- advise the patient not to take a catch up dose if one dose is missed; the flare-up of disease is unlikely
- make a carer responsible for giving the drug if the patient appears to have cognitive or severe sensory difficulties

Most of these principles are relevant when advocating unusual or atypical regimens. The consequences of incorrect dosage can be fatal but are often preventable.[3]

REFERENCES

1. Methotrexate misadventures – a need for care and counselling. Aust Adv Drug React Bull 1999;18:14.
2. Methotrexate – name the day. Aust Adv Drug React Bull 1998;17:7.
3. Low dose methotrexate therapy – toxic if not taken correctly. Adverse Drug Reactions Advisory Committee. Med J Aust 1994;161:152.

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 Board 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 Board is prepared to do this. Before new drugs are prescribed, the Board 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.

Anagrelide

Agrylin (Orphan)

0.5 mg capsules

Approved indication: essential thrombocythaemia

Australian Medicines Handbook Section 7

Essential thrombocythaemia is an uncommon abnormality of the bone marrow. This clonal stem cell disorder results in the production of abnormal platelets and an increased platelet count. Patients are not only at risk of thrombosis, but also bleeding.[1]

Patients require treatment if they develop complications or if their platelet count exceeds 1000 x 10^9/L. While some patients require plateletpheresis, many patients are treated with hydroxyurea. This drug can have serious adverse effects so anagrelide will offer an alternative treatment.

Anagrelide was originally developed as an inhibitor of platelet aggregation, but was found to cause thrombocytopenia. It is thought to impair the maturation of megakaryocytes.

A clinical trial investigated anagrelide in 577 patients with conditions such as polycythaemia vera and chronic granulocytic leukaemia. The trial included 335 patients with essential thrombocythaemia, but only 262 were evaluable. After completing at least four weeks of treatment, 247 had a platelet count which had reduced by half or fallen below 600 x 10^9/L.[2]

Patients begin treatment with 0.5 mg four times a day or 1 mg twice a day for at least a week. The dose is adjusted to the lowest dose able to keep the platelet count under control. The platelet count should be measured every two days in the first week, then weekly until the maintenance dose is found. In clinical studies the mean duration of treatment was 65 weeks, but more than 20% of patients took anagrelide for two years.

The drug is rapidly absorbed. Although food reduces bioavailability the effect is not significant. Anagrelide has a half-life of 1.3 hours and is extensively metabolised. Most of the metabolites are excreted in the urine. Patients with liver or kidney disease must be monitored carefully as anagrelide may alter liver function and possibly cause renal failure.

Anagrelide causes vasodilatation. Patients may develop hypotension, palpitations, tachycardia and heart failure. These symptoms led to the withdrawal of some patients from the clinical trials. In total 15% of the patients withdrew. Other reasons for withdrawal included headache, diarrhoea and abdominal pain which are common adverse reactions to anagrelide.

Anaemia is common and thrombocytopenia can develop. In addition to full blood counts, renal and liver function should also be checked during treatment.

REFERENCES

1. Bentley MA, Taylor KM, Wright SJ. Essential thrombocythaemia. Med J Aust 1999;171:210-3.
2. Anagrelide Study Group. Anagrelide, a therapy for thrombocythemic states: experience in 577 patients. Am J Med 1992;92:69-76.

Varicella vaccine

Varilix (SmithKline Beecham)

vials containing a powder pellet for reconstitution

Approved indication: immunisation

Australian Medicines Handbook Section 20.1

Chickenpox is usually a mild childhood infection. It can, however, be fatal in immunocompromised patients. In the USA the cost of managing chickenpox is estimated to be US$400 million.[1] Universal vaccination is now recommended for all American children.

The vaccine which has been approved for use in Australia is a live attenuated strain of the varicella-zoster virus. A single dose is recommended for children more than nine months old. Older children and adults have two doses at least six weeks apart. The deltoid area is the preferred site for the subcutaneous injection.

In children a single dose of vaccine has an efficacy of 88%. Children who catch chickenpox despite vaccination appear to develop an attenuated infection.

Injection site reactions occur in 27% of cases. Some vaccinees develop a mild varicella-like disease within a month.

Although varicella vaccines have been available overseas for

several years, there are unanswered questions about their role. The duration of immunity is unknown; will immunising children result in more infections in later life? It will be many years before we know if the vaccine influences the incidence and severity of shingles. An economic analysis in the USA has found that the vaccine may not be cost-beneficial from the perspective of 'payers' such as governments or health funds. For every dollar spent the payer only saves US 90 cents. However, from a societal perspective, including costs such as time lost from work, the community saves US$5.40 for every dollar spent.[1] A New Zealand study found similar results. For every dollar spent the payer saves NZ 67 cents, but society saves NZ$2.79.[2]

REFERENCES

1. Strassels SA, Sullivan SD. Clinical and economic considerations of vaccination against varicella. Pharmacotherapy 1997;17:133-9.
2. Scuffham P, Devlin N, Eberhart-Phillips J, Wilson-Salt R. The cost-effectiveness of introducing a varicella vaccine to the New Zealand immunisation schedule. Soc Sci Med 1999;49:763-79.

NEW FORMULATIONS

Phytomenadione

Konakion MM Paediatric (Roche)

2 mg/0.2 mL in glass ampoules

Approved indication: prevention of haemorrhagic disease of the newborn

Australian Medicines Handbook Section 7.4

Injecting neonates with vitamin K (phytomenadione) has been an effective method of preventing haemorrhagic disease of the newborn. In the early 1990s a possible link between these injections and childhood cancer was reported.[1] Although other studies have not confirmed this link, the National Health and Medical Research Council advised that vitamin K could be given orally as an alternative to injection. The intramuscular formulation was not ideal for oral use and has now been replaced by a formulation which is approved for oral and intramuscular use.

Health professionals need to be aware that the new formulation has different regimens. Not only are repeat oral doses required for babies given vitamin K by mouth, but also for babies who are breast-fed following an injection. The regimens for prophylaxis are:

Healthy breast-fed neonates

2 mg orally at birth, at 3–5 days and every two weeks thereafter while breast feeding

OR

1 mg intramuscularly at birth followed by either 1 mg intramuscularly or 2 mg orally at 6–8 weeks (if the second dose is given orally, further doses every two weeks should be considered)

Healthy formula-fed neonates

2 mg orally at birth and at 3–5 days

OR

1 mg intramuscularly at birth

Neonates at risk of haemorrhagic disease

- 1 mg intramuscularly at birth
- second dose if fully breast-fed:

  1 mg intramuscularly at 6–8 weeks

  OR

  2 mg orally at 6–8 weeks and 2 mg orally every two weeks thereafter while breast feeding

To reduce the risk of late-onset bleeding, it is important to remind parents to ensure that the recommended repeat doses are given.

REFERENCE

1. Golding J, Greenwood R, Birmingham K, Mott M. Childhood cancer, intramuscular vitamin K, and pethidine given during labour. Br Med J 1992;305:341-6.

Ocreotide

Sandostatin LAR (Novartis)

10 mg, 20 mg and 30 mg modified-release intramuscular injection

NEW STRENGTHS

Desferrioxamine mesylate

Desferal (Novartis)

2 g powder for injection

NEW PROPRIETARY BRANDS

Clomipramine

DBL Clomipramine (Faulding)

25 mg tablets

Diltiazem

DBL Diltiazem (Faulding)

60 mg tablets

Gemfibrozil

DBL Gemfibrozil (Faulding)

600 mg tablets

Gliclazide

Glyade (Alphapharm)

80 mg tablets

Moclobemide

DBL Moclobemide (Faulding)

150 mg and 300 mg tablets

Prazosin hydrochloride

DBL Prazosin (Faulding)

1 mg, 2mg and 5 mg tablets

Ticlopidine hydrochloride

Ticlohexal (Hexal)

250 mg tablets