
AUSTRALIAN PRODUCT INFORMATION – NEULACTIL (PERICIAZINE)

1. NAME OF THE MEDICINE

Periciazine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Neulactil tablets contain periciazine (2.5 mg and 10 mg)

List of excipients with known effect: Contains gluten and sugars as lactose.

For the full list of excipients, see Section 6.1 List of excipients..

3. PHARMACEUTICAL FORM

Tablets

2.5 mg: yellow, scored, marked NEULACTIL

10 mg: yellow, scored, marked 10

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Severe anxiety and tension states and the maintenance treatment of the psychotic patient. It is useful in controlling such symptoms as impulsiveness and aggression.

4.2 Dose and method of administration

In all cases, dosage may be progressively increased until the most effective level is reached after which the dosage should be adjusted to maintain control of symptoms.

Mild to Moderate Conditions in General Practice

Adults

The initial daily dosage is 15 to 30 mg divided into two portions with the larger dose given in the evening.

Geriatric Patients

The starting dose is 10 mg/day, increasing according to therapeutic effect and patient tolerance, to a maximum of about 30 mg daily in divided doses.

Moderate to Severe Conditions

Hospitalised Adult Patients

Initial dosage is 25 to 75 mg/day orally, administered in divided doses.

Children

The initial daily dosage should not exceed 0.5 mg per year of age. Use in children below 1 year of age is contraindicated. In older children (16 years) the twenty four hour dose should be about 1 mg/year of age. Dosages up to 75 mg/day are used in hospitals without any untoward effects.

4.3 Contraindications

Periciazine should never be used in the following circumstances:

- Circulatory collapse.
- Acute intoxication with central depression and coma.
- Previous history of blood dyscrasias. or agranulocytosis.
- Hypersensitivity to periciazine, other phenothiazines or to any of the other ingredients contained in the tablets (see Section 6.1 List of excipients).
- Hypersensitivity or intolerance to gluten, because the medicinal product contains wheat starch (gluten).
- Risk of angle-closure glaucoma.
- Risk of urinary retention due to urethroprostatic disorders.
- Periciazine should not be administered in association with spinal or regional anaesthetics.
- Periciazine should not be used in patients with convulsive disorders that are not receiving appropriate anticonvulsive medication.
- In children younger than 1 year, due to a possible association between use of phenothiazine-containing products and Sudden Infant Death Syndrome (SIDS).
- Periciazine is contraindicated in combination with dopaminergic antiparkinsonism agents (see Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS.)
- Neuroleptics should be avoided 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.

Hypersensitivity reactions including urticaria and angioedema have been reported with Neulactil use. In case of allergic reaction, treatment with Neulactil must be discontinued and appropriate symptomatic treatment initiated (see Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)).

When Neulactil 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 Neulactil 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.

Neulactil should be avoided in patients with liver or renal dysfunction, epilepsy, Parkinson's disease, hypothyroidism, cardiac failure, pheochromocytoma, myasthenia gravis, or prostate hypertrophy, or in patients with a history of narrow angle glaucoma or agranulocytosis.

Acute withdrawal symptoms, including nausea, vomiting, headache, anxiety, agitation, dyskinesia, dystonia, disturbed temperature regulation, and insomnia, have very rarely been reported following the abrupt cessation of high doses of neuroleptics. Relapse may also occur, and the emergence of extrapyramidal reactions has been reported. Therefore, gradual withdrawal is advisable. Symptoms of withdrawal can occur following treatment at any dose. Withdrawal of treatment should occur under close medical supervision.

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 of prolongation of QT because of a risk of worsening of long QT-syndrome, which may also elevate the risk for developing torsade de pointes, tachycardia and sudden death. As with other neuroleptics, cases of QT interval prolongation have been reported with periciazine. If the clinical situation allows, relevant examinations of e.g. ECG and serum potassium should be performed and control of blood pressure to exclude possible risk factors before the treatment is started. The same examinations should be repeated during the treatment (see Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)).

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 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)).

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. Neulactil should be used with caution in patients with stroke risk factors.

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

As agranulocytosis has been reported, regular monitoring of the complete blood count is recommended. The occurrence of unexplained infections or fever may be evidence of blood dyscrasia (see Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)), and requires immediate hematological investigation.

All patients should be advised that, if they experience fever, sore throat or any other infection, they should inform their physician immediately and undergo a complete blood count. Treatment should be discontinued if any marked changes (hyperleucocytosis, granulocytopenia) are observed in the blood count.

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

It is essential that periciazine treatment should be discontinued in the event of unexplained fever as this may be one of the signs of the 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 blood pressure 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.

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 Neulactil is required in epileptics due to a possible lowering of the seizure threshold. The occurrence of convulsive seizures necessitates the discontinuation of periciazine treatment. Periciazine should not be used in patients with convulsive disorders that are not receiving appropriate anticonvulsive medication (see Section 4.3 CONTRAINDICATIONS).

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

Apart from exceptional situations, periciazine should not be used in patients with Parkinson's disease. In such patients, careful monitoring is required and caution should be exercised if constipation develops. The onset of paralytic ileus, which can manifest itself as abdominal bloating and pain, requires emergency treatment.

Prolonged administration of any phenothiazine may result in tardive dyskinesia, particularly in the elderly and children.

Phenothiazines may be additive with, or may potentiate the action of, other CNS depressants such as opiates or other analgesics, barbiturates or other sedatives, general anaesthetics, or alcohol.

Use in hepatic impairment

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

Use in renal impairment

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

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.

Careful monitoring of treatment with periciazine is required when administering in elderly patients exhibiting greater susceptibility to orthostatic hypotension, sedation and extrapyramidal effects; chronic constipation (risk of ileus paralytic); possible prostatic hypertrophy.

Neulactil should be used cautiously in the elderly owing to their susceptibility to drugs acting on the central nervous system and a lower initial dosage is recommended. There is an increased risk of drug-induced Parkinsonism in the elderly particularly after prolonged use.

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

The elderly are particularly susceptible to postural hypotension, careful monitoring is required.

Paediatric use

- Use in children < 1 year of age – contraindicated (see Section 4.3 CONTRAINDICATIONS).
- Use in children 1-3 years of age – not recommended.
- Use in children 3-6 years of age 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 an 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.
- Neulactil has been associated with dystonic reactions. It should therefore be used cautiously in children.

Effects on laboratory tests

No data available

4.5 Interactions with other medicines and other forms of interactions

The use of dopaminergic antiparkinsonism agonist agents with periciazine is contraindicated due to reciprocal antagonism between the dopaminergic agonist and neuroleptics (see Section 4.3 CONTRAINDICATIONS).

Contraindicated combinations:

Dopaminergics, except in patients with Parkinson's disease.

Antiparkinsonism dopaminergic agonist agents: Reciprocal antagonism between the dopaminergic agonist and neuroleptics. Neuroleptic-induced extrapyramidal syndrome should be treated with an anticholinergic rather than a dopaminergic antiparkinsonism agent.

Where treatment for neuroleptic-induced extrapyramidal symptoms is required, anticholinergic antiparkinsonian agents should be used in preference to levodopa, since neuroleptics antagonize the antiparkinsonian action of dopaminergics.

Drug combinations not recommended or requiring precaution:

Dopaminergics in patients with Parkinson's disease.

Dopaminergics may cause or exacerbate psychotic disorders. If treatment with neuroleptics is required in patients with Parkinson's disease treated with a dopaminergic, the latter should be tapered off gradually (sudden discontinuation of dopaminergic agents exposes the patient to a risk of "neuroleptic malignant syndrome"). For parkinsonian patients who require treatment with both a neuroleptic and a dopaminergic agent, use the minimum effective doses of both medications.

The action of some drugs may be opposed by phenothiazine neuroleptics; these include amphetamine, clonidine, adrenaline.

Sulopride: Increased risk of ventricular arrhythmias, particularly of the torsades de pointes type, by addition of electrophysiological effects. There is an increased risk of arrhythmias when antipsychotics are used with concomitant QT prolonging drugs (including certain antiarrhythmics, antidepressants and other antipsychotics) and drugs causing electrolyte imbalance.

Caution is required with the use of the following medicines due to the risk of QT prolongation (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE):

- Class Ia antiarrhythmic agents such as quinidine and disopyramide.
- Class III antiarrhythmic agents such as amiodarone and sotalol.
- Other medications such as bepridil, cisapride, sulopride, 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 (amphotericin), glucocorticoids, tetracosactides (tetracosactrins).
- Other antipsychotics.

Lithium: concomitant use might increase the risk of QT prolongation and can 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 while being treated with periciazine.

The CNS depressant actions of neuroleptic agents may be intensified (additively) by alcohol, other sedatives, and other central nervous system depressants: morphine derivatives, barbiturates, benzodiazepines,

anxiolytics other than benzodiazepines, hypnotics, sedative antidepressants, sedative H1 antihistamines, central antihypertensives, baclofen, thalidomide. Enhanced central depression and respiratory depression may occur. Impaired vigilance may make it dangerous to drive or use machines.

Cytochrome P450 2D6 Metabolism: Some phenothiazines are moderate inhibitors of CYP2D6. There is a possible pharmacokinetic interaction between inhibitors of CYP2D6, such as phenothiazines, and CYP2D6 substrates. Co-administration of periciazine with amitriptyline/amitriptylinoxide, a CYP2D6 substrate, may lead to an increase in the plasma levels of amitriptyline/amitriptylinoxide. Monitor patients for dose-dependent adverse reactions associated with amitriptyline/amitriptylinoxide.

Because of convulsive risk, the combined use of medicinal products which lower the seizure threshold should be carefully assessed.

Antihypertensives (especially alpha adrenoceptor blocking agents): increased antihypertensive effect and risk of orthostatic 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, adrenaline (epinephrine).

Guanethidine: inhibition of the antihypertensive effect of guanethidine

Adrenaline must not be used in patients overdosed with neuroleptics.

Anticholinergic agents may reduce the antipsychotic effect of neuroleptics.

Gastro-intestinal agents that are not absorbed (e.g. antacids), antiparkinsonian agents, lithium: Reduced gastro-intestinal absorption of phenothiazine neuroleptics may occur. Such gastro-intestinal agents 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 (phenobarbitone) have been observed but were not of clinical significance.

Administration of Neulactil in patients taking antidiabetic agents can lead to an increase in blood sugar levels. Forewarn the patient and advise increased self-monitoring of blood and urine levels. If necessary, adjust the antidiabetic dosage during and after discontinuing neuroleptic treatment.

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: Imipramine antidepressants, sedative H1 antihistamines, anticholinergic antiparkinsonian agents, atropine-like antispasmodics, disopyramide: cumulative side effects such as urinary retention, constipation and dry mouth (i.e. atropine-like side effects).

4.6 Fertility, pregnancy and lactation

Effects on fertility

No data available.

Use in pregnancy – Pregnancy Category C

The use of Neulactil is not recommended during pregnancy and in women of childbearing potential not using contraception, unless the potential benefits outweigh the potential risks.

Advise patients to inform their healthcare provider of a known or suspected pregnancy.

Advise patients to avoid becoming pregnant while receiving this medicine.

Advise female patients of reproductive potential to use effective contraception.

Safety in pregnancy has not been established. Available human data are insufficient to exclude a risk of congenital malformation in children exposed in utero to Neulactil. Neonates exposed to antipsychotic drugs (including periciazine) during the third trimester of pregnancy are at risk of experiencing extrapyramidal neurological disturbances and/or withdrawal symptoms following delivery. There have been post-market reports of neurological disorders such as extrapyramidal symptoms including agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, and feeding disorder in these neonates. These complications have varied in severity; while in some cases symptoms have been self-limiting, in other cases neonates have required additional medical treatment or monitoring.

The following effects have also 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 mother receiving Neulactil are recommended.

Periciazine should be used during pregnancy only if the anticipated benefit outweighs the risk and the administered dose and duration of treatment should be as low and as short as possible.

Precaution is needed when both neuroleptics and antiparkinsonian agents are used together towards the end of pregnancy, due to their additive atropine-like effects. 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.

Use in lactation

Safety in lactation has not been established. Phenothiazines may be excreted in milk, therefore, breastfeeding is not recommended during treatment with Neulactil.

4.7 Effects on ability to drive and use machines

Patients should be warned about drowsiness, dizziness, and blurred vision and advised not to drive or operate machinery, particularly during the early days of treatment, until they know how Neulactil affects them.

4.8 Adverse effects (Undesirable effects)

Behavioural

Indifference, confusional state, delirium, anxiety, mood altered

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.

Paradoxical effects, such as agitation, insomnia, inversion of sleep, increased aggressiveness and activation of psychotic symptoms, have been occasionally observed.

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.

Jaundice cholestatic and liver injury, mainly of cholestatic or mixed type, are very rarely reported in patients treated with periciazine.

Cardiovascular

Orthostatic hypotension 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.

Torsade de pointes, ECG changes include QT prolongation, ST depression, U-waves and T-wave changes. Cardiac arrhythmias, including ventricular arrhythmias and atrial arrhythmias, atrioventricular (A-V) block, ventricular tachycardia, which may result in ventricular fibrillation or cardiac arrest have been reported during neuroleptic phenothiazine 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.

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 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

There have been isolated reports of sudden death, with possible causes of cardiac origin (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE), as well as cases of unexplained sudden death, in patients receiving neuroleptic phenothiazines.

Gastrointestinal

Vomiting, nausea, constipation, faecal impaction, diarrhoea and paralytic ileus may occur.

Respiratory

Respiratory depression is possible in susceptible patients, nasal congestion

Haematological

Agranulocytosis, leukopenia, eosinophilia, thrombocytopenia (including thrombocytopenic purpura)

A mild leukopaenia occurs in up to 30% of patients on prolonged high dosage of neuroleptics. 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.

Positive serology for anti-nuclear antibodies without clinical lupus erythematosus has been reported, weight increased, liver function test abnormal

Nervous system

Early dyskinesia has been reported.

Dystonia, tardive dyskinesia occurring during long-term treatment.

Extrapyramidal syndrome: 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; akinesia with or without hypertonia, hyperkinetic-hypertonic movements, motor excitation, akathisia.

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.

Commonly just tremor.

Sedation or somnolence, dizziness, insomnia, anticholinergic effects such as dry mouth, constipation, ileus paralytic (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE), accommodation disorder, risk of urinary retention have been reported. Seizure.

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.

Skin and eyes

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 reaction and rash may also be seen in patients treated with drug. Patients should be warned that they may develop photosensitivity reaction in sunny weather and should avoid exposure to direct sunlight and that retinal changes may occur. Pigmentation disorder.

In some patients blurred vision and aggravation of glaucoma have been reported. Abnormal pigmentation, including deposits in the anterior segment of the eye, due to accumulation of the product, have been observed, usually when high doses of phenothiazines are given for prolonged periods.

Accommodation disorder, corneal deposits.

Endocrine

Hyperprolactinaemia which may result in galactorrhoea, gynaecomastia, amenorrhoea, erectile dysfunction; frigidity. Other effects include delayed ovulation, menstrual irregularities, lactation, gynaecomastia, changes in libido, inhibition of ejaculation, false positive pregnancy tests, weight gain and oedemas, have been known to occur. Increased appetite and weight gain have been reported in some patients on periciazine therapy.

Temperature regulation disorder.

Metabolism and nutrition disorders

Glucose tolerance impaired, hyperglycemia, hyponatremia, inappropriate antidiuretic hormone secretion

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.

Allergic and Toxic Reactions

Hypersensitivity, urticaria, angioedema, asthma, laryngeal oedema, angioneurotic oedema, hyperpyrexia and other allergic reactions may also occur.

Other

Dry mouth (sometimes with oral infections and dental caries), perspiration and changes in body temperature.

Pregnancy, puerperium and perinatal conditions

Neonatal abstinence syndrome has been reported. Drug withdrawal syndrome neonatal.

Reproductive system and breast disorders

Very rare: priapism, ejaculation disorder

Miscellaneous

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.

In post-marketing surveillance cases of intolerance to glucose, hyperglycaemia have been reported (see Section 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE).

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at <http://www.tga.gov.au/reporting-problems>

4.9 Overdose

Symptoms

High doses cause depression of the central nervous system, presenting as lethargy, dysarthria, ataxia, stupor; reduction of consciousness into coma with areflexia, convulsions; mydriasis; patients with early or mild intoxication may experience restlessness, confusion, agitation, excitement or a delirious state. Other symptoms include cardiovascular symptoms (related to QT interval prolongation), such as hypotension, ventricular tachycardia, 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 may occur. Severe 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).

For information on the management of overdose, contact the Poison Information Centre on 13 11 26 (Australia).

In the event of overdose of Neulactil, take all appropriate measures immediately.

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 benzotropine or another antiparkinsonian agent (intramuscular dose in adults: 1 to 2mg, children 0.2 to 0.25mg initially with increments if necessary).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

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.

Clinical trials

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.

5.2 Pharmacokinetic properties

Absorption

Periciazine is well absorbed after oral administration. However, like other phenothiazines, periciazine appears to be subject to extensive first pass metabolism in the gut and/or liver with low plasma levels of parent compound.

Metabolism

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

Genotoxicity

No data available

Carcinogenicity

No data available

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Neulactil tablets contain the following excipients: microcrystalline cellulose, lactose monohydrate, magnesium stearate, colloidal anhydrous silica and wheat starch.

6.2 Incompatibilities

Please see Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

2.5 mg: PVC/PVDC/Al Blister pack in packs of 100;

10 mg: PVC/PVDC/Al Blister pack in packs of 100.

6.6 Special precautions for disposal

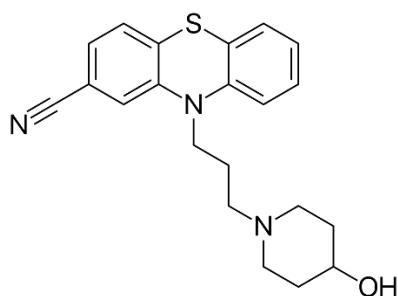
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 Physicochemical properties

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

Periciazine is 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.

Chemical Structure



CAS Number

2622-26-6

7. MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Medicine (Schedule 4)

8. SPONSOR

Clinect Pty Ltd

120 – 132 Atlantic Drive

Keysborough VIC 3173

Australia

Free Call Australia: 1800 899 005

9. DATE OF FIRST APPROVAL

21 October 1991

10. DATE OF REVISION

21 September 2023

Summary table of changes

Section Changed	Summary of new information
All	Changes to format
2	Wording amended to align with declarations printed on the proposed labels.
8	Update to Sponsor Details