DATA SHEET

1 NEULACTIL TABLETS

Neulactil 2.5 mg tablets

Neulactil 10 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Periciazine 2.5mg

Periciazine 10mg

Excipients with known effect: lactose monohydrate and wheat starch

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Neulactil tablets

2.5 mg: yellow, scored, marked NEULACTIL

10 mg: yellow, scored, marked 10

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Periciazine is indicated:

1. In adults with schizophrenia or other psychoses, for the treatment of symptoms or prevention of relapse.
2. In anxiety, psychomotor agitation, violent or dangerously impulsive behaviour. periciazine is used as an adjunct to the short-term management of these conditions.

Periciazine tablets are not recommended for children (see Section 4.3 and 4.4).

4.2 DOSE AND METHOD OF ADMINISTRATION

Dosage requirements vary with the individual and the severity of the condition being treated. Initial dosage should be low with progressive increases until the desired response is obtained, after which dosage should be adjusted to maintain control of symptoms.

Severe conditions (Indication 1)

Adults

Initially 75 mg per day in divided doses. Dosage should be increased by 25 mg per day at weekly intervals until optimum effect is achieved. Maintenance therapy would not normally be expected to exceed 300mg per day.

Elderly

Initially 15-30 mg per day in divided doses. If this is well tolerated the dosage may be increased if necessary for optimum control of behaviour.

Mild or moderate conditions (Indication 2)

Adults

Initially 15-30 mg daily, divided into two portions, with a larger dose being given in the evening.

Elderly

5-10mg per day is suggested as a starting dose. It may be divided so that a larger portion is given in the evening. Half or quarter the normal adult dose may be sufficient for maintenance therapy.

4.3 CONTRAINDICATION

Periciazine should not be used in the following circumstances:

- Hypersensitivity to periciazine, phenothiazines or any of the ingredients.
- Circulatory collapse.
- Acute intoxication with central depression and coma.
- History of blood dyscrasias or agranulocytosis
- Risk of angle-closure glaucoma.
- Risk of urinary retention due to urethroprostatic disorders.
- Hypersensitivity or intolerance to gluten, because the medicinal product contains wheat starch (gluten).

- Periciazine should not be administered in association with spinal or regional anaesthetics.
- Periciazine should not be combined with dopaminergic antiparkinsonism agents (**see Section 4.5**)
- Periciazine should not be used in patients with convulsive disorders that are not receiving appropriate anticonvulsive medication.
- Periciazine should not be used in children younger than 1 year, due to a possible link between use of phenothiazine-containing products and Sudden Infant Death Syndrome (SIDs)
- Neuroleptics should not be used in patients with phaeochromocytoma or liver dysfunction.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

WARNING: Periciazine may cause a mild leukopenia or agranulocytosis in some patients.

Suicide. The possibility of a suicide attempt is inherent in schizophrenia and bipolar disorder, and close supervision of high-risk patients should accompany therapy.

When periciazine is prescribed in conjunction with other centrally acting drugs, the usual dose of these compounds should be reduced by at least half while the new treatment is being introduced. Caution should be exercised when periciazine is prescribed with other phenothiazine derivatives or CNS depressants such as barbiturates, analgesics, narcotics or antihistamines as it may potentiate their effects.

Activities such as the control of vehicles or machinery should not be undertaken until it is evident that any soporific effect has subsided. Patients should be warned about drowsiness, slowing of reaction time and impaired judgement.

Neuroleptics should be avoided in patients with renal dysfunction, epilepsy, Parkinson's disease, hypothyroidism, cardiac failure and myasthenia gravis. As periciazine has an anticholinergic action, it should be avoided in patients who have a history of prostatic hypertrophy.

Patients should be strongly advised against ingesting alcohol or any medication containing alcohol while under treatment.

Patients with the following diseases/disorders should be monitored closely during treatment: Cardiovascular disorders, bradycardia, hypokalaemia or familial history or prolongation of QT, because of a risk of worsening of long QT-syndrome, which may also elevate the risk of developing torsade de pointes, tachycardia and sudden death. As with other neuroleptics, cases of QT interval prolongation have been reported with periciazine. Neuroleptic phenothiazines may potentiate QT interval prolongation which increases the risk of onset of serious ventricular arrhythmias of the torsade de pointes type, which is potentially fatal (sudden death). QT prolongation is exacerbated, in particular, in the presence of bradycardia, hypokalaemia, and congenital or acquired (i.e., drug induced) QT prolongation. If the clinical situation permits, medical and laboratory evaluations (e.g. ECG and serum potassium) and control of blood pressure

should be performed to rule out possible risk factors before initiating treatment with a neuroleptic agent and as deemed necessary during treatment (**see Section 4.8**).

Caution should be taken in patients with cardiovascular disease or family history of QT prolongation. Concomitant use with QT prolonging drugs should be avoided.

An increased risk of cerebrovascular events has been reported in elderly patients with dementia treated with atypical antipsychotic drugs. An increase in the risk of cerebrovascular events with other antipsychotic drugs or other populations of patients cannot be excluded. Periciazine should therefore be used with caution in patients with stroke risk factors.

Cases of venous thromboembolism, sometimes fatal, have been reported with antipsychotic drugs. Therefore, periciazine should be used with caution in patients with risk factors for thromboembolism (**see Section 4.8**).

Hyperglycaemia or intolerance to glucose has been reported in patients treated with periciazine. Patients with an established diagnosis of diabetes mellitus or with risk factors for the development of diabetes who are started on periciazine, should get appropriate glycaemic monitoring during treatment (**see Section 4.8**).

It is essential that treatment should be discontinued in the event of unexplained fever as this may be one of the signs of neuroleptic malignant syndrome described with neuroleptics, the clinical manifestations of which include pallor, hyperthermia, autonomic disturbances, altered consciousness and muscle rigidity. Signs of autonomic dysfunction such as sweating and arterial instability may precede the occurrence of hyperthermia and thus constitute early presenting signs. Although this effect of neuroleptics may be idiosyncratic in origin, certain risk factors such as dehydration or organic brain damage appear to be predisposing factors.

Apart from exceptional situations, periciazine should not be used in patients with Parkinson’s disease. The onset of paralytic ileus, which can manifest itself as abdominal bloating and pain, requires emergency treatment.

Use with caution in patients with certain cardiovascular conditions, because of the quinidine-like, tachycardia-inducing and hypotensive effects of this class of products.

Careful monitoring of treatment with periciazine is required in epileptics due to a possible lowering of the seizure threshold. The occurrence of convulsive seizures necessitates the discontinuation of treatment.

Careful monitoring of treatment with periciazine is required in patients with severe hepatic impairment and/or renal impairment, due to the risk of accumulation.

Because of the risk of photosensitisation, patients should be advised to avoid exposure to direct sunlight.

Use in the Elderly

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Although the causes of death in clinical trials with atypical antipsychotics were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g. pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear.

Paralytic ileus has occurred in patients, particularly in the elderly, taking one or more drugs with anticholinergic action for extended periods. In such patients, caution should be exercised if constipation develops.

It should be used with caution in the elderly, particularly during very hot or very cold weather (risk of hyper-, hypothermia).

Careful monitoring of treatment with periciazine is required in the elderly who are particularly susceptible to postural hypotension, sedation and extrapyramidal effects; chronic constipation (risk of paralytic ileus); possible prostatic hypertrophy.

Use in Children

Periciazine is not recommended in children under 3 years of age. Use in children under the age of 6 years is reserved for exceptional situations in specialist units. When it is prescribed in this population, neurological signs or symptoms should be carefully monitored.

It is advisable to perform annual clinical examination to evaluate learning abilities in children, due to the cognitive impact, and dosage should be regularly adapted depending on the child's clinical condition.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

Dopaminergic antiparkinsonism agonist agents are contraindicated due to reciprocal antagonism between dopaminergic agonists and neuroleptics. Neuroleptic-induced extrapyramidal syndrome should be treated with an anticholinergic rather than a dopaminergic antiparkinsonism agent. Patients being treated for Parkinson's disease with a dopaminergic antiparkinsonism agent and requiring a neuroleptic, should cease antiparkinsonism therapy since such agents exacerbate psychotic disorders and cannot act on receptors blocked by neuroleptics.

Caution is required with the use of the following medicines due to the risk of QT prolongation (**see Section 4.8**):

- Class Ia antiarrhythmic agents such as quinidine and disopyramide.
- Class III antiarrhythmic agents such as amiodarone and sotalol.

- Other medications such as bepridil, cisapride, sultopride, thioridazine, methadone, intravenous erythromycin, intravenous vincamine, halofantrine, pentamidine, sparfloxacin lithium.
- Medicines which induce bradycardia, such as bradycardia-inducing calcium channel blockers (diltiazem, verapamil), beta-blockers, clonidine, guanfacine, digitalis.
- Medicines which can cause hypokalaemia, such as diuretics, stimulant laxatives, intravenous amphotericin B, glucocorticoids, tetracosactides.
- Other antipsychotics.

Concomitant use of Lithium might increase the risk of the appearance of neuropsychiatric signs, suggestive of neuroleptic malignant syndrome or lithium poisoning. Regular clinical and biological monitoring of serum (lithium) should be performed, especially when the combination is initiated.

Intensification of the sedative effects of neuroleptics may be intensified by alcohol. Impaired vigilance may make it dangerous to drive or use machines. Avoid consumption of alcoholic beverages and medications containing alcohol.

The CNS depressant actions of neuroleptic agents may be intensified (additively) by alcohol, barbiturates, morphine derivatives, benzodiazepines and other sedatives, anxiolytics other than benzodiazepines, hypnotics, sedative antidepressants, sedative H1 antihistamines, central antihypertensives, baclofen and thalidomide. Enhanced central depression and respiratory depression may occur. Impaired vigilance may make it dangerous to drive or use machines.

Phenothiazines are potent inhibitors of CYP2D6. Co-administration of phenothiazines with amitriptyline, a CYP2D6 substrate, may lead to an increase in the plasma levels of amitriptyline. Monitor patients for dose-dependent adverse reactions associated with amitriptyline.

The hypotensive effect of most antihypertensive drugs especially alpha adrenoceptor blocking agents may be exaggerated by neuroleptics, increasing the risk of postural hypotension.

The mild anticholinergic effect of neuroleptics may be enhanced by other anticholinergic drugs possibly leading to constipation, heat stroke, etc.

The action of some drugs may be opposed by neuroleptics; these include amphetamine, levodopa clonidine, guanethidine (inhibition of the antihypertensive effect), epinephrine. In patients with Parkinson’s disease, use the minimum effective doses of levodopa and periciazine.

Adrenaline must not be used in patients overdosed with neuroleptics.

Anticholinergic agents may reduce the antipsychotic effect of neuroleptics.

Some drugs interfere with absorption of phenothiazine neuroleptic agents: topical gastro-intestinal agents (e.g.antacids), antiparkinsonian agents, lithium. Antacids should not be taken at the same time as phenothiazine neuroleptics.

Increases or decreases in the plasma concentrations of a number of drugs, e.g. propranolol, phenobarbital have been observed but were not of clinical significance.

High doses of neuroleptics may reduce the response to hypoglycaemic agents the dosage of which might have been raised.

Simultaneous administration of desferrioxamine and prochlorperazine has been observed to induce a transient metabolic encephalopathy characterised by loss of consciousness for 48-72 hours.

It is possible that this may occur with periciazine since it shares many of the pharmacological activities of prochlorperazine.

Atropine and other atropine-like substances (e.g. imipramine antidepressants, sedative H1 antihistamines, anticholinergic antiparkinsonian agents, atropine-like antispasmodics and disopyramide) may cause cumulative atropine-like side effects such as urinary retention, constipation and dry mouth.

4.6 FERTILITY, PREGNANCY AND LACTATION

Use in Pregnancy (Category C)

Available human data are insufficient to exclude a risk of congenital malformation in children exposed *in utero* to periciazine.

When given in high doses during late pregnancy, phenothiazines have caused prolonged extrapyramidal disturbances in the child.

The following effects have been reported (in postmarketing surveillance) in neonates exposed to phenothiazines during the third trimester of pregnancy:

- various degrees of respiratory disorders ranging from tachypnoea to respiratory distress, bradycardia and hypotonia, most often when other drugs such as psychotropic or antimuscarinic drugs were coadministered.
- signs related to the atropinic properties of phenothiazines such as meconium ileus, delayed meconium passage, initial feeding difficulties, abdominal bloating, tachycardia;
- neurological disorders such as extrapyramidal symptoms including tremor and hypertonia, somnolence, agitation.

Appropriate monitoring and treatment of neonate born to mothers receiving periciazine is recommended.

If possible, it is preferable to taper the dosage of both neuroleptics and antiparkinsonians, which potentiate the atropine-like effects of neuroleptics, at the end of pregnancy.

A period of monitoring of the neurological and gastro-intestinal functions of the neonate appears warranted.

As a precautionary measure, the use of periciazine should be avoided during pregnancy unless the potential benefits outweigh the potential risks.

Use in Lactation

Safety in lactation has not been established. In the absence of data on excretion in breast milk, breastfeeding is not recommended during treatment.

Fertility

No data currently available.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients, and especially those who drive or operate machines, should be informed of the risk of somnolence associated with this medication, particularly at the beginning of treatment.

4.8 UNDESIRABLE EFFECTS

a. Summary of the safety profile

Most serious and/or most frequently occurring adverse effects of periciazine include the following:

Behavioural: At the start of treatment, some drowsiness is not uncommon but this effect usually wears off within a few days. Adjustment of dosage, e.g. by giving the larger portion in the evening, will invariably lessen the effect, but care should be exercised when barbiturates or other sedatives are prescribed with periciazine, particularly for children or elderly patients.

Impaired psychomotor activity is a frequent initial untoward reaction. If a toxic-confusional state appears, the medication should be stopped immediately.

Hepatic: Jaundice, occurs in a very small percentage of patients taking neuroleptics. A premonitory sign may be a sudden onset of fever after one to three weeks of treatment followed by the development of jaundice. Neuroleptic jaundice has the biochemical and other characteristics of obstructive jaundice and is associated with obstruction of the canaliculi by bile thrombi; the frequent presence of an accompanying eosinophilia indicates the allergic nature of this phenomenon. Treatment should be withheld on the development of jaundice.

Cardiovascular: Hypotension, usually postural, commonly occurs. Elderly or volume depleted subjects are particularly susceptible. These reactions occur more often at the beginning of treatment or when initial high dosages are used.

Haematological: Agranulocytosis may occur rarely; it is not dose related. These may occur suddenly or follow a fall in blood count usually during the first 2 or 3 months of treatment. The occurrence of unexplained infections or fever requires immediate haematological investigation.

Nervous system: Extrapyramidal: Acute dystonias or dyskinesias, usually transitory are commoner in children and young adults, and usually occur within the first 4 days of treatment or after dosage increases.

Akathisia characteristically occurs after large initial doses.

Parkinsonism is more common in adults and the elderly. It usually develops after weeks or months of treatment. One or more of the following may be seen: tremor, rigidity, akinesia or other features of Parkinsonism.

Skin: Contact skin sensation is a serious but rare complication in those frequently handling preparations of phenothiazines; the greatest care must be taken to avoid contact of the drug with the skin. Skin rashes of various kinds may also be seen in patients treated with drug. Patients on high dosage should be warned that they may develop photosensitivity in sunny weather and should avoid exposure to direct sunlight and that retinal changes may occur.

Tardive Dyskinesia: Tardive Dyskinesia may appear in some patients on long term therapy or may appear after drug therapy has been discontinued. The risk appears to be greater in elderly patients on high dose therapy, especially females. The symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterised by rhythmical involuntary movement of tongue, face, mouth or jaw (e.g. protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these may be accompanied by involuntary movements of extremities.

Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of the drug increases. Less commonly, the syndrome can develop after relatively brief treatment periods at low doses. The risk seems to be greater in elderly patients, especially females.

The syndrome may become clinically recognisable either during treatment, upon dosage reduction, or upon withdrawal of treatment. The dosage of antipsychotic drug should be reduced periodically (if clinically possible) and the patient observed for signs of the disorder, since the syndrome may be masked by a higher dose. In patients requiring long-term treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought.

There is no known effective treatment for tardive dyskinesia. Anti-parkinsonian agents usually do not alleviate symptoms. It is suggested that anti-psychotic agents be discontinued if symptoms of tardive dyskinesia appear.

Neuroleptic Malignant Syndrome: A potentially fatal syndrome called neuroleptic malignant syndrome has been reported in association with anti-psychotic drugs. The syndrome is

characterised by muscular rigidity, fever, hyperthermia, altered consciousness and autonomic instability (eg tachycardia, labile blood pressure, profuse sweating, dyspnoea).

The management of neuroleptic malignant syndrome should include immediate discontinuation of anti-psychotic drugs, intensive monitoring and treatment of symptoms, and treatment of any associated medical problems.

b. Tabulated list of adverse reactions

The following adverse effects have been reported for periciazine or phenothiazines in general. The adverse drug reactions are presented in the following table by system organ class (SOC), and are ranked by frequency, using the following convention:

Very common ≥1/10
Common ≥1/100 to <1/10
Uncommon ≥1/1,000 to <1/100
Rare ≥1/10,000 to <1/1,000
Very rare < 1/10,000
Not known cannot be estimated from the available data

Such adverse reactions as listed in the below table may occur. Patients should be carefully monitored, and in the event of an abnormality, appropriate measures such as reduction of the dose and suspension of administration should be taken.

System organ class	Frequency and symptom
Blood and lymphatic system disorders	Very Common:
	A mild leukopaenia occurs in up to 30% of patients on prolonged high dosage of neuroleptics.
	Rare:
	Agranulocytosis
Endocrine disorders	Not known:
	Hyperprolactinaemia which may result in galactorrhoea, gynaecomastia, amenorrhoea, frigidity and impotence.
	Delayed ovulation, menstrual irregularities, lactation, gynaecomastia, changes in libido, inhibition of ejaculation, false positive pregnancy tests and oedemas.
	Increased appetite and weight gain.
	Temperature dysregulation.
Metabolism and nutrition disorders	Not known:
	Intolerance to glucose, hyperglycaemia have been reported (**see Section 4.4**).
Psychiatric disorders	Not known:
	Indifference, anxiety reactions, mood variations, agitation.

System organ class	Frequency and symptom
Nervous system disorders	At the start of treatment, some drowsiness is not uncommon.
	Paradoxical effects e.g.agitation, insomnia, inversion of sleep, increased aggressiveness and activation of psychotic symptoms, have been occasionally observed.
	Common:
	impaired psychomotor activity.
	Tremor.
	Not known:
	Extrapyramidal syndrome: Acute dystonia or dyskinesias, akathisia, akinesia with or without hypertonia, hyperkinetic-hypertonic movements and motor excitation.
	Parkinsonism: rigidity, akinesia or other features of Parkinsonism.
	Tardive dyskinesia occurring during long-term treatment.
	Early dyskinesia.
	Neuroleptic malignant syndrome.
	Nasal stuffiness, dry mouth (sometimes with oral infections and dental caries), perspiration and changes in body temperature.
	Anticholinergic effects such as dry mouth, constipation, paralytic ileus, accommodation disorders, risk of urinary retention.
	Sedation or somnolence
Eye disorders	Not known:
	Blurred vision and aggravation of glaucoma. Abnormal pigmentation, including deposits in the anterior segment of the eye, due to accumulation of the product, generally without effects on vision, have been observed, usually when high doses of phenothiazines are given for prolonged periods.
Cardiac disorders	Not known:
	Cardiac arrhythmias, including atrial arrhythmia, A-V block, ventricular tachycardia and fibrillation have been reported during neuroleptic therapy, possibly related to dosage. Pre-existing cardiac disease, old age, hypokalaemia and concurrent tricyclic antidepressants may predispose.
	ECG changes, usually benign, include, ST depression, U-waves and T-wave changes. Risk of QT interval prolongation.
	There have been isolated reports of sudden death, with possible causes of cardiac origin (**see Section 4.4**), as well as cases of unexplained sudden death, in patients receiving neuroleptic phenothiazines.
	Positive serology for antinuclear antibodies without clinical lupus erythematosus.
Vascular disorders	Common:
	Postural hypotension.
	Not known:
	Cases of venous thromboembolism, including cases of pulmonary embolism, sometimes fatal, and cases of deep vein thrombosis have been reported with antipsychotic drugs (**see Section 4.4**).

System organ class	Frequency and symptom
Respiratory disorders	Not known:
	Respiratory depression is possible in susceptible patients.
	Phenothiazine therapy, historically, has been associated with hypostatic pneumonia and unexpected sudden deaths with possible causes of cardiac origin. The reports of unexpected sudden death with periciazine are very rare. The physician should also be alerted to the possible development of "silent pneumonias" with phenothiazine therapy.
Gastrointestinal disorders	Not known:
	Vomiting, nausea, constipation, faecal impaction, diarrhoea and paralytic ileus.
Hepatobiliary disorders	Very rare:
	Cholestatic jaundice and liver injury, mainly of cholestatic or mixed type, are reported in patients treated with periciazine.
Skin and subcutaneous tissue disorders	Rare:
	Contact skin sensation.
	Not known:
	Skin rashes, photosensitivity reactions, allergic skin reactions.
Pregnancy, puerperium and perinatal conditions	Not known:
	Neonatal abstinence syndrome.
Reproductive system and breast disorders	Very rare:
	Priapism has been reported in patients treated with periciazine.
General disorders and administration site conditions	Not known:
	Allergic and Toxic Reactions: Asthma, laryngeal oedema, angioneurotic oedema, hyperpyrexia and other allergic reactions.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 OVERDOSE

Symptoms:

The symptoms of overdosage with phenothiazines include CNS depression, presenting as lethargy, dysarthria, ataxia, stupor progressing from drowsiness to coma with areflexia, patients with early or mild intoxication may experience restlessness, confusion, agitation, excitement or a delirious state. Other symptoms include cardiovascular symptoms (related to risk of QT prolongation), such as hypotension, ventricular tachycardia and arrhythmias, ECG changes: respiratory depression, hypothermia, pupillary dilation or constriction, tremor, muscle twitching, spasm or rigidity, convulsions, arrhythmias and hypotension, dystonic movements, muscular

hypotonia, difficulty in swallowing and breathing, cardiovascular collapse, cyanosis and respiratory and/or vasomotor collapse, possibly with sudden apnoea. Polyuria has also been noted which may result in dehydration. Severe extra-pyramidal dyskinesias may occur.

These effects may be potentiated by other medicines or by alcohol. Anticholinergic syndrome is of importance. Extremely serious parkinsonian syndrome may occur.

Acute toxicity has been determined in animals. LD 50 values range from 44 mg/kg (intravenous, mouse) to 530 mg/kg (oral mouse).

Treatment:

The stomach should be emptied by aspiration and lavage. Emetics should not be used, not only because the antiemetic action of phenothiazines prevents the effect of the emetic agent, but also because the sedative and extrapyramidal side effects increase the risk of pulmonary aspiration should vomiting occur.

To counter acute hypotension the patient should be placed in the head down position and noradrenaline or phenylephrine administered intravenously. Adrenaline is contraindicated.

The central nervous depression should generally be allowed to recover naturally, however artificial respiration may be required. Appropriate antibiotic therapy should be instituted for any respiratory infections.

Hypothermia should be allowed to recover naturally unless the temperature approached levels at which cardiac arrhythmias may be feared (e.g. 29.4°C). Shivering is a sign of the waning effects of the drug.

Severe extrapyramidal reactions should be treated with benztropine or another antiparkinsonian agent.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Periciazine is 2 -cyano - 10 - 3' - (4 - hydroxpiperidino-propyl) phenothiazine.

Neulactil contains a yellow crystalline powder, almost without odour, non-hygroscopic and sensitive to light. It melts at about 115°C. The molecular weight is 365.48. It is insoluble in water, slightly soluble in ether, fairly soluble in ethanol, acetone and benzene and freely soluble in chloroform.

Periciazine is a phenothiazine with a piperidine side chain. It has similar antipsychotic action to other phenothiazines but produces more sedation. It also has adrenolytic, anticholinergic and extrapyramidal effects.

5.2 PHARMACOKINETIC PROPERTIES

A group of 12 healthy human volunteers were administered two 10mg periciazine capsules. A peak concentration of 150 ng/ml (410 nmol/l) was achieved 2 hours after drug administration and the half-life was approximately 12 hours. In some subjects, detectable amounts of periciazine were still present in the blood after 36 hours. There is high inter-patient variability.

The majority of the product undergoes conjugation in the liver and is excreted in the urine.

As with other phenothiazines, high inter-patient variability is to be expected.

5.3 PRECLINICAL SAFETY DATA

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the Data Sheet.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Colloidal dioxide 0.48mg (aerosil)

Microcrystalline cellulose 115.3mg

Wheat starch 24mg (LMS)

Lactose monohydrate 87.96mg

Magnesium stearate 2.4mg

6.2 INCOMPATIBILITIES

None known.

6.3 SHELF LIFE

36 months from date of manufacture.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

Both strengths come in blister packs of 100 tablets made from PVC/PVDC/AI.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

None stated.

7 MEDICINE SCHEDULE

Prescription Medicine.

8 SPONSOR

sanofi-aventis new zealand limited
Level 8, 56 Cawley Street, Ellerslie
Auckland New Zealand

Toll Free Number (medical information): 0800 283 684
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

31 December 1969

10 DATE OF REVISION OF THE TEXT

04 December 2018

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
2	Chemical name moved to section 5.1; addition of excipients with known effect
3	Physical/chemical properties of the active ingredient moved to section 5.1; editorial changes
4.1	Editorial changes
4.2	Editorial changes
4.3	Editorial changes

Section changed	Summary of new information
4.6	Additional pregnancy warnings
5.1	Movement of text from previous sections
8	Addition of contact email