The Western Australian Drugs and Therapeutics Committee wishes to inform all prescribers of recent major changes in the Product Information for thioridazine (Aldazine, Melleril), arising from recognition of ECG changes induced by the drug (see below).

**SINGLE INDICATION FOR THIORIDAZINE USE**

The only indication now approved by the Therapeutic Goods Administration is thioridazine use in the management of schizophrenia in patients who have failed to respond adequately to treatment with at least two other antipsychotic drugs, at an adequate dose and for an adequate duration, either because of poor effectiveness or significant side-effects.

**INDICATIONS DELETED**

Indications NOT now approved in the revised thioridazine Product Information include:

- treatment of acute functional psychoses eg schizophrenia, mania or psychotic depression;
- long-term treatment of schizophrenia;
- short-term treatment of agitation and/or behavioural disturbance in patients with delirium or dementia;
- short-term treatment of agitation and severe depression; and
- adjunctive treatment of children with severe behavioural disorders, as can be found in some children with mental retardation or autism, including the treatment of self-injurious and aggressive behaviour or overactivity.

**NEW CONTRAINDICATIONS**

Thioridazine has been shown to prolong the QTc interval in a dose-related manner. Other drugs with this potential have been associated with torsade-de-pointes type arrhythmias and sudden death. Thioridazine is thus now contraindicated:

- with other drugs that inhibit cytochrome P450 2D6 isoenzyme activity (eg fluoxetine, paroxetine, cimetidine, moclobemide);
• with drugs that appreciably inhibit the metabolism of thioridazine by other pathways (eg fluvoxamine, propranolol, pindolol);

• with drugs that potentially prolong the QTc interval (eg disopyramide, procainamide, quinidine, sotalol, tricyclic antidepressants, terfenadine);

• in patients known to have reduced expression of cytochrome P450 2D6 isoenzyme; and

• in patients with congenital long QT syndrome or a history of cardiac arrhythmias

IMPACT ON PRACTICE GUIDELINES

Use of thioridazine in the treatment of acute arousal is no longer an approved indication. Thioridazine was recently recommended as a therapeutic option in the WADTC Psychotropic Drug Guidelines (Algorithm: Acute Arousal including Treatment of Elderly Patients), and in Therapeutic Guidelines: Psychotropic Version 4 as an adjunct to acute mania and for sedation of acutely disturbed patients. Use of thioridazine for this indication requires careful consideration by prescribers.

WADTC also recommends that though thioridazine remains approved for resistant schizophrenia, newer “atypical” antipsychotic agents should be used as the first line drugs for the treatment of schizophrenic and related disorders, and resistant schizophrenia.

The Committee now recommends that patients being considered for treatment with thioridazine should have a baseline ECG and measurement of serum $K^+$, and monitoring of these during treatment, especially during dose adjustment. Patients with a QTc interval greater than 450 msec should not receive thioridazine, and it should be discontinued at a QTc interval over 500 msec. Thioridazine should be discontinued or avoided in patients with actual or potential hyper- or hypokalemia.

Treatment of thioridazine overdose should include but is not restricted to cardiovascular and ECG monitoring, and correction of electrolyte abnormalities.

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