

Book review

Goodman & Gilman's The pharmacological basis of therapeutics. 11th ed. Brunton L, Lazo J, Parker K, editors.

**New York: McGraw-Hill; 2005.
2021 pages. Price \$155.95**

John S. Dowden, Editor, Australian Prescriber

This textbook of therapeutics was first published in 1940, so it is not surprising that the original authors were not involved in the 11th edition. The book is now made up of chapters written by individual authors, creating a challenge for the editors. All but three of the authors work in the USA, but the textbook has an international appeal.

As in previous editions, the book is divided into sections dealing with drugs that act on each of the body's systems. There have been a few changes in this format such as the section on vitamins being absorbed into other chapters, and the chapter on the treatment of poisoning being moved into

the toxicology section. New chapters include pharmacogenetics and drug metabolism.

Several sections begin with a chapter that reviews the physiology of a body system. In other sections these reviews are incorporated within the chapters. The usual pattern is to explain how a class of drugs acts and then to briefly discuss individual members of that class. The explanations of mechanisms of action are usually easy to understand especially when accompanied by diagrams. There is a bibliography at the end of each chapter for people who want to check the original research.

The problem with any textbook is that parts of it quickly go out of date. This edition was compiled recently enough to include the downfall of rofecoxib.

Unless it is already available in the USA, a new drug marketed in Australia may not be included in Goodman and Gilman. (*Australian Prescriber* is an up-to-date source of brief information on new drugs.) However, the book is a useful resource. It does not need to be on every prescriber's desk, but it is a very helpful reference for learning, or recalling, how drugs work.

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.

Lumiracoxib

Prexige (Novartis)

400 mg tablets

Approved indication: analgesia

Australian Medicines Handbook section 15.1

Lumiracoxib is a non-steroidal anti-inflammatory drug which selectively inhibits the COX-2 isoenzyme. Like celecoxib, lumiracoxib may have fewer gastrointestinal adverse effects than similar drugs which inhibit the COX-1 and COX-2 isoenzyme (see COX-2 inhibitors, *Aust Prescr* 2000;23:30–2).

A small study randomised 65 men to take lumiracoxib, naproxen or a placebo for eight days. While none of the volunteers who took lumiracoxib developed gastroduodenal erosions, 13 of those taking naproxen developed duodenal erosions and one man developed a gastric ulcer.¹

A larger trial compared lumiracoxib with naproxen and ibuprofen in 18 325 people over 50 years old with osteoarthritis.²

Although 39% of the patients did not complete the one-year trial, there was a significant difference in the incidence of gastrointestinal adverse effects. Complications occurred in 29 of the 9117 people (0.32%) in the lumiracoxib group compared with 83 of the 9127 people (0.91%) who took another non-steroidal anti-inflammatory drug.

At the time lumiracoxib was approved in Australia much of the information about its efficacy was only publicly available as conference abstracts. Several papers were presented at the 2003 congress of the European League against Rheumatism.³

One of the conference abstracts describes a comparison of lumiracoxib, celecoxib and placebo in 1600 patients with osteoarthritis of the knee. After 13 weeks the effect of lumiracoxib on pain and function was greater than with placebo and similar to the effect of celecoxib. There was no significant difference in the efficacy of once-daily lumiracoxib 200 mg and lumiracoxib 400 mg.³

An extension of another study found celecoxib and lumiracoxib had similar efficacy after nine months of treatment.³

In addition to osteoarthritis, lumiracoxib has also been approved for the treatment of acute pain. Few of the studies of primary dysmenorrhoea, postoperative dental pain and postoperative surgical pain have been published in full.

Lumiracoxib can cause the same problems as other non-steroidal anti-inflammatory drugs. It can affect hepatic and renal function and should be used with caution in patients with hypertension or heart failure as it can cause fluid retention. Lumiracoxib is contraindicated in patients with ischaemic heart disease, cerebrovascular disease and peripheral arterial disease.

In the comparison with naproxen and ibuprofen the incidence of cardiovascular events was higher in patients taking lumiracoxib, but the difference was not significant.⁴ If the patients were taking low-dose aspirin lumiracoxib lost its significant gastrointestinal advantage over the other drugs.²

Most of a dose is metabolised, primarily by cytochrome P450 2C9. Although lumiracoxib therefore has several potential interactions it is not clear which will be clinically significant.

Although there is now published information about using lumiracoxib for osteoarthritis it should probably not be prescribed for other conditions until more data are available.

T manufacturer had no objection to providing data but did not actually provide it

References

1. Rordorf C, Kellett N, Mair S, Ford M, Milosavljev S, Branson J, et al. Gastroduodenal tolerability of lumiracoxib vs. placebo and naproxen: a pilot endoscopic study in healthy male subjects. *Aliment Pharmacol Ther* 2003;18:533-41.
2. Schnitzer TJ, Burmester GR, Mysler E, Hochberg MC, Doherty M, Ehram E, et al. Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), reduction in ulcer complications: randomised controlled trial. *Lancet* 2004;364:665-74.
3. <http://www.eular.org/index.cfm?framePage=/eular2003.cfm> [cited 2006 Jan 13]
4. Farkouh ME, Kirshner H, Harrington RA, Ruland S, Verheugt FW, Schnitzer TJ, et al. Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), cardiovascular outcomes: randomised controlled trial. *Lancet* 2004;364:675-84.

Moxonidine

Physiotens (Solvay)

0.2 and 0.4 mg tablets

Approved indication: hypertension

Australian Medicines Handbook section 6.4.8

Centrally-acting antihypertensive drugs such as methyldopa and clonidine are no longer widely used to control blood pressure.

Their usefulness is limited by their adverse effects. Moxonidine has been developed as a more tolerable centrally-acting drug.

The imidazoline receptors are found in the brainstem and in the kidney. Stimulation of these receptors by an agonist, such as moxonidine, reduces sympathetic activity, lowering peripheral vascular resistance, and thereby reducing blood pressure.

The tablet formulation of moxonidine is well absorbed with a bioavailability of 88%. Most of the dose is excreted unchanged in the urine. Although the half-life is only around 2.2 hours, blood pressure can be controlled by a single daily dose.

Placebo-controlled trials show that moxonidine works better than placebo and that the effect on blood pressure is similar to enalapril. Other studies have shown no statistical difference between moxonidine and hydrochlorothiazide, atenolol and nifedipine.¹

Moxonidine has been available in the UK since 1996. Analysis of prescribing data from 409 general practitioners shows that moxonidine is not extensively used. It seems to be prescribed when several other treatments have failed to control hypertension. Out of 71 775 people with hypertension only 830 took moxonidine and 80% of these patients were taking it with at least one other antihypertensive.²

Although moxonidine may cause fewer adverse effects than clonidine, dry mouth and somnolence can still occur. Approximately 5% of the patients withdrew from clinical trials because of adverse events. Although the trials were short, rebound hypertension does not appear to be a major problem when moxonidine is stopped. Rebound hypertension may occur if the patient stops a beta blocker at the same time. Patients ceasing this combination should therefore withdraw the beta blocker first.

A trial of moxonidine in patients with heart failure had to be stopped because of increased mortality compared to treatment with placebo.³ Moxonidine is therefore contraindicated in any degree of heart failure. It is also contraindicated in patients with bradycardia, heart block or renal impairment and in people more than 75 years old. Caution is required if a patient has a history of unstable angina, severe coronary artery disease or angioneurotic oedema.

X manufacturer did not respond to request for data

References

1. Messerli F. Moxonidine: a new and versatile antihypertensive. *J Cardiovasc Pharmacol* 2000;35(Suppl 4):S53-S56.
2. Schachter M, Mitchell G, Niziol C, Abhyankar BA. Antihypertensive efficacy of moxonidine in primary care: a 'real-life' study. *Int J Clin Pract* 2003;57:479-82.
3. The MOXCON Investigators. Adverse mortality effect of central sympathetic inhibition with sustained-release moxonidine in patients with heart failure (MOXCON). *Eur J Heart Fail* 2003;5:659-67.

Rabies vaccine

Rabipur (CSL)

vials containing lyophilised powder for reconstitution

Approved indication: rabies prophylaxis and treatment

Australian Medicines Handbook section 20.1

Rabies is caused by a lyssavirus and usually occurs after a bite by a rabid dog. A similar illness can result from infection with Australian bat lyssavirus.

Rabies vaccine is used prophylactically for people who will spend a prolonged time in areas where rabies is endemic. It is also used with immunoglobulin in the management of people who have been exposed to the virus.

This product differs from the currently available vaccine in that a different strain of virus is used and it is prepared using chick embryo cells rather than human diploid cells. Both vaccines will produce adequate amounts of antibody after the series of three injections.

Several injections are required for post-exposure prophylaxis. Protective antibody titres can be achieved within 14 days if the recommended regimen is followed.

People with a continuing risk of exposure to rabies may need a booster dose every 2–5 years to maintain their immunity. Some people developed serum sickness after boosters of diploid cell vaccines. It is uncertain if this will be a problem with the chick embryo vaccine, but it is approved for use as a booster in people previously immunised with diploid cell vaccine.

Many people will get pain at the injection site. Other reactions include headache, myalgia and rash. Rarely a vaccinee may develop anaphylaxis or a neurological disorder such as Guillain-Barré syndrome.

T**T** manufacturer provided some data

The T-score (**T**) is explained in 'Two-way transparency', Aust Prescr 2005;28:103.

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- | | | |
|----------|----------|----------|
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| 2. False | 4. True | 6. False |
| 7. True | | |
| 8. False | | |

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