Data Sheet

MERSYNDOL® Tablet

*Paracetamol 450mg per tablet*

*Codeine Phosphate 9.75mg per tablet*

*Doxylamine Succinate 5mg per tablet*

MERSYNDOL FORTE® Tablet

*Paracetamol 450mg per tablet*

*Codeine Phosphate 30mg per tablet*

*Doxylamine Succinate 5mg per tablet*

Presentation

MERSYNDOL Tablets are yellow, round, flat faced bevelled edged tablets with a diameter of 12.7mm. One face is marked "M" within two concentric circles, the other "MERSYNDOL 008" and has a breakline.

MERSYNDOL FORTE Tablets are white round flat faced bevelled edged tablets with a diameter of 12.7mm. One face is marked "M" within two concentric circles, the other "MERSYNDOL FORTE" and has a breakline.

Uses

Actions

Paracetamol is an effective and fast acting analgesic and antipyretic which acts centrally to relieve mild to moderate pain. Like the salicylates, paracetamol reduces fever by a direct action on the heat regulating centres to increase the dissipation of heat.

Codeine phosphate is an effective oral analgesic, which provides relief from mild to moderate pain. The abuse potential of codeine is lower than other opiates.

Doxylamine succinate belongs to the ethanolamine class of antihistamines with sedative properties.

Pharmacokinetics

Paracetamol is rapidly and completely absorbed from the gastrointestinal tract after oral administration with peak plasma levels occurring 30 to 60 minutes after administration. It is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol.

The elimination half-life varies from about 1 to 4 hours.
The apparent volume of distribution is 1 to 1.2 L/kg. Plasma protein binding is negligible at usual therapeutic concentrations but increases with increased concentrations. Paracetamol can cross the placenta and is excreted in milk. Food intake delays paracetamol absorption.

**Codeine phosphate** is well absorbed after oral administration. It is metabolised in the liver, mainly to the glucuronide conjugates, morphine (about 10%) and norcodeine (about 10%), which, with codeine, are excreted in the urine. Most of the excretion products appear in the urine within 6 hours and excretion of up to 86% of the dose is almost complete in 24 hours. The volume of distribution of codeine is 3.5L/kg and at therapeutic blood levels about 30% is protein bound.

**Doxylamine succinate** has an elimination half-life of approximately 9 hours.

### Indications

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

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

MERSYNDOL is a suitable alternative for those individuals who cannot tolerate aspirin.

MERSYNDOL FORTE is indicated only for relief of severe pain not responding to other analgesics.

### Dosage and Administration

**Mersyndol and Mersyndol Forte**

Adults, children 12 years and older: 1 or 2 tablets every four to six hours as needed for relief.

Do not exceed 8 tablets in a 24 hour period.

Not recommended for children under 12 years.

### Contraindications

Known hypersensitivity to paracetamol, codeine, doxylamine succinate or any excipients of Mersyndol or Mersyndol Forte

Pre-existing respiratory depression

Asthma

Patients with known glucose-6-phosphate-dehydrogenase deficiency

Patients with known analgesic intolerance

### Warnings and Precautions

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 ingestion of a single dose of 10 to 15 g (200 to 250 mg/kg) and a dose of more than 25 g is potentially fatal. 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. There have been reports of kidney damage, disturbances in clotting mechanisms, metabolic acidosis, hypoglycaemia, agranulocytosis, thrombocytopenia, methaemoglobinemia and myocardial necrosis.
Paracetamol should be used with caution in patients with severe hepatic or renal dysfunction.

Products containing codeine should not be given for prolonged periods. Codeine phosphate may occasionally cause constipation. Codeine may be habit forming.

Both doxylamine succinate and codeine may cause drowsiness in some patients. Patients should be cautioned about operating vehicles or machinery, or engaging in activities which require them to be fully alert.

Alcohol should be avoided. To avoid more serious adverse reactions, special caution must be exercised and intervals between doses must be increased and/or the dose reduced, when paracetamol is used in patients with chronic alcohol abuse.

**Use in Pregnancy**

Safe use in pregnancy has not been established in human studies; this medication should not be used in pregnancy unless in the opinion of the prescribing doctor the potential benefits outweigh the potential risks. There is epidemiological evidence of safety in pregnancy for paracetamol and doxylamine succinate. There is inadequate evidence of safety of codeine in pregnancy, but it has been in wide use for many years without any apparent ill consequence.

Although the embryo-toxicity/teratogenicity of doxylamine succinate has not been proven in humans, animal studies have demonstrated adverse effects on chondrogenesis.

**Use in Lactation**

Both codeine and paracetamol are excreted in breast milk. Mersyndol & Mersyndol Forte should not be used during lactation without a thorough assessment of possible risks and benefits by a physician.

**Adverse Reactions**

Side effects with MERSYNDOL and MERSYNDOL FORTE are infrequent. However among those reported are anorexia, drowsiness, depression, dizziness, gastrointestinal discomfort (nausea and diarrhoea), dry mouth and on rare occasions, redness of the skin or rash.

Hypersensitivity reactions such as, sweating, angioneurotic oedema, difficulty breathing and drop in blood pressure may occur.

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

Paracetamol may occasionally cause skin reactions. Isolated cases of agranulocytosis and thrombocytopenic purpura have been reported with paracetamol. Changes in blood picture are possible (thrombopenia, leucopenia, agranulocytosis and pancytopenia).

Prolonged or high dosage use may result in impaired liver or kidney function.

Doxylamine succinate may cause drowsiness in some individuals.

Constipation may occur in association with codeine.

Very rarely, pancreatitis may occur.
Interactions

Patients receiving CNS depressants such as anaesthetics, hypnotics, sedatives, tranquilizers and alcohol concomitantly with MERSYNDOL or MERSYNDOL FORTE may exhibit an additive CNS depression.

Barbiturates and prolonged alcohol ingestion may increase the metabolism of paracetamol to metabolites toxic to the liver.

Certain hypnotics, antiepileptics (Phenobarbital, phenytoin and carbamazepine) and rifampicin when administered concomitantly with paracetamol products can result in liver damage.

Paracetamol may considerably slow down the excretion of chloramphenicol, resulting in toxicity.

Concurrent use of paracetamol and zidovudine increases the tendency for neutropenia to develop and should be avoided.

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

When Mersyndol tablets are taken after a meal, the onset of action may be delayed.

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.

Overdosage

Reactions associated with doxylamine succinate overdosage may vary from central nervous depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms - dry mouth; fixed, dilated pupils; flushing and gastrointestinal symptoms may also occur. Severe rhabdomyolysis after doxylamine succinate overdose has been reported in humans.

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 micrograms per ml in eight adults whose deaths were attributed to codeine 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 10-15g (200 to 250 mg/kg) and a dose of more than 25g is potentially fatal. 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 1 week. Non-fatal hepatic damage is usually reversible. Lavage or emesis induced by ipecac is recommended. The antidote, N-acetylcysteine, should be administered as early as possible.

Pharmaceutical Precautions

Store below 30°C.
Medicine Classification

MERSYNDOL: Pharmacist-Only Medicine
MERSYNDOL FORTE: Prescription Medicine

Package Quantities

In blister packs of 20 tablets (both presentations)

Further Information

Nil

Name and Address

Distributed by:-
sanofi-aventis new zealand limited
James & Wells Tower
Part Level 8, 56 Cawley St, Ellerslie
Auckland, New Zealand

Date of Preparation

Approved July 1997
Address details updated 18 August 2004
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