures. The greatest risk of fracture in the elderly comes from falls, not osteoporosis
- For the management of glucocorticoid-induced osteoporosis, refer to the NOGG guideline.
- Male osteoporosis is often secondary to other medical conditions; consider specialist referral if a secondary cause is suspected or if a z score is less than -2

6.6.1 Drugs for the treatment and management of Osteoporosis

6.6.1.1Calcium and Vitamin D

Choice	Drug	Dosage
1st choice	Adcal-D3® Caplets (300mg calcium and 200IU vitamin D)	Dose: Two tablets to be taken twice a day
	or	
	Accrete D3® film-coated tablets (600mg calcium and 400IU vitamin D)	Dose: One tablet twice a day
	or	
	Accrete D3® One a Day 1000mg / 880 IU Chewable Tablets	Dose: One tablet daily
2nd Choice **Reserve for swallowing difficulties**	Adcal-D3® Dissolve effervescent tablets(1500mg calcium carbonate/ 400 IU vitamin D)	Dose: 1 tablet twice a day

Prescribing Notes

- Supplementation with calcium and vitamin D alone has been shown to reduce fracture rates in housebound elderly patients

without previous fracture. Evidence in other patient groups is lacking

- Those with, or at risk of, osteoporosis should maintain adequate supply of calcium and vitamin D. If deficiency is suspected, this should be corrected by increasing dietary intake or taking supplements.
    - Dietary sources of calcium are the preferred option, see Royal Osteoporosis Society website for information on calcium rich food and a calcium calculator
    - With the introduction of licensed vitamin D preparations, many clinicians are moving away from the use of combined calcium and vitamin D preparations in favour of single agent vitamin D preparations (in patients who are calcium replete)
- For vitamin D guidance, see section 9.6.4 and for single agent calcium supplements, see section 9.5.1.1 (*add jumps)*

6.6.1.2 Bisphosphonates

Choice	Drug	Dose
Formulary choices	Alendronic acid tablets 70mg	70mg once weekly. Take with a full glass of water on an empty stomach at least 30minutes before breakfast and other medication (e.g calcium supplements). Stand or sit upright for at least 30mins and do not lie down until after breakfast.
	OR	
	Risedronate sodium tablets 35mg	35mg once weekly.Take with a full glass of water on an empty stomach at least 30minutes before breakfast and other medication (e.g calcium supplements). Stand or sit upright for at least 30mins and do not lie down until after breakfast.

Prescribing Notes

- See NICE TA464 Bisphosphonates for treating osteoporosis
- People receiving drug treatment for osteoporosis (unless confident that the patient is receiving an adequate dietary intake) should receive a vitamin D supplement (+/- calcium). Click here for formulary choices – *add jump*
- Before starting treatment, calcium, phosphate, alkaline phosphatase and renal function should be checked
- Due to concerns about these potential side effects of long-term bisphosphonate therapy, patients should be assessed for benefit and on-going need after 5 years of oral bisphosphonate therapy:
    - Where a 'drug holiday' is deemed appropriate, note this is a **pause** not a stop.
        - For risedronate and ibandronate, place the patient on a 1-2year bisphosphonate drug holiday
        - For alendronic acid place the patient on a 2-3year drug holiday
        - Once drug holiday period has elapsed, reassess fracture risk and restart treatment if appropriate
    - For those patients who are then deemed at continued high risk of fracture and who continue to receive treatment, local expert opinion is that no patient should receive continuous oral bisphosphonate therapy for more than 10 years without referral to a specialist
    - Refer to Osteoporosis Medication Review Tool and NOGG guideline for further information
- **GI Side Effects**
    - Bisphosphonates have complex administration instructions. GI side effects are minimised by following these instructions
    - Oral bisphosphonates should be avoided in anyone with a history of oesophageal stricture or severe oesophagitis and in anyone who is unable to follow the

administration instructions e.g. unable to sit upright after swallowing the tablet
    - Risedronate may be preferable in those patients that have a history of (recent) proven peptic ulcer disease, active GORD, or develop significant GI side effects on alendronate. See BNF for risedronate prescribing information
    - PPIs are unlikely to be helpful as this is due to a local irritant effect
- Long term adherence is poor and patients should be encouraged to continue taking their bisphosphonate
- Monthly oral ibandronate is an alternative option for younger patients who have predominantly spinal osteoporosis (no data is available for hip fracture)
- The intravenous bisphosphonates zoledronic acid and ibandronic acid are red list drugs for specialist use only

Cautions

- Renal impairment:
    - Alendronate should be avoided if Creatinine Clearance <35mL/min
    - Risedronate should be avoided if Creatinine Clearance < 30mL/min
- High dose IV bisphosphonate therapy is associated with osteonecrosis of the jaw. It is rarely associated with oral bisphosphonates. History of poor dentition is a risk factor. Refer to MHRA advice
- Atypical femoral fracture has been reported rarely with bisphosphonate treatment, mainly in patients receiving long-term treatment for osteoporosis. Patients should be advised to report any thigh, hip or groin pain. The need to continue bisphosphonate treatment for osteoporosis should be re-evaluated periodically based on the benefits and potential risks of bisphosphonate therapy for individual patients, particularly after 5 or more years of use and should not exceed 10 years. See MHRA warning for further details

- Osteonecrosis of the external auditory canal has been reported very rarely with bisphosphonates. For full details see MHRA warning

6.6.1.3 Other drug therapies used in osteoporosis

Denosumab

- Denosumab is an amber list drug indicated for post-menopausal women at increased risk of fracture. Further details can be found in the Shared Care Guideline
- Withdrawal of denosumab is associated with a rapid fall in bone density and the potential for rebound vertebral fractures. Patients should not stop denosumab without specialist review
- Given the difficulties in stopping denosumab treatment, particularly careful consideration is needed before starting denosumab in younger postmenopausal women, and men

Hormone Replacement Therapy (HRT) *add jump to HRT section*

- HRT should be considered for women who have experienced a premature menopause to reduce their risk of osteoporotic fractures and for relief of menopause symptoms
- HRT should not be considered first-line therapy for the long-term prevention of osteoporosis in women over 50 years of age. It is an option where other therapies are contraindicated, cannot be tolerated, or if there is a lack of response. For most women the benefits of HRT outweigh the small risks up to the age of 60 years and women will gain bone protection if they are taking HRT for symptom relief

Raloxifene

- Raloxifene is an alternative option for patients for the secondary prevention of osteoporotic fractures in postmenopausal women in line with NICE TA161. It is not recommended for primary prevention

- Raloxifene has not been shown to prevent non-vertebral fractures

Red list treatments for specialist use only

- Romosozumab
- Teriparatide

Anabolic drug treatments (romosozumb or teriparatide) are sometimes considered as first-line treatment options (before bisphosphonates) in postmenopausal women at very high fracture risk, particularly in those with vertebral fractures, where NICE criteria are met

Strontium

- When other antiresorptive and anabolic treatments are contraindicated or not tolerated, strontium can be used to treat postmenopausal osteoporosis and men with severe osteoporosis, provided the risk-benefit in relation to cardiovascular and thromboembolic events is considered. Initiation by a specialist who is an expert in osteoporosis management is advised

6.7.4 Growth hormone disorders

The primary treatment of acromegaly is usually pituitary surgery. Management and treatment requires specialist involvement.

Prescribing Notes

- Refer to BNF Chapter 6 for drugs used in the management of growth hormone disorders
- See BNF Chapter 8 for the use of the somatostatin analogues (lanreotide, octreotide and pasireotide)
- A shared care guideline for lanreotide is available here
- A shared care guideline for octreotide is available here