

'system' operates may be responsible. When an additional drug is identified it should not be administered before its possible relevance to the patient's condition is considered.

This case once again emphasises that traditional dictum that

diagnosis begins with obtaining a detailed medical history, including the drug history. It also shows that patients need to be told what symptoms to watch for if they are taking a drug with potentially serious adverse effects.

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 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.

Sulesomab

LeukoScan (Australian Radioisotopes)

3 mL vials containing 0.31 mg powder for reconstitution

Approved indication: diagnosis of osteomyelitis

Prompt treatment of osteomyelitis may prevent bone necrosis. Early diagnosis is therefore important, but the infection may not show up on a plain X-ray. A technetium (^{99m}Tc) bone scan will detect most cases, but sometimes cannot distinguish infection from other causes of inflammation. Using sulesomab may overcome this problem.

Sulesomab is a monoclonal antibody which binds to antigens on the surface of neutrophils. If it is labelled with ^{99m}Tc it will reveal areas where there is intense inflammation. *In vitro* studies suggest that labelled sulesomab binds more avidly to activated granulocytes.

After the sulesomab and the ^{99m}Tc are mixed they are given by intravenous injection. Imaging can take place between one and eight hours after the injection. Most of the dose is renally excreted, with 41% of the radioactivity appearing in the urine within 24 hours of the dose.

Sulesomab has been studied in 122 patients with diabetes who were thought to have osteomyelitis secondary to foot ulcers. The performance of the scan was assessed by bone biopsy. The scan detected 74 of the 81 patients with osteomyelitis and excluded it in 23 of the 41 patients who did not have osteomyelitis. Sulesomab therefore has a sensitivity of 91% and a specificity of 56%. The sensitivity compares favourably with the technique of using radiolabelled white blood cells, which has a sensitivity of 79%. Sulesomab imaging has slightly greater accuracy (81% versus 75%) and the results are likely to influence the patients' management.¹

Leucocyte numbers fall after the injection, but usually recover within 10 days. Other reported adverse effects include eosinophilia and rashes. The production of sulesomab involves mice, but no anti-mouse antibody reactions occurred in the trial.

Sulesomab is safer and easier to use than radiolabelled white blood cells, so it is being studied in other conditions, such as inflammatory bowel disease, where the detection of inflammation is important.

REFERENCE

1. Harwood SJ, Valdivia S, Hung G-L, Quenzer RW. Use of sulesomab, a radiolabeled antibody fragment, to detect osteomyelitis in diabetic patients with foot ulcers by leukoscintigraphy. *Clin Infect Dis* 1999;28:1200-5.

Tegaserod

Zelmac (Novartis)

6 mg tablets

Approved indication: irritable bowel syndrome in women

Australian Medicines Handbook Section 12.2.1

The cause of irritable bowel syndrome is uncertain. As there are several possible mechanisms a variety of drugs have been used in treatment. There has been interest in drugs acting on 5-HT receptors because of the effects of serotonin in the gastrointestinal tract.

Tegaserod is a partial agonist of the 5-HT₄ receptor. It stimulates the peristaltic reflex and accelerates gastrointestinal transit. Tegaserod may therefore have a role in patients with irritable bowel syndrome who are predominantly troubled by constipation.

A double-blind trial randomised 881 patients with constipation-predominant irritable bowel syndrome to take tegaserod or a placebo for 12 weeks. Tegaserod produced statistically significant subjective improvements in bowel movements and abdominal discomfort. There was a non-significant improvement in bloating.¹

Patients take tegaserod twice a day before meals. Its bioavailability is only 10% and this is reduced by food. Most of the dose is excreted unchanged in the faeces, but a metabolite is produced which is excreted in the urine. Liver impairment increases the plasma concentrations of tegaserod.

Adverse reactions to tegaserod most frequently involve the gastrointestinal tract. The effect of the drug will result in approximately 9% of patients developing diarrhoea. Other adverse events occur with a frequency similar to that of placebo.

There is a large placebo response in patients with irritable bowel syndrome. In the largest study of tegaserod 43.5% of patients responded, but so did 38.8% of the patients given a placebo. The therapeutic advantage of tegaserod appears to decline with time so it should be discontinued if there has been no response after one month of treatment. In patients who respond, the maximum duration of treatment should be 12 weeks. As the number of men in the clinical trials was limited, tegaserod is only approved for women with constipation-predominant irritable bowel syndrome.

REFERENCE

1. Müller-Lissner SA, Fumagalli I, Bardhan KD, Pace F, Pecher E, Nault B, et al. Tegaserod, a 5HT₄ receptor partial agonist, relieves symptoms in irritable bowel syndrome patients with abdominal pain, bloating and constipation. *Aliment Pharmacol Ther* 2001;15:1655-66.

Travoprost

Travatan (Alcon)

0.004% solution in 2.5 mL dispenser

Approved indication: raised intraocular pressure

Australian Medicines Handbook Section 11.2.5

Travoprost adds to the choice of prostaglandin analogues available to treat conditions such as glaucoma. Latanoprost is already widely used for this indication (see 'New drugs for glaucoma' *Aust Prescr.* in press 2002).

As travoprost is an analogue of prostaglandin F_{2α}, it reduces intraocular pressure by increasing the outflow of aqueous humour. Only a single daily dose is required as the effect lasts for at least 24 hours.

A clinical trial compared 801 patients treated with travoprost, latanoprost or timolol for a year.¹ Intraocular pressure was reduced by 30% or to below 17 mmHg in 54.7% of the patients using travoprost, 50% of those using latanoprost and 39% of those using timolol. The mean intraocular pressure with travoprost was 0.8 mmHg less than with latanoprost. Another study confirmed that travoprost has a significantly greater effect than timolol on intraocular pressure.²

More than 37% of patients may experience ocular hyperaemia while taking travoprost. This occurs more frequently than in patients using latanoprost or timolol. Other ocular adverse effects include itching, discomfort and changes in the eyelashes. Travoprost can also cause a slow discolouration of the iris which may be permanent.

In addition to monotherapy, travoprost can also be used as adjunctive therapy with timolol. If the patient is using two drugs they should be instilled at least five minutes apart.

While the efficacy of travoprost is similar to that of latanoprost, its local adverse effects may reduce its acceptability to patients.

REFERENCES

1. Netland PA, Landry T, Sullivan EK, Andrew R, Silver L, Weiner A, et al. Travoprost compared with latanoprost and timolol in patients with open-angle glaucoma or ocular hypertension. *Am J Ophthalmol* 2001;132:472-84.
 2. Goldberg I, Cunha-Vaz J, Jakobsen J-E, Nordmann J-P, Trost E, Sullivan EK, et al. Comparison of topical travoprost eye drops given once daily and timolol 0.5% given twice daily in patients with open-angle glaucoma or ocular hypertension. *J Glaucoma* 2001;10:414-22.

Answers to self-test questions

1. True	3. False	5. False
2. True	4. False	6. True
7. True	9. False	
8. True	10. True	

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