PRODUCT INFORMATION
MERSYNDOL

NAME OF THE MEDICINE

Non-proprietary Name
Paracetamol, codeine phosphate and doxylamine succinate

DESCRIPTION

Mersyndol contains paracetamol 450 mg, codeine phosphate 9.75 mg, doxylamine succinate 5 mg. Paracetamol is an odourless, crystalline powder or crystals with a bitter taste. Codeine phosphate is an odourless, crystalline powder or small colourless crystals with a bitter taste. Doxylamine succinate is a powder with a characteristic odour.

Mersyndol also contains sodium starch glycollate, purified talc, magnesium stearate, microcrystalline cellulose, quinoline yellow CI 47005 and sunset yellow FCF 15985.

Mersyndol is aspirin-free.

PHARMACOLOGY

Paracetamol is an effective and fast-acting analgesic which relieves mild to moderate pain. It is rapidly absorbed from the gastrointestinal tract with peak plasma levels usually reached half to one hour after oral administration. It also reduces fever by a direct effect on the heat-regulating centres to increase dissipation of body heat.

Codeine phosphate is an effective oral analgesic which provides relief from mild to moderate pain. It is also well absorbed from the gastrointestinal tract after oral administration. The abuse potential of codeine is lower than that of other opiates.

Doxylamine succinate belongs to the ethanolamine class of antihistamines with sedative properties. Its calmative effect is useful in enhancing the effects of analgesics.

INDICATIONS

Symptomatic relief of moderate to severe pain including headache, toothache, backache or pain associated with trauma or surgery.

The calmative properties of Mersyndol may be especially useful in the treatment of tension headache, migraine and period pain and the antipyretic properties may be useful in controlling fever.

CONTRAINDICATIONS

Known hypersensitivity to paracetamol, codeine or doxylamine succinate; patients with pre-existing respiratory depression. Patients with glucose-6-phosphate-dehydrogenase deficiency. Mersyndol is contraindicated during breast-feeding (see PRECAUTIONS).
PRECAUTIONS
Mersyndol should be used with caution in severe hepatic or renal dysfunction. Hepatotoxicity may occur with paracetamol even at therapeutic doses, after short treatment duration and in patients without pre-existing liver dysfunction. Both doxylamine succinate and codeine may cause drowsiness in some patients, thus patients should be cautioned about operating vehicles or machinery or engaging in activities which require them to be fully alert. Avoid alcohol.

Products containing codeine should not be given for prolonged periods as they may be habit-forming.

This medication may be dangerous when used in large amounts or for long periods. Hepatotoxicity may develop following a dose of 10 g of paracetamol and hepatic failure is known to occur occasionally with the long term use of paracetamol.

Patients with known analgesic intolerance or known bronchial asthma must only use Mersyndol after having consulted a physician (hypersensitivity reactions including bronchospasm are possible).

In ultra-rapid opiate/codeine metabolisers, there is an increased risk of developing opioid toxicity even at low doses. Symptoms of opioid toxicity include nausea, vomiting, constipation, lack of appetite and somnolence. In severe cases this may include symptoms of circulatory and respiratory depression.

Use in Pregnancy
Category A. There have been no observations of an increase in the frequency of malformations or other direct or indirect harmful effects on the foetus in pregnant women and women of child-bearing age who have taken those drugs found in Mersyndol. Codeine may cause respiratory depression and withdrawal syndrome in neonates born to mothers who use codeine during the third trimester of pregnancy. As a precautionary measure, use of Mersyndol should be avoided during the third trimester of pregnancy and during labour.

Use in Lactation
Mersyndol is contraindicated during breast-feeding (see CONTRAINDICATIONS). There are no data available on the use of Mersyndol during lactation. Paracetamol and codeine is excreted into human breast milk. Codeine is partially metabolized by cytochrome P450 2D6 (CYP2D6) into morphine, which is excreted into breast milk. If nursing mothers are CYP2D6 ultra-rapid metabolisers, higher levels of morphine may be present in their breast milk. This may result in symptoms of opioid toxicity in both mother and the breast-fed infant. Life-threatening adverse events or neonatal death may occur even at therapeutic doses (see PRECAUTIONS).

INTERACTIONS WITH OTHER MEDICINES
Patients receiving other CNS depressants eg. hypnotics, sedatives, tranquillisers, including alcohol, concomitantly may exhibit an additive CNS depression. Barbiturates and other antiepileptics (including phenytoin and carbamazepine), rifampicin and prolonged alcohol ingestion may increase the metabolism of paracetamol to metabolites toxic to the liver.

Paracetamol may increase the risk of bleeding in patients taking warfarin and other coumarin derivatives, particularly if paracetamol is taken in high doses or for several days. Patients
taking paracetamol and coumarin derivatives should be monitored for appropriate coagulation and bleeding complications.

Paracetamol may considerably slow down the excretion of chloramphenicol, entailing the risk of increased toxicity. When used concurrently with zidovudine, an increased tendency for neutropenia may develop. Combination of Mersyndol and zidovudine should be avoided.

Concurrent intake of drugs, which delay gastric emptying, such as propantheline, may slow down the uptake of paracetamol, thereby retarding its onset of action. Conversely, drugs, which accelerate gastric emptying, such as metoclopramide, may accelerate the uptake of paracetamol and its onset of action.

ADVERSE EFFECTS

Side-effects with Mersyndol are infrequent. However, among those reported are: anorexia, drowsiness, depression, dizziness, sweating, anaphylactic shock, angioneurotic oedema, difficulty in breathing, drop in blood pressure, gastrointestinal discomfort such as nausea and diarrhoea, dry mouth and, on rare occasions, rash.

Paracetamol may occasionally cause skin reactions and isolated cases of agranulocytosis and thrombocytojaenic purpura have been reported. Changes in blood picture (rarely thrombocytopenia, leukopenia, and, in isolated cases, pancytopenia) may occur.

Bronchospasm may be triggered in patients having a tendency of analgesic asthma.

Toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), acute generalised exanthematous pustulosis, fixed drug eruption and cytolytic hepatitis, which may lead to acute hepatic failure, have also been reported.

Doxylamine succinate may cause drowsiness in some individuals. Constipation and pancreatitis may occur in association with codeine.

DOSAGE AND ADMINISTRATION

Adults and children 12 years of age and older

One or two tablets every 4 to 6 hours as needed for relief. Do not exceed 8 tablets in 24-hour period. Not recommended to be used for long periods.

Children under 12 years

Not recommended.

OVERDOSAGE

It has been reported that paracetamol may produce symptoms of acute toxicity in adults, following the ingestion of more than 15g. Hepatotoxicity may develop after the ingestion of a single dose of 10 to 15g (200 to 250 mg/kg) and a dose of more than 25g is potentially fatal.

Nausea, vomiting, anorexia, pallor and abdominal pain generally appear during the first 24 hours of overdosage with paracetamol. Overdosage with paracetamol may cause hepatic cytolysis which can lead to hepatocellular insufficiency, metabolic acidosis, encephalopathy, coma and death. Increased levels of hepatic transaminases, lactate deshydrogenase and bilirubin with a reduction in prothrombin level can appear 12 to 48 hours after acute overdosage. It can also lead to pancreatitis and acute renal failure. Patients may be asymptomatic for several days following ingestion of large doses of paracetamol and laboratory evidence of hepatotoxicity may be delayed for up to one week. Non-fatal hepatic
damage is usually reversible. The antidote, N-acetylcysteine, should be administered as early as possible.

In an evaluation of codeine intoxication in children, symptoms ranked by decreasing order of frequency included sedation, rash, miosis, vomiting, itching, ataxia and swelling of the skin. Respiratory failure may occur. Blood concentrations of codeine ranged from 1.4 to 5.6 µg/mL in eight adults whose deaths were attributed primarily to codeine overdosage.

Reactions associated with doxylamine overdosage may vary from CNS depression to stimulation. Stimulation is particularly likely in children; insomnia, nervousness, euphoria, irritability, tremors, nightmares, hallucinations and convulsions can occur. Atropine-like signs and symptoms such as dry mouth, fixed, dilated pupils, flushing and gastrointestinal symptoms may also occur.

For information on the management of overdose contact the Poisons Information Centre on 131126 (Australia).

PRESENTATION AND STORAGE CONDITIONS
Mersyndol is available as 20 tablets or caplets, each containing paracetamol 450 mg, codeine phosphate 9.75 mg and doxylamine succinate 5 mg.
The tablets are yellow, marked with ‘M’ inside two concentric circles on one side and ‘Mersyndol 008’ and a breakline on the reverse.
The caplets are yellow, capsule-shaped tablets with ‘Mersyndol’ on one side and a breakline on the other.
Storage Conditions: store below 30 °C

NAME AND ADDRESS OF THE SPONSOR
sanofi-aventis australia pty ltd
12-24 Talavera Road
Macquarie Park NSW 2113

POISON SCHEDULE OF THE MEDICINE
Pharmacist Only Medicine (Schedule 3)

DATE OF FIRST INCLUSION IN THE ARTG
8 July 1991

DATE OF MOST RECENT AMENDMENT
11 July 2012