

(and some special disadvantages). Buprenorphine can be taken on alternate days.

The risk of overdose is minimal but people on large doses of heroin may experience some withdrawal symptoms. Although buprenorphine is more expensive than methadone it may become the treatment of choice for detoxification.

### **Leva-alpha-acetylmethadol (LAAM)**

LAAM (also known as levomethadyl acetate) is a methadone derivative. It has a longer half-life than methadone, but has similar effects. Administration on alternate days reduces the cost of providing the drug and also reduces the burden on patients who are doing well. The metabolites are active and other drugs can interfere with the production of the metabolites. LAAM may be available in Australia within the next few years.

### **Sustained release oral morphine (SROM)**

Few studies have been conducted. A trial has commenced in Australia.

### **Prescription heroin**

Heroin prescription has been available for the management of heroin dependence in the UK since 1926. It has never been studied or utilised commonly in that country. A handful of papers of variable quality suggest that results might be comparable to methadone. A heroin trial conducted in Switzerland in the 1990s obtained some impressive results but lacked a control group. Nevertheless, results were sufficiently impressive to stimulate research in other European countries. The major argument in favour of heroin prescription is for the management of heroin injectors refractory to other treatments.

### **Intravenous methadone**

Intravenous methadone has been prescribed in the UK for decades although evaluation studies are scant.

### **Non-pharmacological treatments**

These include drug-free outpatient counselling, residential rehabilitation (therapeutic communities) and self-help groups (Narcotics Anonymous). Retention is often poor and good

evidence of benefit is difficult to find. Residential rehabilitation is more expensive than outpatient pharmacological treatment and is difficult to combine with continued employment.

### **Summary**

Pharmacotherapeutic treatments attract and retain large numbers of heroin-dependent patients. Evaluation studies show that agonist treatments are safe, effective and cost-effective. The range of pharmacotherapeutic options for management of heroin dependency in Australia is now being expanded. Demand for all forms of treatment (especially pharmacological treatments) for heroin dependence far outstrips supply.

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### **Self-test questions**

*The following statements are either true or false (answers on page 23)*

1. Buprenorphine is taken sublingually because of its low oral bioavailability.
2. The long half-life of methadone allows it to be given once a day.

## **Thyroxine interacts with celery seed tablets?**

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### **Introduction**

Interactions between so-called 'natural therapies' and clinical medicines are an unquantified problem in the Australian community, due to a lack of awareness and reporting from consumers and health professionals alike.

The Queensland Medication Helpline is a direct link to consumers and their medication concerns. Over the past five years we have reported, to the Adverse Drug Reactions Advisory Committee, a variety of suspected adverse effects and interactions between clinical and herbal/nutritional

medicines. An interesting example is the potential interaction between thyroxine and celery seed tablets.

### Case reports

Our first case involved a 55-year-old woman who, after considerable monitoring, had finally been stabilised on a daily dose of thyroxine 100 microgram. A month later, her doctor found that her  $T_4$  levels were low again and her dose was doubled. The patient then remembered that in the past month she had also started taking celery seed tablets for osteoarthritis. Suspecting a potential interaction, she ceased the celery seed tablets without increasing the thyroxine dose as the doctor had advised. Next time her thyroxine levels were checked they had increased to within the normal range. She tried recommencing celery seed a month later but after a week she felt lethargic, bloated and had dry skin. When she stopped the celery seed tablets, she reported that her 'general energy levels improved'.

A second report was received from a 49-year-old woman who had taken thyroxine for many years. When her  $T_4$  became extremely low her doctor suspected that she had not been taking her tablets. The patient argued that she had taken her thyroxine, but she had recently commenced taking celery seed tablets to treat arthritis. She ceased the celery seed tablets and one month later her thyroxine levels had returned to within the normal range.

### Evidence

Celery seed extracts (*Apium graveolens*) are a popular herbal remedy for the treatment of arthritis, gout, fluid retention and cystitis. Celery seed/fruit should not be confused with the edible celery stem.<sup>1</sup> Studies have shown that celery plant extracts have anti-inflammatory activity against carrageenan-induced rat paw oedema.<sup>2</sup> Hypotensive and hypoglycemic activities have also been reported.<sup>1</sup> In preliminary research, five of 23 celery-based preparations showed antiarthritic

effects, but no anti-inflammatory or antipyretic effects. The celery seed activity was thought to be dependent on processing at low temperatures.<sup>3</sup>

An extensive literature search did not find other reports of an interaction between celery seed extracts and thyroxine. However, when reference was made to these case studies in an article in a Queensland newspaper, the Queensland Medication Helpline received a flood of calls about similar experiences. A total of 10 cases are now on file. Although the validity of these anecdotal reports needs to be tested, as their number accumulates so too does the suspicion that the interaction is real. A pharmacokinetic study of the  $T_4$ -celery interaction is under consideration by the Mater Hospital Pharmacy Services' Therapeutic Advisory Service.

### Conclusion

Anecdotal evidence indicates a potential interaction between thyroxine and celery seed tablets. Since consumers often fail to volunteer details of self-medication with complementary medicines, prescribers and pharmacists should ask directly what herbal/nutritional medicines consumers are taking. If celery seed tablets are being co-administered with thyroxine, it is strongly recommended that thyroid function tests are closely monitored and any suspected interaction reported.

### R E F E R E N C E S

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## Your questions to the PBAC

### Celecoxib

The listing of celecoxib as a general benefit on the Pharmaceutical Benefits Scheme (PBS) from 1 August 2000 was welcomed by arthritis sufferers Australia-wide. However, the decision to list the 200 mg capsules with an issue quantity of 60 rather than 30 has surprised many pharmacists. This exceeds the 30 day supply rule, taking into account the manufacturer's recommended one capsule a day dosage.

A more serious problem is the number of potential adverse sulfonamide-type reactions that may occur around Australia, and the subsequent waste of Commonwealth funds when celecoxib is discontinued by the patients. In our town of 5000 there has been a high demand for celecoxib and within one week of listing we had six adverse sulfonamide-type reactions, with swelling of the throat, body rash and fever. One patient ended up in Moruya Hospital and the rest were referred to their general practitioner.

As a medication review pharmacist, I am concerned about the incidence and severity of these reactions. They usually occur within a few days of commencing celecoxib and the patient has to cease the medication. As celecoxib 200 mg is the most commonly prescribed dose, I believe that the decision by the Pharmaceutical Benefits Advisory Committee to list the 200 mg capsules in a quantity of 60 was a poor one, and will result in a significant waste of PBS funds.

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### PBAC response:

The Pharmaceutical Benefits Advisory Committee (PBAC) recommends the maximum quantity and the number of repeats that should apply to the prescribing of a particular medication. The maximum quantity recommended for listing by the PBAC