usually corresponds to the pack size produced by the manufacturer.

For drugs which are intended for use in chronic conditions, the PBAC recommends a maximum quantity and number of repeats which will provide sufficient supply of the drug for six months' therapy at normal dosage levels.

The current dosage of celecoxib for the treatment of osteoarthritis is 200 mg once daily or 100 mg twice daily, with some patients requiring 200 mg twice daily. The dosage for rheumatoid arthritis is 100 mg or 200 mg twice daily. The PBAC therefore recommended a maximum quantity of 60 capsules for both the 100 mg and 200 mg strengths of celecoxib in an attempt to encompass the complete dosage range required by patients. The maximum quantity listed in the Pharmaceutical Benefits Scheme (PBS) Schedule for celecoxib 200 mg provides for one month's therapy at maximum dosage levels and for two months' therapy at minimum dosage levels. The maximum number of repeats (three, for consistency with the listings of the non-steroidal anti-inflammatory drugs) provides for a supply of four months or eight months of medication depending on the patient's dose.

Doctors are under no obligation to prescribe the full maximum quantity specified in the Schedule for a particular drug. They may, at their discretion, prescribe smaller quantities than those listed in the Schedule.

The mechanism via which adverse drug reactions are monitored in Australia is administered by the Adverse Drug Reactions Advisory Committee (ADRAC) of the Therapeutic Goods Administration. Pharmacists who see unexpected reactions can notify the ADRAC Secretariat by filling out the blue report card which is enclosed in every copy of the PBS Schedule.

Australian Prescriber storage boxes

Many readers of Australian Prescriber keep their copies for reference. To help readers keep their back issues in good condition, a limited number of storage boxes are now available. The boxes are vinyl covered and will hold all the issues published over the last 5 years. To order a box, send your name and address to the Editorial office (see page 23). A limit of one box per Australian health professional will apply.

Medications which may lower seizure threshold

Neil Buchanan, Emeritus Professor, University of Sydney, Sydney

Most people who have epilepsy are warned that certain substances, especially other medications and alcohol, 'do not mix with their pills'. This is partly correct and is more valid with the older, enzyme-inducing drugs (phenytoin, phenobarbitone and carbamazepine) than with the newer antiepileptic drugs.

What people with epilepsy are not sufficiently informed about are the factors which lower the seizure threshold and make them more liable to have seizures. Such factors include stress, sleep deprivation, alcohol, menstruation and, especially in children, intercurrent infection and fever. Antiepileptic drugs may occasionally make seizures worse, either idiosyncratically when being introduced, or if the dose is excessive. Table 1 shows some medications which may provoke seizures by lowering the seizure threshold, rather than by interacting with antiepileptic drugs.

We do not know how often seizures occur because a drug has altered the seizure threshold. Many reports are anecdotal. In the past two years of specialist practice I have seen 25 patients where clinical judgement would suggest a particular medication has provoked a seizure. The commonest seizure-provoking drug was pethidine. With hindsight, 19 of the 25 patients might have avoided this problem if they had known that it could have occurred. The severity of the seizures varied, but three patients were admitted to intensive care units.

The list of potential seizure-provoking medications shown in Table 1 is probably incomplete. The list has been compiled from personal observations, discussions with colleagues, data from the Adverse Drug Reactions Advisory Committee (ADRAC) and published product information. The purpose of compiling such a list does not imply the use of these drugs is prohibited. Rather it aims to alert doctors and people with epilepsy to medications that could provoke seizures. Attention to the mention of epilepsy in the precautions section of published product information would identify most potential problems.

With regard to anaesthetic agents, there are reports of seizures post-anaesthesia. Whether this relates to the anaesthetic agent itself or withdrawal seizures after an anaesthetic is not clear. While propofol is effectively used in the management of status epilepticus, there are definite reports of seizures after its use as an anaesthetic. From the patient's point of view, the reason why is not of great concern.

The implications are:

- medical practitioners should be aware of the possibility of a change in seizure threshold
- people with epilepsy should be aware of the possibility that medicines may lower their seizure threshold
- medications which may alter the seizure threshold should only be used if really necessary and no safer alternative exists.

Table 1

Medications which may lower seizure threshold

Medications	*Relative frequency of seizure provocation*	*Comments*
Anaesthetic drugs		
enflurane	rare	
isoflurane	rare	
propofol	well described	
Antiarrhythmics		
lignocaine	uncommon	
mexiletine	rare	
Antibiotics		
penicillins, cephalosporins, amphotericin, imipenem	relatively common in high dosage	• with big intravenous doses • probably cannot be avoided
Antidepressants		
tricyclics	uncommon	• patients should be informed of risk • increased seizures usually occur within 2–6 weeks of starting antidepressant
selective serotonin reuptake inhibitors	uncommon	
monoamine oxidase inhibitors	uncommon	
doxepin	rare	
nefazodone	uncommon	
Antihistamines		
azatadine, cyproheptadine, dexchlorpheniramine, methdilazine, pheniramine maleate, promethazine	probably quite rare	• widely used and found in many over-the-counter medicines • suggest avoiding unless essential • use non-sedating antihistamines in preference
Antimigraine		
sumatriptan	rare	
Antipsychotics		
chlorpromazine	uncommon	avoid – if possible
clozapine	common	avoid – if possible
flupenthixol	rare	
fluphenazine	rare	
haloperidol	uncommon	
olanzapine	uncommon	See ADRAC Bulletin 1999;18:3
pimozide	uncommon	
risperidone	uncommon	
thioridazine	uncommon	
thiothixene	uncommon	
trifluoperazine	uncommon	
Bronchodilators		
aminophylline, theophylline	well described	avoid – if possible
Cough and cold remedies		
triprolidine and pseudoephedrine, pseudoephedrine	probably quite rare	• widely used and found in many over-the-counter medicines • suggest avoiding unless essential
Hormonal preparations		
oral contraceptives	uncommon	• patients should be warned of risk • increased seizures occur within 1–4 weeks of starting oral contraceptives or hormone replacement therapy
hormone replacement therapy	uncommon	
Immunomodifiers		
cyclosporin	common	
Narcotic analgesics		
pethidine	common	avoid – use morphine See ADRAC Bulletin 1997;16:3
fentanyl	uncommon	avoid – if possible
Stimulant medications		
dexamphetamine	uncommon	parents/patients should probably be made aware of a quite low risk
methylphenidate	anecdotal reports	