New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may have been little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained either from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Eplerenone

Inspra (Pfizer)

25 mg and 50 mg tablets

Approved indication: heart failure post-myocardial infarction

Australian Medicines Handbook section 6.4.2

Low doses of spironolactone have a role in regimens for the treatment of severe heart failure. The beneficial effects of spironolactone are probably related to its antagonism of aldosterone. As aldosterone concentrations are increased in heart failure, it is a target for drug therapy.

Like spironolactone, eplerenone is a potassium-sparing diuretic. It blocks the attachment of aldosterone to its receptor. As this can reduce blood pressure, eplerenone has been approved as an antihypertensive drug in the USA.

In a study of patients with hypertension and left ventricular hypertrophy eplerenone was found to reduce left ventricular mass, particularly if it was combined with enalapril.[1] If eplerenone can prevent ventricular remodelling it may be beneficial after acute myocardial infarction.

A multinational clinical trial enrolled several thousand patients with left ventricular dysfunction and heart failure 3–14 days after a myocardial infarction. In addition to standard therapy (excluding spironolactone), 3319 patients were assigned to take eplerenone while 3313 patients took a placebo. The dose of eplerenone was 25 mg daily increasing to 50 mg daily after four weeks. After follow-up for an average of 16 months, 478 of the patients taking eplerenone had died compared with 554 of the placebo group. This was a 15% reduction in relative risk. Most of the deaths were from cardiovascular causes, particularly sudden death.[2]

Patients taking eplerenone are at risk of hyperkalaemia. In the heart failure trial serious hyperkalaemia (6.0 mmol/L) occurred in 5.5% of patients compared with 3.9% of the placebo group.[2] Apart from hyperkalaemia, other reasons for discontinuing eplerenone include dizziness and altered renal function.

Eplerenone is mainly metabolised by the liver with most of the metabolites being excreted in the urine. The drug is contraindicated in patients with moderate to severe renal impairment. As it is metabolised by cytochrome P450 3A4 it should not be prescribed with drugs, such as ketoconazole, that inhibit this enzyme.

As eplerenone is said to have relative selectivity for mineralocorticoid receptors, it may not have as many adverse effects as spironolactone. However, gynaecomastia and breast pain can still occur. Although the trials cannot be directly compared, spironolactone reduces the relative risk of death by 30% in patients with severe heart failure.[3] Although there is a risk of hyperkalaemia[4], spironolactone is a well-known and inexpensive drug and is unlikely to be superseded until more data about eplerenone are available.

T T T manufacturer provided all requested information

References

1. Pitt B, Reichek N, Willenbrock R, Zannad F, Phillips RA, Roniker B, et al. Effects of eplerenone, enalapril, and eplerenone/enalapril in patients with essential hypertension and left ventricular hypertrophy. Circulation 2003;108:1831-8.
2. Pitt B, Remme W, Zannad F, Neaton J, Martinez F, Roniker B, et al. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. N Engl J Med 2003;348:1309-21.
3. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. N Engl J Med 1999;341:709-17.
4. ADRAC. Evidence-based medicine: pitfalls of overlooking safety. Aust Adv Drug React Bull 2005;24:7-8.

Insulin detemir

Levemir FlexPen (Novo Nordisk)

3 mL cartridges containing 100 U/mL

Approved indication: diabetes mellitus

Australian Medicines Handbook section 10.1.1

Analogues of insulin enable patients with diabetes to be treated with regimens that follow the pattern of normal insulin secretion.[1] Insulin detemir is a soluble analogue designed to provide the basal requirements for insulin.

The genetically engineered molecule has a fatty acid side chain which delays absorption and degradation. Insulin detemir is active for 3–14 hours after subcutaneous injection. Depending on the dose, the duration of action can extend to 24 hours, so some patients can manage with a single daily dose.

An open-label study compared insulin detemir with the intermediate acting NPH insulin. The 56 patients, with type 1

diabetes, used one insulin at night for six weeks then switched over to the other insulin. Larger doses of insulin detemir were required to maintain good glycaemic control and serum glucose concentrations were higher for the first few hours after a dose. During the last week of treatment, hypoglycaemia occurred in 60% of the patients injecting insulin detemir and 77% of those injecting NPH insulin.[2]

A larger study compared twice-daily doses of the two insulins. After 16 weeks, the 267 patients given insulin detemir had a lower fasting blood glucose than the 124 patients who had taken NPH insulin. The mean concentration of glycated haemoglobin (HbA_{1c}) decreased slightly more in patients given insulin detemir (mean difference between groups 0.18%).[3]

Studies lasting up to a year show that the effect of insulin detemir on HbA_{1c} is equivalent to the effect of NPH insulin.

As insulin detemir only gradually reduces blood glucose during the night, nocturnal hypoglycaemia is less likely than with NPH insulin. However, there are no significant differences in the frequency of major hypoglycaemia.[2]

To achieve good glycaemic control, patients taking insulin detemir for their basal requirements should also be prescribed a short-acting insulin. Although insulin detemir has been studied in type 2 diabetes it is not currently approved for this indication unless there is no longer a response to oral hypoglycaemic drugs.

The activity profile of insulin detemir may have some advantages over older insulins. It is unknown if this difference will actually improve the outcomes for patients.

☒ manufacturer declined to supply data

References

1. Phillips P. Insulins in 2002. Aust Prescr 2002;25:29-31.
2. Hermansen K, Madsbad S, Perrild H, Kristensen A, Axelsen M. Comparison of the soluble basal insulin analog insulin detemir with NPH insulin. Diabetes Care 2001;24:296-301.
3. Home P, Bartley P, Russell-Jones D, Hanaire-Broutin H, Heeg J-E, Abrams P, et al. Insulin detemir offers improved glycemic control compared with NPH insulin in people with type 1 diabetes. Diabetes Care 2004;27:1081-7.

Answers to self-test questions

1. False
2. True
3. True
4. False
5. True
6. True

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