Prescription drugs uses and effects

ACE inhibitors

cardiovascular disease

Angiotensin-converting enzyme (ACE) inhibitors reduce the strain on the cardiovascular system

ACE inhibitors disrupt the renin-angiotensin-aldosterone system. This controls blood pressure and fluid balance. ACE inhibitors block the formation of angiotensin II. Therefore, they:

- Decrease blood pressure (BP). With less angiotensin II, blood vessels relax.
- Increase salt and water loss, reduce fluid retention and relieve heart failure.
- Improve the effectiveness of a failing heart.
- Disrupt the mechanisms which maintain BP on standing.
- Protect the linings of blood vessels, particularly in diabetes.
- Decrease the sensation of thirst.

ACE inhibitors also prevent breakdown of inflammatory mediators. Accumulation of these substances is responsible for drug-induced cough and other 'allergic-type' adverse effects. Changing the ACE inhibitor in these circumstances is unlikely to help.

Indications

Heart failure Prescribed preferentially in the treatment of moderate-to-severe heart failure. Diuretics are usually co-prescribed.

Hypertension First choice therapy for patients with heart failure or kidney damage due to diabetes and for Caucasian patients younger than 55. Otherwise, they are prescribed if other treatments are not tolerated, contraindicated or fail to control blood pressure.

Diabetic nephropathy Reduce deterioration in renal function in patients with proteinuria or microalbuminuria.

Myocardial infarction Commenced within 24 hours of myocardial infarction, provided systolic BP >100mmHg and the patient is stable. Administration is either for five to six weeks, or, if the left ventricle is underperforming, indefinitely.

Angiotensin-II receptor antagonists These include losartan and irbesartan. Their therapeutic effects are similar to ACE inhibitors. However, they block the action (rather than formation) of angiotensin II. Their main role is control of hypertension in patients who have responded to ACE inhibitors, but who are unduly troubled by drug-induced cough.

Administration

ACE inhibitors should be taken at the same time each day, with a constant relation to meals, as absorption may be affected by food.

Captopril prescribed alone to treat hypertension is commenced at 12.5mg twice daily. The initial dose is 6.25mg for older people, or if co-prescribed with a diuretic. Usual maintenance dose is 25mg twice daily. Maximum dose is 50mg three times a day.

Lisinopril is administered as a single daily dose. The usual starting dose is 2.5mg/day, which can be increased to 40mg/day.

Due to the potential for a profound drop in blood pressure after the first dose of ACE inhibitors, it is usual to recommend patients taking these for the first time at home to take them just before retiring to bed. Bed rest should be maintained for a minimum of three hours following first dose. If possible, check for orthostatic (postural) hypotension before the patient gets up.

Doses are adjusted at two to four week intervals in relation to BP readings and assessed immediately before a dose is due. The lowest possible dose is prescribed if systolic BP is below 100-120mmHg.

Cautions and contraindications

- Heart failure – ACE inhibitors should be initiated under specialist supervision if patients are receiving multiple-dose or high-dose diuretic therapy (equivalent to 80mg furosemide [frusemide] daily), or high-dose vasodilator therapy or have:
  - Severe or unstable heart failure.
  - Hypovolaemia.
  - Serum sodium concentration <130mmol/litre.
  - Systolic blood pressure <90mmHg.
  - Plasma-creatinine concentration >150micromol/litre.
  - Age >70.
- Poor blood flow in the kidneys (renovascular disease) may be worsened. Without pre-therapy checks this may go undiagnosed. Patients with peripheral vascular disease are at particular risk.
- Bilateral renal artery stenosis – ACE inhibitors reduce or abolish urine formation, causing severe, progressive renal failure.
- Impaired renal function hinders elimination of ACE inhibitors. Any administration of ACE inhibitors to such patients is usually under specialist supervision.
- Previous hypersensitivity response to any ACE inhibitor or other forms of angioedema. Risk of angioedema is very high.
- Conditions reducing cardiac output, such as aortic stenosis. Risk of hypotension is very high.
- Dialysis – extra precautions are detailed by manufacturers.
- Pregnancy – ACE inhibitors are contraindicated, as they can damage fetal kidneys and cause bone defects.
- Breastfeeding – Manufacturers advise to avoid.

Drug interactions

Increased risk of hyperkalaemia possible if co-administered with heparins, beta blockers, NSAIDs, ciclosporin, potassium-sparing diuretics (18-24 per cent increase in potassium levels) and potassium salts (including marketed salt substitutes). With careful monitoring, combining spironolactone with ACE inhibitors improves survival in severe heart failure. However, careful monitoring is needed to prevent a potentially dangerous rise in potassium levels.

Low dose aspirin may be co-prescribed to reduce risks of cardiovascular events as it is not known to clinically reduce the efficacy of ACE inhibitors. High dose aspirin is reported to reduce antihypertensive efficacy of ACE inhibitors by up to 50 per cent.

Ciclosporin with ACE inhibitors can result in acute kidney failure or a more gradual accumulation of potassium.

Hypotension This is accentuated by all anti-hypertensives, diuretics, alcohol, alpha-blockers, antipsychotics, anxioloytics/hypnotics, baclofen, beta-blockers, vasodilators, clonidine, levodopa and anti-depressants.

Antagonism – of anti-hypertensive effect by corticosteroids, oestrogens and NSAIDs, which not only antagonise the hypotensive effects but also increase risks of kidney damage.

Hypoglycaemia The hypoglycaemic effects of insulin, metformin and sulphonylureas are enhanced.

Others Lithium, digoxin, allopurinol and procainamide are likely to accumulate.

Desensitisation treatments These should not be undertaken concurrently due to risks of anaphylaxis.

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Managing the common adverse effects of ACE inhibitors

Problem	Prevention
Profound first dose hypotension	
Particularly in patients taking diuretics or antihypertensives If BP falls suddenly, patients with previous myocardial infarction (MI) or stroke are at increased risk of recurrence	If possible, withdraw or reduce diuretics two to three days before initiation. Monitor cardiovascular condition prior to administration, and following first dose (see cautions). If patient becomes dizzy or hypotensive, place him or her in a supine position and offer oral fluids. Ensure intravenous fluids and atropine are available. Following MI, withdraw ACE inhibitor if systolic BP is <90mmHg for more than one hour.
Hypotension/postural hypotension	
	Monitor postural hypotension and advise appropriately (see diuretics). Ask patients to report any dizziness, avoid fluid depletion and ensure prompt rehydration during vomiting, diarrhoea or sweating. Prior to surgery, including emergency procedures, ensure anaesthetic team are aware that ACE inhibitors have been administered.
Deterioration in renal function	
	Measure concentrations of creatinine and potassium in venous blood samples and concentrations of albumin and microalbumin in urine pre-therapy, one to two weeks after initiation and regularly thereafter. Refer to specialist if creatinine >150micromol/l. Following MI, serum creatinine >177micromol/l and proteinuria >500 mg/24hours precludes therapy. Particular vigilance is advised in patients with heart failure, peripheral vascular disease, dehydration and diuretic therapy.
Hyperkalaemia	
	Monitor potassium concentrations. Avoid concurrent administration of drugs increasing serum potassium (see interactions), including non-prescription products. Caution against regular self-medication with NSAIDs. Advise patients to avoid excessive consumption of potassium-rich foods. Particular caution if renal function is poor.
Allergic responses	
Persistent dry cough – affects 5 to 20 per cent of patients, particularly women and non-smokers. This may arise at any dose, any time during therapy	For hypertensive patients, co-prescription of nifedipine or indometacin may ameliorate symptoms and allow dose reduction. Advise that cough may spontaneously remit and will disappear four days after discontinuation of therapy.
Sinusitis and rhinitis	Ensure symptoms are not due to infection and manage symptoms conservatively.
Skin rash – sometimes associated with pruritus, urticaria, photosensitivity and hair loss	Mild symptoms may respond to dose reduction, emollients or a brief course of antihistamines.
Severe symptoms (epidermal necrolysis)	Withhold drug if severe symptoms occur.
Angioedema – of nose, throat, mouth, larynx, lips and tongue, affecting 0.1-0.2 per cent of patients within the first few hours or days of therapy	Advise patients to discontinue medication and seek urgent medical opinion. Ensure patient is observed, as swelling may progress to airway. If airway is involved, adrenaline (epinephrine), oxygen, antihistamines, corticosteroids and intubation may be necessary. If swelling is confined to the face, anti-histamine treatment will suffice .
Leucopenia and other blood disorders (rare)	Ask patients to report infections, as these may indicate serious adverse reactions. Obtain full blood count (FBC) to evaluate these symptoms. Patients with collagen vascular diseases, such as systemic lupus, need regular FBC.
Gastrointestinal side effects	
Indigestion	Advise regular meals.
Nausea, vomiting and diarrhoea	Ensure prompt rehydration.
Constipation	Advise regarding constipation (see vasodilators).
Alteration or loss of sense of taste and thirst (particularly captopril)	Reassure that this common problem reverses on cessation of treatment. Encourage good mouth care/dental hygiene. Monitor diet and weight in older people.
Altered liver function, cholestatic jaundice, hepatitis and pancreatitis (rare)	Inform prescriber, withdrawal of therapy may be necessary. Incidence of hepatic adverse reactions reported to be 0.09 per 1,000 patients, however this may be underestimated. Encourage fluids.
Neurological side effects	
Headache, dizziness, fatigue, malaise, insomnia, parasthesia, myalgia, mood changes and blurred vision	Advise patients to ensure they are not adversely affected before driving.
Impotence	Discuss quality of life and compliance with same-gender nurse.
Therapeutic failure	
	Advise patient against high salt intake and co-administration of NSAIDs. Co-administration with antacids reduces absorption – separate administration by two hours.

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