AUSTRALIAN PRODUCT INFORMATION – SYMMETREL (AMANTADINE HYDROCHLORIDE) CAPSULES

1 NAME OF THE MEDICINE

Amantadine hydrochloride.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains amantadine hydrochloride 100 mg.

Excipients with known effect: contains hydroxybenzoates and sulfites.

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

3 PHARMACEUTICAL FORM

100 mg capsules: brown, soft gelatin, marked "GEIGY" on one side and "GB" on reverse.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Parkinson's Disease

Idiopathic Parkinson's disease; post-encephalitic parkinsonism; symptomatic parkinsonism (e.g. following CNS injury from carbon monoxide poisoning); arteriosclerotic parkinsonism; drug-induced extrapyramidal reactions.

Symmetrel can be given alone for initial therapy or combined with anticholinergic drugs or L-dopa (see section 4.2 Dose and method of administration).

Note: Symmetrel is not indicated for the treatment of tardive dyskinesia.

Type A Virus Influenza

Prophylaxis of respiratory tract illness caused by Influenza Type A.
Prophylaxis in non-immunised individuals (including children) for whom influenza may have serious consequences (e.g. persons with chronic respiratory disease or diabetes mellitus).

4.2 DOSE AND METHOD OF ADMINISTRATION

Before use in elderly patients or those with impaired liver or kidney function, refer to section 4.4 Special warnings and precautions for use and section 5.2 Pharmacokinetics properties. In patients over 65 years of age, both age and renal function should be taken into consideration. By age 65, renal function will typically have declined to a level at which reduced doses of Symmetrel or increased dosing interval are appropriate. Specific dosage schedules for patients over 65 years of age and those with impaired renal function are shown below.

Recommended Dosages

Parkinson's disease

Adults to 65 years

When used alone, 100 mg daily for the first week of treatment, increasing in the second week to 100 mg twice daily. The dose can be titrated against signs and symptoms. Amounts exceeding 200mg daily may provide some additional relief but may also be associated with increasing toxicity. In these cases the dose should be raised gradually, at intervals of not less than 1 week.

Adults over 65 years

Since patients in this age group tend to have lower renal clearance and consequently higher plasma concentrations (see section 5.2 Pharmacokinetic properties), the recommended dose is 100 mg daily. If the patient has, or develops, any renal impairment, the dosing interval should be adjusted (see section 4.2 Dose and method of administration - Dosage in Renal Impairment).

Note: Patients deriving benefit initially from Symmetrel not uncommonly experience a reduction in effectiveness after a few weeks. Temporary discontinuation of Symmetrel for several weeks, followed by re-introduction of therapy, may result in regaining of benefit in some patients. The use of other anti-Parkinson drugs may be necessary. Treatment with Symmetrel must be reduced gradually because abrupt discontinuation may exacerbate Parkinson's syndrome, regardless of the patient's response to therapy (see section 4.4 Special warnings and precautions for use).

Combined treatment

Any anti-Parkinson drug with which the patient is already being treated should be continued during the first stage of treatment with Symmetrel. In many cases it is then possible to gradually reduce the dosage of the other drug without prejudicing the treatment response. If increased side effects occur, however, its dosage should be reduced more quickly. In patients receiving high doses of L-dopa or anticholinergic drugs, the initial period of low dosage with Symmetrel should be extended to two weeks.

Drug-induced extrapyramidal reactions

Adults

The most appropriate treatment is to reduce the dosage of the drug inducing the reactions. Where this is not practical the usual dose of Symmetrel is 100 mg twice daily. Occasionally, a patient may require 100 mg three times daily in order to obtain an optimal response.

As drug-induced extra-pyramidal reactions may decrease or disappear without treatment, an attempt should be made to discontinue treatment with Symmetrel when the reactions have been controlled for a period.

Type A virus influenza

Children aged 5-9 years: 100 mg once daily.

Children and adults aged 10-65 years: 100 mg twice daily. Effective prevention of influenza A has been reported with a dosage of 100 mg daily. This dosage may be indicated for persons who have demonstrated intolerance to 200 mg daily.

Adults over 65 years: 100 mg daily.

Dosage with Symmetrel should start immediately after suspected exposure and continue for at least 10 days. When exposure to infection is recurrent or prolonged, treatment throughout the epidemic may be indicated. Symmetrel is effective for prophylaxis only during the period of its administration. The recommended dosage should not be exceeded.

Dosage in renal impairment
In patients with compromised renal function and in those on haemodialysis the elimination half-life of amantadine is substantially prolonged, resulting in elevated plasma concentrations (see section 5.2 Pharmacokinetic properties). Careful adjustment of the dose of Symmetrel by increasing the dosing interval according to the creatinine clearance (see Table 1) is required in these patients. Ideally, amantadine plasma concentrations should be monitored. Careful surveillance of the patient is recommended (see section 5.2 Pharmacokinetic properties - Renal failure, haemodialysis).

Loading dose on the first day of treatment with Symmetrel: Starting dose as recommended for patients without renal impairment (see section 4.2 Dose and method of administration - Parkinson's disease, Type A virus influenza).

Dose thereafter: 100 mg at interval shown below

Table 1. Dose interval

Measured or calculated creatinine clearance (mL/min/1.73 m^2 or mL/min)	100 mg dose interval
< 15	7 days
15-25	3 days
26-35	2 days
36-75	1 day
> 75	12 hours

When it is not possible to measure creatinine clearance, the value may be estimated in patients with stable renal function using the formula of Cockcroft and Gault:

Calculation of creatinine clearance (mL/minute):

Males: $\frac{(140 - \text{age [yr]}) \times (\text{body weight [kg]}) \times 0.0885}{72 \times \text{serum creatinine (mmol/L)}}$

Females: 0.85 x value as calculated above

This formula should only be used if the patient is in a steady state with respect to serum creatinine concentration.

4.3 CONTRAINDICATIONS

Pregnancy; lactation, hypersensitivity to amantadine or to any of the excipients in Symmetrel.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Medical supervision during treatment with Symmetrel is essential. The margin between the therapeutically effective dose and that producing toxic manifestations may be only 100 to 200 mg per day. The usual daily dose should, therefore, not be exceeded.

Use with caution in the following circumstances

Patients with pre-existing seizure disorders have been reported to develop an increased frequency of major motor seizures during amantadine ingestion. A reduction in dosage may minimise this risk. These patients should be closely monitored.

Those patients with confusional, hallucinatory or psychotic states should receive Symmetrel with caution as an increase in confusion, hallucinations, and nightmares may occur in patients with underlying psychiatric disorders.

Because of the possibility of serious adverse effects, caution should be observed when prescribing Symmetrel to patients being treated with drugs having CNS effects or for whom the potential risks outweigh the benefit of treatment. Because some patients have attempted suicide by using an overdose of amantadine, prescriptions should be written for the smallest quantity consistent with good patient management.

Particular care is called for in patients suffering from or with a history of recurrent eczema, gastric ulceration or cardiovascular disorders.

Peripheral oedema probably due to local vascular disturbance may occur in some patients during treatment with Symmetrel capsules. This should be considered if Symmetrel is prescribed for patients with a history of heart failure.

The dosage of Symmetrel may need careful adjustment in patients with orthostatic hypotension.

The possible occurrence of anticholinergic effects should be borne in mind, particularly when treating patients with glaucoma or prostatic enlargement.

Symmetrel should be used with care in patients suffering from or with a history of recurrent eczematoid rash, and should be withdrawn if allergic skin reactions occur.

Isolated cases of corneal lesions have been reported, e.g. punctate sub-epithelial opacities which might be associated with superficial punctate keratitis, corneal epithelial oedema and markedly reduced visual acuity.

Because amantadine has anticholinergic effects, it should not be given to patients with untreated angle closure glaucoma.

If blurred vision or other visual problems occur an ophthalmologist should be contacted to exclude corneal oedema. In case that corneal oedema is diagnosed treatment with amantadine should be discontinued.

Discontinuation of Symmetrel in Parkinson's disease

Abrupt discontinuation of anti-parkinsonian drugs, including Symmetrel, may result in worsening of the symptoms of Parkinson’s disease or in symptoms resembling neuroleptic malignant syndrome (NMS), catatonia as well as in cognitive manifestations (e.g. confusion, disorientation, worsening of mental status, delirium). There have been isolated reports on a possible association between the aggravation of NMS or neuroleptic-induced catatonia and the withdrawal of amantadine in patients treated concurrently with neuroleptic agents and amantadine, following abrupt cessation of the latter. Therefore treatment with amantadine should not be stopped abruptly.

Development of resistance during use for influenza A

Resistance to amantadine is readily achieved by serial passage of influenza virus strains

in vitro or *in vivo* in the presence of the drug. Influenza A viruses (cross-) resistant to amantadine can emerge when this drug is used to treat influenza infections. Apparent transmission of drug-resistant viruses may have been the reason for failure of prophylaxis and treatment in household contacts and in nursing home patients. However, there is no evidence to date that the resistant virus produces a disease that is in any way different from that produced by sensitive viruses.

Impulse control disorders

Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists including Symmetrel. Dose reduction/tapered discontinuation should be considered if such symptoms develop.

Use in renal or liver impairment

Symmetrel should be used cautiously in patients with renal or liver disorders. In cases of impaired renal function the dosage should be adjusted according to the creatinine clearance of the individual patient and, ideally, amantadine plasma concentrations should be monitored. Since only small amounts of amantadine are eliminated by patients undergoing haemodialysis for renal failure, these patients should have their dosage carefully adjusted in order to avoid adverse reactions (see section 5.2 Pharmacokinetic properties and section 4.2 Dose and method of administration).

Use in the elderly

Elderly patients are often especially susceptible to adverse reactions or exacerbation of pre-existing central nervous system symptoms (see section 5.2 Pharmacokinetic properties and section 4.2 Dose and method of administration).

Plasma amantadine concentrations are influenced by renal function. In the elderly, the elimination half-life tends to be longer and renal clearance lower than in younger subjects. A dose not exceeding 100 mg daily is recommended in elderly patients without renal disease. If the patient has any renal function impairment, the dosing interval should be adjusted (see section 4.2 Dose and administration - Adults over 65 years and Dosage in renal impairment).

Paediatric use

Symmetrel is not recommended for use in patients below the age of 5 years. Hypothermia has been observed in children. Caution should be exercised when prescribing Symmetrel to children for the prevention and treatment of influenza type A virus (see section 4.2 Dose and method of administration).

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Observed interactions resulting in concomitant use not being recommended
Concomitant administration of amantadine and anticholinergic agents may increase confusion, hallucinations, nightmares, gastrointestinal disturbances or other atropine-like side effects (also see section 4.9 Overdose).

In isolated cases psychotic decompensation has been reported in patients receiving amantadine and concomitant antipsychotic drugs or levodopa.

Concomitant administration of amantadine with fixed dose combination of hydrochlorothiazide and triamterene may reduce the systemic clearance of the drug leading to increased plasma concentrations and toxic effects (confusion, hallucinations, ataxia, and myoclonus).

Anticipated interactions to be considered
Drugs acting on the central nervous system: Concomitant administration of amantadine and drugs or substances (e.g. alcohol) acting on the central nervous system may result in additive CNS toxicity. Close observation is recommended (also see section 4.9 Overdose).

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

Symmetrel administered to both male and female rats at a dose equivalent to the maximum recommended human dose on a mg/m2 basis impaired fertility.

Use in pregnancy – Pregnancy Category B3

Amantadine-related complications during pregnancy have been reported. Symmetrel is contraindicated during pregnancy. Women of child-bearing potential must use highly effective contraception during treatment, and for 5 days after their last dose of amantadine.

Use in lactation

Amandine passes into breast milk. Adverse drug reactions have been reported in breast-fed infants. Nursing mothers should not take Symmetrel.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients receiving treatment with Symmetrel should be warned that dizziness, blurred vision and other central nervous symptoms may occur and impair the patient's reactions, in which case they should not drive, operate potentially dangerous machinery or engage in other activities that may become hazardous because of decreased alertness (see section 4.8 Adverse effects (Undesirable effects) – Nervous system disorders).

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The undesirable effects of amantadine usually appear within the first 1-4 days of treatment and promptly disappear in 24-48 hours after discontinuation of amantadine.

A direct relationship between dose and incidence of side effects has not been demonstrated. However, there seems to be a tendency towards more common adverse drug reactions, particularly affecting the central nervous system, with increasing doses.

The adverse reactions (Table 2) are listed by MedDRA system organ class. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention (CIOMS III):

Very common	≥ 1/10 (≥ 10%)
Common	≥ 1/100 to < 1/10 (≥ 1% to < 10%)
Uncommon	≥ 1/1,000 to < 1/100 (≥ 0.1% to < 1%)
Rare	≥ 1/10,000 to < 1/1,000 (≥ 0.01% to < 0.1%)
Very rare	< 1/10,000 (< 0.01%)
Not known	frequency has not been assessed

Table 2. Adverse drug reactions

Nervous system disorders	
Common:	dizziness, light headedness, headache, lethargy, ataxia, dysarthria
Rare:	tremor, dyskinesia, convulsion
Very rare:	neuroleptic malignant syndrome (NMS)-like symptoms
Psychiatric disorders:	
Common:	depression, anxiety, elevated mood, agitation, nervousness, nervous excitement, increased drive, difficulty in concentration, insomnia, hallucinations[1], nightmares[1]
Rare:	confusional state[1], disorientation, psychotic disorder
Not known:	delirium[2], hypomania[2], mania[2]
Cardiac disorders:	
Common:	palpitations
Very rare:	cardiac failure, congenital heart lesions
Vascular disorders:	
Common:	orthostatic hypotension
Blood and lymphatic system disorders:	
Very rare:	leukopenia, neutropenia
Investigations:	
Very rare:	reversible elevation of liver enzymes, abnormal liver function tests
Gastrointestinal disorders:	
Common:	indigestion, dry mouth, nausea, vomiting, constipation
Rare:	diarrhoea
Metabolism and nutrition disorders:	
Common:	decreased appetite
Skin and subcutaneous tissue disorders:	
Very common:	livedo reticularis
Common:	hyperhidrosis
Rare:	rash, eczematoid dermatitis, exanthema
Very rare:	photosensitivity reaction
Not known:	hair loss
Eye disorders:	
Common:	vision blurred

Rare:	corneal lesions (see section 4.4 Special warnings and precautions for use), e.g. punctate subepithelial opacities which might be associated with superficial punctate keratitis, corneal epithelial oedema, and markedly reduced visual acuity
Other:	sudden loss of vision, oculogyric crisis
Renal and urinary disorders:	
Rare:	urinary retention, urinary incontinence
Respiratory, thoracic, and mediastinal disorders:	
Other:	dyspnoea
General disorders and administration site conditions:	
Very common:	oedema peripheral
Common:	fatigue, weakness
Other:	hypothermia[3]

[1]Hallucinations, confusional state, and nightmares are more common when amantadine is administered concurrently with anticholinergic agents or when the patient has an underlying psychiatric disorder
[2]These ADRs have been reported but the incidence cannot be readily deduced from literature
[3]Reported in children (also see section 4.4 Special warnings and precautions for use); frequency cannot be established

Impulse control disorders:

Pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists including Symmetrel (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 www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Overdose (acute overdose with multiples of the maximum recommended dose or overexposure due to high dosages for elderly and/or renally impaired patients) with Symmetrel capsules can lead to a fatal outcome (see section 4.4 Special warnings and precautions for use).

Signs and Symptoms

Neuromuscular disturbances and symptoms of acute psychosis are prominent features of acute poisoning with amantadine.

Central nervous system:

Hyperreflexia; motor restlessness; convulsions; extrapyramidal signs: torsion spasms, dystonic posturing; confusion; disorientation; delirium; visual hallucinations; dilated pupils; dysphagia, and myoclonus, aggression/hostility, depressed level of consciousness and coma.

Respiratory system:

Hyperventilation, pulmonary oedema, respiratory distress including adult respiratory distress syndrome.

Cardiovascular system:

Disturbances of fluid, electrolyte and acid-base balance, sinus tachycardia, arrhythmia, and hypertension. Cardiac arrest and sudden cardiac death have been reported.

Gastrointestinal system:

Nausea, vomiting, dry mouth.

Renal function:

Urinary retention, renal dysfunction including increase in blood urea nitrogen (BUN) and decreased creatinine clearance.

Overdose from combined drug treatment:

The peripheral and central adverse effects of anticholinergic drugs are increased by the concomitant use of amantadine, and acute psychotic reactions, which may be identical to those caused by atropine poisoning, may occur, especially when large doses of anticholinergic agents are used (see section 4.5 Interactions with other medicines and other forms of interactions). When overdosage of amantadine has occurred in conjunction with the use of alcohol or central nervous system stimulants, the signs and symptoms of acute poisoning with Symmetrel may be aggravated or otherwise modified.

Treatment

There is no specific amantadine hydrochloride antidote.

Removal and/or inactivation of poisoning agent(s): Induction of vomiting and/or gastric aspiration and lavage if patient is conscious, activated charcoal, saline cathartic, if judged appropriate. Since amantadine is largely excreted unchanged in the urine, maintenance of renal excretory function, copious diuresis, and forced diuresis, if necessary, are effective in removing it from the blood stream. Acidification of the urine favours the excretion of amantadine in the urine. Haemodialysis does not remove significant amounts of amantadine.

Monitoring of blood pressure, heart rate, ECG, respiration, body temperature, and treatment for possible hypotension and cardiac arrhythmias, as necessary. Caution is required when administering adrenergic substances in case of cardiac arrhythmias and hypotension as the clinical status may deteriorate due to arrhythmogenic nature of the adrenergic drugs.

Convulsions and excessive motor restlessness: Administer anticonvulsants such as diazepam i.v., paraldehyde i.m. or per rectum, or phenobarbital i.m.

Acute psychotic symptoms, delirium, dystonic posturing, myoclonic manifestations Physostigmine by slow i.v. infusion (1 mg doses in adults, 0.5 mg in children) in repeated administration according to initial response and subsequent need has been reported.

Retention of urine: The bladder should be catheterized; an indwelling catheter can be left in place for the time required.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Therapeutic/pharmacological group: antiparkinsonian agent and anti-influenzal virostatic (ATC code N04B B01)

Mechanism of action

As antiparkinsonian agent

The mechanism of action of amantadine is not fully understood. There is evidence to suggest that amantadine acts as an indirect dopamine receptor agonist, by enhancing the synthesis and release of dopamine from central neurons and delaying the reuptake into synaptic vesicles. Other evidence suggests an alteration of striatal D2 receptors towards a high affinity state. Amantadine may also exert some anticholinergic activity. When administered either alone or in combination with other drugs, amantadine produces an improvement in the cardinal signs and symptoms of parkinsonism and improves functional capacity. In Parkinson's disease, the clinical response usually occurs within 24 to 48 hours or, at the most, one week. An optimal effect is obtained during a period extending from several days to a few weeks.

As anti-influenzal virostatic

Amantadine specifically inhibits the replication of influenza A viruses at low concentrations. Using a sensitive plaque-reduction assay human influenza viruses, including H1N1, H1N2, H2N2, H3N2 subtypes, are inhibited by 0.2 to 0.7 microgram/mL or less of amantadine. It is recognised, however, that not all strains susceptible under *in vitro* conditions will be similarly affected in clinical practice. The exact mechanism of action of amantadine is unclear.

Amantadine does not completely prevent the host immune response to influenza A infection. Individuals who take this drug may still develop immune responses to natural disease or vaccination and may be protected when later exposed to antigenically related viruses.

Clinical trials

No data available

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Symmetrel is completely absorbed from the gastrointestinal tract after oral administration, producing a peak concentration of amantadine in plasma 1 to 4 hours after ingestion. Peak plasma concentrations of approximately 250 nanograms/mL and 500 nanograms/mL are attained after single oral administration of 100 mg and 200 mg amantadine, respectively. Following repeated administration of 200 mg daily, the trough steady-state plasma concentration is approximately 300 nanograms/mL within 3 days.

Distribution

67% of amantadine is bound to plasma proteins *in vitro*. A substantial amount of amantadine is bound to red blood cells. The erythrocyte amantadine concentration in normal healthy volunteers is 2.66 times the plasma concentration. The apparent volume of distribution of the drug is

approximately 5-10 L/kg, suggesting extensive tissue binding. It declines with increasing doses. The concentration of amantadine in the lung, heart, kidney, liver and spleen is higher than in the blood. The drug accumulates after several hours in nasal secretions, is found in saliva in concentrations similar to those in plasma, and in CSF in concentrations about 60% of those in plasma.

Metabolism

Amantadine is metabolised to a minor extent, principally by N-acetylation. Whether this metabolic pathway is affected by acetylator phenotype remains to be determined.

Excretion

Amantadine is eliminated in healthy young adults with a mean plasma elimination half-life of approximately 15 hours (10-31 hours). The total plasma clearance is about the same as renal clearance (250 mL/min). Renal clearance of amantadine is much higher than the creatinine clearance, suggesting renal tubular secretion.

A single dose of amantadine is excreted over 72 hours as follows: 65-85% unchanged, 5-15% as the acetyl metabolite in urine and 1% in the stool. After 4-5 days, approximately 90% of the dose appears unchanged in the urine. The rate is considerably influenced by urinary pH, a rise in pH bringing about a fall in excretion.

Effect of Age and Disease on Pharmacokinetics

Elderly patients

Compared with data from healthy young adults, the elimination half-life is doubled and renal clearance is diminished. The renal/creatinine clearance ratio in elderly subjects is smaller than in young people. Tubular secretion diminishes more than glomerular filtration. In elderly patients, repeated administration of 100 mg amantadine daily may raise the plasma concentration into the toxic range.

Renal failure

Accumulation of amantadine may occur in renal failure, causing severe adverse reactions. A creatinine clearance of less than 40 mL/ (min 1.73 m2) causes a 3 to 5-fold increase in elimination half-life and a 5-fold decrease in total and renal clearance. Renal elimination is dominant even in cases of renal failure.

Renal function declines steadily after early adulthood (at about 10% per decade from the fourth decade on). By age 65, renal function will typically have declined to a level at which reduced doses of Symmetrel (or increased dosing interval) are appropriate. Elderly patients or patients with renal failure should receive an adequately reduced dosage in accordance with the individual creatinine clearance (see section 4.2 Dose and method of administration). The target plasma amantadine concentration should not exceed a maximum of 300 nanograms/mL.

Haemodialysis

Little amantadine is removed by haemodialysis. This inefficiency may be related to its extensive tissue binding. Less than 5% (7-15mg) of a single 300 mg dose is eliminated after a 4-hour haemodialysis. The mean elimination half-life reaches 24 dialysis-hours.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Symmetrel soft capsules also contain the inactive ingredients: rape seed oil, lecithin, beeswax-yellow, soya oil-hydrogenated and soya oil-partially hydrogenated. The capsule shell contains: sodium ethyl hydroxybenzoate, sodium propyl hydroxybenzoate, gelatin, glycerol, iron oxide red, Karion 83 (sorbitol, mannitol and starch-hydrolysed maize as 70% aqueous solution), titanium dioxide, edible ink-white.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

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 moisture.

6.5 NATURE AND CONTENTS OF CONTAINER

White plastic bottles of 100 capsules, fitted with a push & turn closure.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

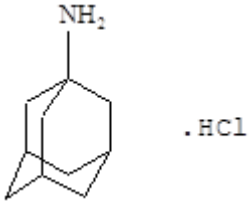
6.7 PHYSICOCHEMICAL PROPERTIES

Amantadine, the active ingredient of Symmetrel, is a stable, white crystalline powder with a bitter taste, readily soluble in water, and soluble in ethanol and chloroform.

Chemical structure

Chemical name: 1-adamantanamine hydrochloride
Molecular weight: 187.71
Molecular formula: $C_{10}H_{18}NCl$

Chemical structure:



CAS number

665-67-7

7 MEDICINE SCHEDULE (POISONS STANDARD)

(S4) Prescription Only Medicine

8 SPONSOR

NOVARTIS Pharmaceuticals Australia Pty Limited
ABN 18 004 244 160
54 Waterloo Road
NORTH RYDE NSW 2113
Telephone: (02) 9805 3555

9 DATE OF FIRST APPROVAL

02 August 1991 (grandfathered)

10 DATE OF REVISION

06 December 2024

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SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
6.4	Change to storage condition from Store below 30°C to Store below 25°C.

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