Drug monitoring

The tables below show the monitoring requirements of common drugs. It should be noted these are basic guidelines and do not relate to monitoring effectiveness of treatment (e.g. Checking lipids for patients taking a statin)

Cardiovascular drugs

Drug	Main monitoring parameters	Details of monitoring
Statins	LFT	LFTs at baseline, 3 months and 12 months
ACE inhibitors	U&E	U&E prior to treatment U&E after increasing dose U&E at least annually
Amiodarone	TFT, LFT	TFT, LFT, U&E, CXR prior to treatment TFT, LFT every 6 months

Rheumatology drugs

Drug	Main monitoring parameters	Details of monitoring
Methotrexate	FBC, LFT, U&E	The Committee on Safety of Medicines recommend 'FBC and renal and LFTs before starting treatment and repeated weekly until therapy stabilised, thereafter patients should be monitored every 2-3 months'
Azathioprine	FBC, LFT	FBC, LFT before treatment FBC weekly for the first 4 weeks FBC, LFT every 3 months

Neuropsychiatric drugs

Drug	Main monitoring parameters	Details of monitoring
Lithium	Lithium level, TFT, U&E	TFT, U&E prior to treatment Lithium levels weekly until stabilised then every 3 months TFT, U&E every 6 months
Sodium valproate	LFT	LFT, FBC before treatment LFT 'periodically' during first 6 months

Endocrine drugs

Drug	Main monitoring parameters	Details of monitoring
Glitazones	LFT	LFT before treatment LFT 'regularly' during treatment

Aspirin

Aspirin works by blocking the action of both cyclooxygenase-1 and 2. Cyclooxygenase is responsible for prostaglandin, prostacyclin and thromboxane synthesis. The blocking of thromboxane A2 formation in platelets reduces the ability of platelets to aggregate which has lead to the widespread use of low-dose aspirin in cardiovascular disease. Until recent guidelines changed all patients with established cardiovascular disease took aspirin if there was no contraindication. Following the 2010 technology appraisal of clopidogrel this is no longer the case*.

Two recent trials (the Aspirin for Asymptomatic Atherosclerosis and the Antithrombotic Trialists Collaboration) have cast doubt on the use of aspirin in primary prevention of cardiovascular disease. Guidelines have not yet changed to reflect this. However the Medicines and Healthcare products Regulatory Agency (MHRA) issued a drug safety update in January 2010 reminding prescribers that aspirin is not licensed for primary prevention.

What do the *current* guidelines recommend?

- first-line for patients with ischaemic heart disease and following a TIA**

Potentiates

- oral hypoglycaemics
- warfarin
- steroids

*NICE now recommend clopidogrel first-line following an ischaemic stroke (but not for TIAs) and for peripheral arterial disease

**alongside dipyridamole

Cushing's syndrome: causes

ACTH dependent causes

- Cushing's disease (80%): pituitary tumour secreting ACTH producing adrenal hyperplasia
- ectopic ACTH production (5-10%): e.g. small cell lung cancer

ACTH independent causes

- iatrogenic: steroids
- adrenal adenoma (5-10%)
- adrenal carcinoma (rare)
- Carney complex: syndrome including cardiac myxoma
- micronodular adrenal dysplasia (very rare)

Pseudo-Cushing's

- mimics Cushing's
- often due to alcohol excess or severe depression

- causes false positive dexamethasone suppression test or 24 hr urinary free cortisol
- insulin stress test may be used to differentiate

Opioid misuse

Opioids are substances which bind to opioid receptors. This includes both naturally occurring opiates such as morphine and synthetic opioids such as buprenorphine and methadone.

Features of opioid misuse

- rhinorrhoea
- needle track marks
- pinpoint pupils
- drowsiness
- watering eyes
- yawning

Complications of opioid misuse

- viral infection secondary to sharing needles: HIV, hepatitis B & C
- bacterial infection secondary to injection: infective endocarditis, septic arthritis, septicaemia, necrotising fasciitis
- venous thromboembolism
- overdose may lead to respiratory depression and death
- psychological problems: craving
- social problems: crime, prostitution, homelessness

Emergency management of opioid overdose

- IV or IM naloxone: has a rapid onset and relatively short duration of action

Harm reduction interventions may include

- needle exchange
- offering testing for HIV, hepatitis B & C

Management of opioid dependence

- patients are usually managed by specialist drug dependence clinics although some GPs with a specialist interest offer similar services
- patients may be offered maintenance therapy or detoxification
- NICE recommend methadone or buprenorphine as the first-line treatment in opioid detoxification
- compliance is monitored using urinalysis

- detoxification should normally last up to 4 weeks in an inpatient/residential setting and up to 12 weeks in the community

Side-effects of common drugs: anti-hypertensives

The table below summarises characteristic (if not necessarily the most common) side-effects of drugs used to treat hypertension

Drug	Side-effect
ACE inhibitors	• Cough • Hyperkalaemia
Bendroflumethiazide	• Gout • Hypokalaemia • Hyponatraemia • Impaired glucose tolerance
Calcium channel blockers	• Headache • Flushing • Ankle oedema
Beta-blockers	• Bronchospasm (especially in asthmatics) • Fatigue • Cold peripheries
Doxazosin	• Postural hypotension

Prescribing guidance

The BNF issues guidance on good practice when prescribing, selected points include:

- drugs should generally be prescribed by their generic name, except for certain preparations where the clinical effect may differ - please see the list below
- when writing numbers unnecessary decimal points should be avoided e.g. 250 ml not 0.25 l

Drugs which should be prescribed by brand

- modified release calcium channel blockers
- antiepileptics
- ciclosporin and tacrolimus
- mesalazine
- lithium
- aminophylline and theophylline
- methylphenidate
- CFC-free formulations of beclometasone
- dry powder inhaler devices

Digoxin and digoxin toxicity

Digoxin is a cardiac glycoside now mainly used for rate control in the management of atrial fibrillation. As it has positive inotropic properties it is sometimes used for improving symptoms (but not mortality) in patients with heart failure.

Mechanism of action

- decreases conduction through the atrioventricular node which slows the ventricular rate in atrial fibrillation and flutter
- increases the force of cardiac muscle contraction due to inhibition of the Na^+/K^+ ATPase pump

Digoxin toxicity

Plasma concentration alone does not determine whether a patient has developed digoxin toxicity. The BNF advises that the likelihood of toxicity increases progressively from 1.5 to 3 mcg/l.

Features

- generally unwell, lethargy, nausea & vomiting, anorexia, confusion, yellow-green vision
- arrhythmias (e.g. AV block, bradycardia)

Precipitating factors

- classically: hypokalaemia*
- increasing age
- renal failure
- myocardial ischaemia
- hypomagnesaemia, hypercalcaemia, hypernatraemia, acidosis
- hypoalbuminaemia
- hypothermia
- hypothyroidism
- drugs: amiodarone, quinidine, verapamil, spironolactone (compete for secretion in distal convoluted tubule therefore reduce excretion)

Management

- Digibind
- correct arrhythmias
- monitor potassium

*hyperkalaemia may also worsen digoxin toxicity, although this is very small print

Bendroflumethiazide

Bendroflumethiazide (bendrofluazide) is a thiazide diuretic which works by inhibiting sodium absorption at the beginning of the distal convoluted tubule (DCT). Potassium is lost as a result of more sodium reaching the collecting ducts. Bendroflumethiazide has a role in the treatment of mild heart failure although loop diuretics are better for reducing overload. The main use of bendroflumethiazide was in the management of hypertension but recent NICE guidelines now recommend other thiazide-like diuretics such as indapamide and chlortalidone.

Common adverse effects

- dehydration
- postural hypotension
- hyponatraemia, hypokalaemia, hypercalcaemia
- gout
- impaired glucose tolerance
- impotence

Rare adverse effects

- thrombocytopenia
- agranulocytosis
- photosensitivity rash
- pancreatitis

(An eagle eyed user noticed that this entry is very similar to the Wikipedia one. I can assure you that the material has been cut-and-pasted from passmedicine to Wikipedia, and not vice-versa! Note the English spellings of hyponatraemia etc. Check the Wikipedia 'history' page for more details.)

Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk >= 20%
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering*

	Total cholesterol (mmol/l)	**LDL cholesterol**
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

*current NICE guidelines do not recommend a target cholesterol in primary prevention

Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

Clinical uses

- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metatases

Adverse effects

- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw
- increased risk of atypical stress fractures of the proximal femoral shaft in patients taking alendronate

The BNF suggests the following counselling for patients taking oral bisphosphonates

- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

Side-effects of common drugs: antibiotics

The table below summarises characteristic (if not necessarily the most common) side-effects of drugs used antibiotics

Drug	Side-effect
Amoxicillin	• Rash with infectious mononucleosis
Co-amoxiclav	• Cholestasis
Flucloxacillin	• Cholestasis
Erythromycin	• Gastrointestinal upset • Prolongs QT interval
Ciprofloxacin	• Lowers seizure threshold • Tendonitis
Metronidazole	• Reaction following alcohol ingestion
Doxycycline	• Photosensitivity
Trimethoprim	• Rashes, including photosensitivity • Pruritus • Suppression of haematopoiesis

Prescribing in pregnant patients

Very few drugs are known to be completely safe in pregnancy. The list below largely comprises of those known to be harmful. Some countries have developed a grading system - see the link.

Antibiotics

- tetracyclines
- aminoglycosides
- sulphonamides and trimethoprim
- quinolones: the BNF advises to avoid due to arthropathy in some animal studies

Other drugs

- ACE inhibitors, angiotensin II receptor antagonists
- statins
- warfarin
- sulfonylureas
- retinoids (including topical)
- cytotoxic agents

The majority of antiepileptics including valproate, carbamazepine and phenytoin are known to be potentially harmful. The decision to stop such treatments however is difficult as uncontrolled epilepsy is also a risk

Drugs causing ocular problems

Cataracts

- steroids

Corneal opacities

- amiodarone
- indomethacin

Optic neuritis

- ethambutol
- amiodarone
- metronidazole

Retinopathy

- chloroquine, quinine

Sildenafil can cause both blue discolouration and non-arteritic anterior ischaemic neuropathy

Side-effects of common drugs: anti-anginals

The table below summarises characteristic (if not necessarily the most common) side-effects of drugs used to treat angina

Drug	**Side-effect**
Calcium channel blockers	• Headache • Flushing • Ankle oedema Verapamil also commonly causes constipation
Beta-blockers	• Bronchospasm (especially in asthmatics) • Fatigue • Cold peripheries • Sleep disturbances
Nitrates	• Headache • Postural hypotension • Tachycardia
Nicorandil	• Headache • Flushing

• Anal ulceration

Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphotase that activates various transcription factors in T cells

Adverse effects of ciclosporin (note how everything is increased - fluid, BP, K^+, hair, gums, glucose)

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- hyperplasia of gum
- tremor
- impaired glucose tolerance

Indications

- following organ transplantation
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- ulcerative colitis
- pure red cell aplasia

P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include

- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort

- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include

- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

Lithium toxicity

Lithium is mood stabilising drug used most commonly prophylatically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys. Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

Features of toxicity

- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

Management

- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity

- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

Splenomegaly

Massive splenomegaly

- myelofibrosis
- chronic myeloid leukaemia
- visceral leishmaniasis (kala-azar)
- malaria
- Gaucher's syndrome

Other causes (as above plus)

- portal hypertension e.g. secondary to cirrhosis
- lymphoproliferative disease e.g. CLL, Hodgkin's
- haemolytic anaemia
- infection: hepatitis, glandular fever
- infective endocarditis
- sickle-cell*, thalassaemia
- rheumatoid arthritis (Felty's syndrome)

*the majority of adults patients with sickle-cell will have an atrophied spleen due to repeated infarction

Amiodarone: adverse effects

Amiodarone is associated with a wide variety of adverse effects.

- thyroid dysfunction: both hypothyroidism and hyperthyroidism
- corneal deposits: present in most patients, rarely interfere with vision, usually reversible on withdrawal of drug
- pulmonary fibrosis/pneumonitis
- liver cirrhosis/hepatitis
- peripheral neuropathy, myopathy
- photosensitivity
- 'slate-grey' appearance
- prolonged QT interval

- thrombophlebitis and injection site reactions
- bradycardia

Important drug interactions of amiodarone include:

- decreased metabolism of warfarin, therefore increased INR
- increased digoxin levels

Sildenafil

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

Contraindications

- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

Side-effects

- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects
- headache

Drug-induced lupus

In drug-induced lupus not all the typical features of systemic lupus erythematosus are seen, with renal and nervous system involvement being unusual. It usually resolves on stopping the drug

Features

- arthralgia
- myalgia
- skin (e.g. malar rash) and pulmonary involvement (e.g. pleurisy) are common
- ANA positive in 100%, dsDNA negative
- anti-histone antibodies are found in 80-90%
- anti-Ro, anti-Smith positive in around 5%

Causes

- procainamide
- isoniazid
- minocycline
- hydralazine
- chlorpromazine
- anti-epileptics: phenytoin

Adrenaline

Adrenaline is a sympathomimetic amine with both alpha and beta adrenergic stimulating properties

Indications

- anaphylaxis
- cardiac arrest

Recommend Adult Life Support (ALS) adrenaline doses

- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

Management of accidental injection

- local infiltration of phentolamine

  10ml of the 1:10,000 preparation contains 1mg of adrenaline

Isotretinoin

Isotretinoin is an oral retinoid used in the treatment of severe acne. Two-thirds of patients have a long term remission or cure following a course of oral isotretinoin

Adverse effects

- teratogenicity: females should ideally be using two forms of contraception (e.g. Combined oral contraceptive pill and condoms)
- dry skin, eyes and lips: the most common side-effect of isotretinoin
- low mood
- raised triglycerides
- hair thinning
- nose bleeds (caused by dryness of the nasal mucosa)
- benign intracranial hypertension: isotretinoin treatment should not be combined with tetracyclines for this reason

Neuropathic Pain

Neuropathic pain results from damage to the peripheral or central nervous system. Such pain is variously described as shooting/stabbing/burning/itching/pins and needles/hypersensitive.

Pharmacological Management

First line treatment
Diabetic neuropathy = Duloxetine 60-120mg daily
Other neuropathic pain = Amitriptyline 10-75mg daily

Second line treatment
Diabetic neuropathy = Pregabalin
Other neuropathic pain = Pregablain

Third line treatment
Refer to a specialist if unsatisfactory pain reduction is acheived at maximum tolerated doses of second line treatment

Causes

Peripheral

Painful diabetic neuropathy (20% of diabetics experience this)
Post-herpetic neuralgia (8% of patients with shingles have post herpetic neuralgia at 3 months)
Trigeminal neuralgia
Radicular pain
Pain after surgery
Neuropathic cancer pain (chemotherapy-induced neuropathy and neuropathy secondary to tumour infiltration)

Central
Stroke
Spinal cord injury
Multiple sclerosis

Adverse Drug Reaction

Asprin and other Non Steroidal Anti Inflammatories (NSAIDs) are associated with bronchospasm and skin reactions in hypersensitive patients.

Common(er) Side Effects

ACE Inhibitors

- Dry persistent cough, renal impairment, profound hypotension, angioedema.
-

Statins

- Muscle aches, myopathy, rhabdomyloysis, derangement of liver function tests (rarely pancreatitis and liver failure)

Fibrates

- Gastrointestinal side effects, myositis (risk high in renal impairment)

Thiazide diuretics

- Mild gastro-intestinal disturbances, postural hypotension, altered plasma-lipid concentrations, metabolic and electrolyte disturbances including hypokalaemia, hyponatraemia, hypomagnesaemia, hypercalcaemia, hyperglycaemia, hypochloraemic alkalosis, hyperuricaemia, and gout.

Heart Failure

Though diuretics show a clear benefit in practice, no trials have demonstrated a survival benefit. It is unlikely such trials would be sanctioned by an ethics committee.

Pharmacological Management (Heart failure with impaired left venticular function ie <40% ejection fraction)

- For those with asymptomatic heart failure start treatment with either an ACE inhibitor or beta blocker. Both agents reduce morbidity and mortality and improve symptoms
- Symptomatic heart failure patients should start a combination of ACE inhibitor and beta blocker. Add a diuretic if there is fluid retention.
- Severe heart failure patients should be referred to a specialist.
- Additional treatment may include angiotensin receptor antagonists, digoxin and aldosterone antagonists. Angiotensin receptor antagonists may be used in combination with ACE inhibitors in this patient group if the patient remains symptomatic. Digoxin is used as an aid to rate control but does not improve mortality. Aldosterone antagonists (spironlactone, eplerenone) are advised for those with LVEF >35% and severe symptoms (NYHA class 3-4). They improve mortality (RALES study).
- Third line drugs include hydralazine, and amiodarone.
- Non drug treatment options include resynchronisation therapy, implantable cardiac defibrillators and cardiac transplant

Prescribing for UTI

- This lady should not be prescribed a penicillin based antibiotic in view of her past history of penicillin allergy.
- Nitrofurantoin is not effective in patients with a GFR of less than 60 as inadequate concentrations are found in the urine. In addition patients with renal failure may develop peripheral neuropathy if prescribed Nitrofurantoin.
- Gentamicin is not a suitable antibiotic for use in primary care as it cannot be given orally.
- Minocycline is not licensed for the treatment of urinary tract infections.
- Trimethoprim has been cited as the first line choice for the treatment of community acquired urinary tract infection infections however levels of resistance are rising. Nitrofurantoin is now commonly used first line. In this instance Trimethoprim is the best choice.

Acne

Answering The Question

Diagnosis

- Diagnosis is clinical - no investigations required
- Findings are

- Closed comedones (whiteheads), open comedones (blackheads), or inflammatory lesions including pustules, inflamed papules or nodules, there may also be scarring or post-inflammatory hyperpigmentation (especially seen in dark skin). These occur most commonly on the face but can also be on the shoulders and back.
- The cause is blockage or inflammation of the hair follicles and accompanying sebaceous glands.
- Doubt about the diagnosis is an indication for referral.

Severity

- Mild acne predominantly consists of non-inflammatory comedones.
- Moderate acne consists of a mixture of non-inflammatory comedones and inflammatory papules and pustules.
- Severe acne is characterized by the presence of nodules and cysts, as well as a preponderance of inflammatory papules and pustules. Nodulocystic acne is an indication for urgent referral for oral isotretinoin. Scarring often indicates previous episodes of severe acne (its presence may warrant more aggressive treatment to prevent further scarring).

History Points

- The reasons for the person presenting, how long they have had acne, and whether it is worsening.
- Any treatments the person has already tried (for example over-the-counter medication).
- Possible causes or aggravating factors
- Underlying causes of acne should be considered e.g. medication (steroids & antidepressants i.e. SSRI).
- Signs of androgen excess (irregular periods, hirsutism, infertility, obesity) should precipitate investigation for underlying hormonal abnormalities.
- Psychosocial impact ie how is it affecting you at home/work/socially
-

Advice

- Acne is common and improves, treatment takes time to work
- Treatments take 8 weeks to work and can irritate the skin
- Acne is a common problem affecting 80% of 11-30 year olds at some point
- Acne improves in the majority with age without scarring
- Address Acne Myths
    - There is no evidence that any foods worsen acne.
    - Acne is not due to poor skin hygiene (in fact excessive washing of the skin or use of abrasive washes can stimulate oil production and worsen acne, instead patients should be encouraged to wash the skin twice a day without these products)

- Acne is not contagious
- Sun does not improve acne

Management

- Hygiene & self care (for all patients)
  - Do not wash more than twice a day.
  - Use a mild soap or cleanser and lukewarm water (as very hot or cold water may worsen acne).
  - Do not use vigorous scrubbing when washing acne-affected skin, or exfoliating
  - Leave blackheads ?open comedones? alone
  - Use minimum make up (this should be water based) and remove it at night.
  - Use a aqueous cream if dry skin is a problem (several topical acne drugs dry the skin).

- Mild (Topical treatment or oral contraceptive)
  - Prescribe a topical retinoid (tretinoin, isotretinoin, or adapalene) or benzoyl peroxide (especially if papules and pustules are present) as first-line treatment.
  - Prescribe a topical antibiotic or azelaic acid if both topical retinoids and benzoyl peroxide are poorly tolerated.
  - Consider prescribing a standard combined oral contraceptive in women who require contraception, particularly if the acne is having a negative psychosocial impact.

- Moderate (Single or combination topical treatment (oral if refractory))
  - Consider a single topical drug in people with limited acne which is unlikely to scar.
  - Prescribe benzoyl peroxide or a topical antibiotic first-line as they are most effective against inflammatory acne. However, topical retinoids are also effective, and azelaic acid may is an option if other drugs are poorly tolerated.
  - Combined treatment should be considered in all people with moderate acne.
    - Benzoyl peroxide combined with a topical antibiotic is the usual preferred regimen, as it is proven to be effective and may limit the development of bacterial resistance.
  - Consider prescribing an oral antibiotic (tetracycline, oxytetracycline, doxycycline, lymecycline, or erythromycin) if topical treatment cannot be tolerated, if there is moderate acne on the back or shoulders (where it may be particularly extensive or difficult to reach), or if there is a significant risk of scarring or substantial pigment change.
  - Consider prescribing a standard combined oral contraceptive in women who require contraception

- Severe (Refer patients and start combination antibiotic treatment (oral & topical))
    - In severe acne, there are nodules and cysts (nodulocystic acne), as well as inflammatory papules and pustules. There is a high risk of scarring (or scarring may already be evident), and there is likely to be considerable psychosocial morbidity.
    - Refer all people with severe acne for specialist assessment and treatment (for example with oral isotretinoin), and consider prescribing an oral antibiotic in combination with a topical drug whilst waiting for an appointment.
    - Oral tetracycline, oxytetracycline (eg 500mg BD)?, doxycycline, or lymecycline are first-line options.

Oral Contraceptive Pill or Dianette

- There is some evidence from a Cochrane review that the combined oral contraceptive pill can help improve acne, but there is no evidence for use of a particular pill. The progesterone only pill may worsen acne. Dianette (an anti-androgen) can be used for acne treatment if oral antibiotics do not work and will also provide effective contraception. There is an increased risk of venous thrombo-embolism with this treatment and an assessment of risk factors for venous thrombo-embolism should be made first.