# Dental notes

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## Cardiac effects of non-cardiac drugs

Dentists have traditionally been concerned about the potential risk of cardiac effects from the vasoconstrictor, either adrenaline or octapresin, in dental local anaesthetics. However, the evidence shows that there is minimal effect from either of these drugs in appropriate dosage. There is a much greater effect from endogenous production of adrenaline if the dental procedure is painful.

Non-steroidal anti-inflammatory drugs are widely used for dental pain and dentists should be aware of the potential cardiac adverse effects, particularly with long-term use of these drugs. The concept of using these very effective drugs for the shortest time possible at the lowest effective dose is an excellent guiding principle for all patients. Concurrent use of other analgesics, as well as correct diagnosis and timely and effective provision of dental treatment, can go a long way in diminishing the long-term adverse effects of these drugs.

# New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data and 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.

## Canakinumab

Ilaris (Novartis)

vials containing 150 mg lyophilised powder for reconstitution

Approved indication: cryopyrin-associated periodic syndromes

Australian Medicines Handbook section 15.2.2

Cryopyrin-associated periodic syndromes are a group of rare but often severe inflammatory disorders including familial cold autoinflammatory syndrome or familial cold urticaria, Muckle-Wells syndrome and neonatal-onset multisystem inflammatory disease. These disorders are associated with mutations in the gene that encodes cryopyrin, a protein involved in the regulation of interleukin-1β. The defect results in over-production of interleukin-1β and leads to inflammation that can affect the skin, eyes, bones, joints and meninges. Patients may also experience severe fatigue, fever, myalgia, chronic anaemia and learning difficulties.

Currently there are no approved treatments for cryopyrin-associated periodic syndromes in Australia, but colchicine, corticosteroids and sometimes anakinra (Aust Prescr 2004;27:160-1) have been used in these patients. Canakinumab is a human monoclonal antibody that specifically binds to interleukin-1β, neutralising its activity. After subcutaneous administration, peak serum concentrations are reached after 7 days in adults and between 2 and 7 days in children. The average terminal half-life is 26 days in adults and between 22.9 and 25.7 days in children.

In an early study, four patients responded to one intravenous dose of canakinumab 10 mg/kg – urticarial rashes disappeared within 24 hours and patients experienced a complete response by one week. The median time until re-dosing after disease flare was approximately 26 weeks.[1]

In a larger 48-week trial, 34 of 35 patients (aged 4–75 years) responded to a single open-label subcutaneous dose of canakinumab 150 mg (or 2 mg/kg for those under 40 kg) within a month. After 8 weeks, patients who had responded were randomised to receive either canakinumab or placebo (at 8-week intervals) for a further 24 weeks. The 15 patients given canakinumab stayed in remission, whereas 13 of the 16 patients given placebo relapsed. Disease activity seemed to correlate with C-reactive protein and serum amyloid A concentrations – both were elevated in the placebo group but normalised in the canakinumab group. After 32 weeks, 6 of the 15 patients in the canakinumab group said their symptoms had completely gone compared to none of the patients in the placebo group. In a third phase of the trial, 31 patients were given open-label canakinumab (at least 2 doses over 16 weeks). Of the 29 who completed treatment, 28 people were in remission.[2]

As canakinumab suppresses the immune system, infections are a risk. The most frequently reported adverse reactions with canakinumab were upper respiratory tract infections and pharyngitis (up to 33.3%). Also, there were more suspected infections with canakinumab than with placebo (10 patients vs 4 patients).[2] Two patients given canakinumab had serious adverse events – one had urinary tract infection requiring hospitalisation and the other developed vertigo with acute closed-angle glaucoma. Both patients discontinued treatment.[2]

Because of the risk of infections, patients should be tested for latent and active tuberculosis before starting treatment and caution is urged in patients with a history of recurring infections. Canakinumab should not be started or continued in patients with active infection requiring medical treatment. Concomitant use of tumour necrosis factor inhibitors or live vaccines is not