NEW ZEALAND DATA SHEET

1. PRODUCT NAME

METHYLPHENIDATE SANDOZ® XR 18 mg methylphenidate hydrochloride modified release tablet

METHYLPHENIDATE SANDOZ® XR 27 mg methylphenidate hydrochloride modified release tablet

METHYLPHENIDATE SANDOZ® XR 36 mg methylphenidate hydrochloride modified release tablet

METHYLPHENIDATE SANDOZ® XR 54 mg methylphenidate hydrochloride modified release tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One modified release tablet contains 18 mg, 27 mg, 36 mg or 54 mg of methylphenidate hydrochloride.

Excipient(s) with known effect:

Lactose

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

3. PHARMACEUTICAL FORM

METHYLPHENIDATE SANDOZ XR is available as a modified release tablet for once-a-day oral administration containing 18, 27, 36 or 54 mg methylphenidate hydrochloride. It is designed to have a 12-hour duration of effect.

METHYLPHENIDATE SANDOZ XR 18 mg are yellow, round, biconvex film-coated tablets, with a hole in one side of the tablet.

METHYLPHENIDATE SANDOZ XR 27 mg are grey, round, biconvex film-coated tablets, with a hole in one side of the tablet.

METHYLPHENIDATE SANDOZ XR 36 mg are white, round, biconvex film-coated tablets, with a hole in one side of the tablet.

METHYLPHENIDATE SANDOZ XR 54 mg are pink, round, biconvex film-coated tablets, with a hole in one side of the tablet.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

METHYLPHENIDATE SANDOZ XR is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

A diagnosis of Attention Deficit Hyperactivity Disorder (ADHD; DSM-IV) implies the presence of hyperactive-impulsive or inattentive symptoms that caused impairment and were present before age 7 years.

Need for comprehensive treatment programme: METHYLPHENIDATE SANDOZ XR is indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational and social) for patients with this syndrome. Stimulants are not intended for use in the patient who exhibits symptoms secondary to environmental factors and/or other primary psychiatric disorders, including psychosis. Appropriate educational placement is essential and psychosocial intervention is often helpful. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the patient's symptoms.

Long term use: The effectiveness of METHYLPHENIDATE SANDOZ XR for long-term use has not been systematically evaluated in controlled trials. Therefore the physician who elects to use METHYLPHENIDATE SANDOZ XR for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

4.2. DOSE AND METHOD OF ADMINISTRATION

METHYLPHENIDATE SANDOZ XR is administered orally once daily and should be taken in the morning.

METHYLPHENIDATE SANDOZ XR must be swallowed whole with the aid of liquids, and must not be chewed, divided, or crushed.

METHYLPHENIDATE SANDOZ XR may be administered with or without food.

Pre-treatment screening:

Prior to prescribing, it is necessary to conduct a baseline evaluation of a patient's cardiovascular status including blood pressure and heart rate. A comprehensive history should document concomitant medications, past and present co-morbid medical and psychiatric disorders or symptoms, family history of sudden cardiac/unexplained death and accurate recording of pre-treatment height and weight on a growth chart (see section 4.3 Contraindications and section 4.4 Special warnings and precautions for use).

Ongoing monitoring:

Growth, psychiatric and cardiovascular status should be continuously monitored (see also section 4.4 Special warnings and precautions for use).

- Blood pressure and pulse should be recorded on a centile chart at each adjustment of dose and then at least every 6 months;
- height, weight and appetite should be recorded at least 6 monthly with maintenance of a growth chart;
- development of *de novo* or worsening of pre-existing psychiatric disorders should be monitored at every adjustment of dose and then least every 6 months and at every visit.

Patients should be monitored for the risk of diversion, misuse and abuse of methylphenidate.

Dose titration:

Careful dose titration is necessary at the start of treatment with methylphenidate. Dose titration should be started at the lowest possible dose.

Dose

Children (6 years of age and above) and adolescents:

Dosage may be adjusted in 9 mg increments between 18 mg and 36mg and consecutively in 18 mg increments to a maximum of 54 mg/day for children aged between 6-12 years and to a maximum of 72 mg/day for adolescents aged between 13-18 years. In general, dosage adjustment may proceed at approximately weekly intervals.

Adults:

Dosage can be adjusted from an initial dose of 18 or 36 mg/day in 18mg increments to a maximum of 72mg/day taken once daily in the morning. In general, dosage adjustment may proceed at approximately weekly intervals. Patients respond at different dose levels and METHYLPHENIDATE SANDOZ XR must be titrated to effect on an individual patient needs and response basis. A maximum dose of 108 mg/day have been included in clinical trials (see Clinical trials).

Patients New to Methylphenidate: The recommended starting dose of METHYLPHENIDATE SANDOZ XR for patients who are not currently taking methylphenidate, or for patients who are on stimulants other than methylphenidate, is 18 mg once daily for children and adolescents and 18 or 36 mg once daily for adults.

Patients Currently Using Methylphenidate: The recommended dose of METHYLPHENIDATE SANDOZ XR for patients who are currently taking methylphenidate two or three times daily at doses of 10 – 60 mg per day is provided in Table 1.

Table 1: Recommended dose conversions from methylphenidate regimens to METHYLPHENIDATE SANDOZ XR

Previous methylphenidate daily dose	Recommended METHYLPHENIDATE SANDOZ XR starting dose
5 mg methylphenidate three times daily	18 mg every morning
10 mg methylphenidate three times daily	36 mg every morning
15 mg methylphenidate three times daily	54 mg every morning
20 mg methylphenidate three times daily	72 mg every morning

Clinical judgement should be used when selecting the dose for patients currently taking methylphenidate in other regimens. Daily dosage above 54 mg is not recommended for children aged between 6-12 years. Daily dosage above 72 mg is not recommended for adolescents aged between 13-18 years.

Long-term (more than 12 months) use in children and adolescents:

The safety and efficacy of long term use of methylphenidate has not been systematically evaluated in controlled trials. Methylphenidate treatment should not and need not, be indefinite. Methylphenidate treatment is usually discontinued during or after puberty. The physician who elects to use methylphenidate for extended periods (over 12 months) in children and adolescents with ADHD should periodically re-evaluate the long term usefulness of the drug for the individual patient with trial periods off medication to assess the patient's functioning without pharmacotherapy. It is recommended that methylphenidate is de-challenged at least once yearly to assess the child's condition (preferable during times of school holidays). Improvement may be sustained when the drug is either temporarily or permanently discontinued.

Dose reduction and discontinuation:

Treatment must be stopped if the symptoms do not improve after appropriate dosage adjustment over a one-month period. If paradoxical aggravation of symptoms or other serious adverse events occur, the dosage should be reduced or discontinued.

Special Populations

Use in Infants and children

Use of methylphenidate hydrochloride modified-release tablets in patients under six years of age has not been studied in controlled trials. METHYLPHENIDATE SANDOZ XR should not be used in patients under six years old.

Use in Elderly

Use of METHYLPHENIDATE SANDOZ XR in patients over 65 years of age has not been studied in controlled trials.

Method of administration

METHYLPHENIDATE SANDOZ XR must be swallowed whole with the aid of liquids. Tablets should not be chewed, divided or crushed. The medication is contained within a nonabsorbable shell designed to release the drug at a controlled rate. The tablet shell, along with insoluble core components, is eliminated from the body; patients should not be concerned if they occasionally notice in their stool something that looks like a tablet.

4.3. CONTRAINDICATIONS

METHYLPHENIDATE SANDOZ XR is contraindicated:

- in patients with known hypersensitivity to methylphenidate or any inactive ingredient used in this product (see section 6.1 List of excipients);
- during treatment with monoamine oxidase inhibitors, and also within a minimum of 14 days following discontinuation of a monoamine oxidase inhibitor (hypertensive crises may result);
- in patients with hyperthyroidism;
- Phaeochromocytoma;
- Diagnosis or history of severe depression, anorexia nervosa/anorexic disorders, suicidal tendencies, psychotic symptoms, severe mood disorders, mania, schizophrenia, psychopathic/borderline personality disorder;
- Diagnosis or history of severe and episodic (Type I) Bipolar (affective) Disorder (that is not well-controlled);
- pre-existing cardiovascular disorders including severe hypertension, heart failure, arterial occlusive disease, angina, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, potentially life-threatening arrhythmias and channelopathies (disorders caused by the dysfunction of ion channels);
- pre-existing cerebrovascular disorders cerebral aneurysm, vascular abnormalities including vasculitis or stroke.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Use with caution in the following circumstances.

Depression and Psychosis

METHYLPHENIDATE SANDOZ XR should not be used to treat severe depression or for the prevention or treatment of normal fatigue states.

Co-morbidity of psychiatric disorders in ADHD is common and should be taken into account when prescribing stimulant products. In the case of emergent psychiatric symptoms or exacerbation of pre-existing psychiatric disorders, methylphenidate should not be given unless the benefits outweigh the risks to the patient.

Development or worsening of psychiatric disorders should be monitored at every adjustment of dose, then at least every 6 months, and at every visit; discontinuation of treatment may be appropriate.

In psychotic patients administration of methylphenidate may exacerbate symptoms of behaviour disturbance and thought disorder.

Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking or mania in patients without a prior history of psychotic illness or mania can be caused by stimulants at usual doses. If such symptoms occur, consideration should be given to a possible causal role of the stimulant, and discontinuation of treatment may be appropriate.

Suicidal tendency

Patients with emergent suicidal ideation or behaviour during treatment for ADHD should be evaluated immediately by their physician. Consideration should be given to the exacerbation of an underlying psychiatric condition and to a possible causal role of methylphenidate treatment. Treatment of an underlying psychiatric condition may be necessary and consideration should be given to a possible discontinuation of methylphenidate.

Forms of bipolar disorder

Particular care should be taken in using methylphenidate to treat ADHD in patients with comorbid bipolar disorder (including untreated Type I Bipolar Disorder or other forms of bipolar disorder) because of concern for possible precipitation of a mixed/manic episode in such patients. Prior to initiating treatment with methylphenidate, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression. Close ongoing monitoring is essential in these patients (see Depression and Psychosis above and section 4.2 Dose and method of administration). Patients should be monitored for symptoms at every adjustment of dose, then at least every 6 months and at every visit.

Tics and worsening of Tourette's syndrome

Methylphenidate is associated with the onset or exacerbation of motor and verbal tics. Worsening of Tourette's syndrome has also been reported. It is recommended that the family history be assessed, and that the patient is clinically evaluated for tics or Tourette's syndrome before initiating methylphenidate. Regular monitoring for the emergence or worsening of tics or Tourette's syndrome during treatment with methylphenidate is recommended at every dose adjustment and every visit, and treatment discontinued if clinically appropriate.

Drug Dependence

Patients should be carefully monitored for the risk of diversion, misuse and abuse of methylphenidate. METHYLPHENIDATE SANDOZ XR should be given cautiously to patients with a history of drug or alcohol dependence. Chronic abusive use can lead to marked tolerance and psychological dependence with varying degrees of abnormal behaviour.

Patient age, the presence of risk factors for substance use disorder (such as co-morbid oppositional-defiant or conduct disorder and bipolar disorder), previous or current substance abuse should all be taken into account when deciding on a course of treatment for ADHD. Caution is called for in emotionally unstable patients, such as those with a history of drug or alcohol dependence, because such patients may increase the dosage on their own initiative.

For some high-risk substance abuse patients, methylphenidate or other stimulants may not be suitable and non-stimulant treatment should be considered.

Careful supervision is required during withdrawal from abusive use since severe depression may occur. Withdrawal following chronic therapeutic use may unmask symptoms of the underlying disorder that may require follow-up.

Drug Screening

METHYLPHENIDATE SANDOZ XR contains methylphenidate which may induce a false positive laboratory test for amphetamines, particularly with immunoassay screen test.

Potential for Gastrointestinal Obstruction

METHYLPHENIDATE SANDOZ XR tablet is non-deformable and does not appreciably change in shape in the GIT. It should not ordinarily be administered to patients with pre-existing severe GI narrowing (pathologic or iatrogenic) or in patients with dysphagia or significant difficulty in swallowing tablets. Due to the prolonged-release design of the tablet, METHYLPHENIDATE SANDOZ XR should only be used in patients who are able to swallow the tablet whole.

Sudden Death and Pre-existing Structural Cardiac Abnormalities

Although a causal relationship has not been established, sudden death has been reported in patients with structural cardiac abnormalities treated with ADHD drugs with stimulant effects. These treatments should be used with caution in patients with structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant medicine.

Hypertension and Cardiovascular Conditions

Patients who are being considered for treatment with stimulant medications should have a careful history (including assessment for a family history of sudden cardiac or unexplained death or malignant arrhythmia,) and physical exam to assess for the presence of cardiac disease, and should receive further specialist cardiac evaluation if initial findings suggest such history or disease. Patients who develop symptoms such as palpitations, exertional chest pain, unexplained syncope, dyspnoea or other symptoms suggestive of cardiac disease during methylphenidate treatment should undergo a prompt specialist cardiac evaluation.

In the laboratory clinical trials in children both methylphenidate hydrochloride modified-release tablets and methylphenidate three times daily increased resting pulse by an average of 2 to 6 bpm and produced average increases of systolic and diastolic blood pressure of roughly

1 to 4 mm Hg during the day, relative to placebo. In placebo-controlled studies in adults, mean increases in resting pulse rate of approximately 4 to 6 bpm were observed with methylphenidate hydrochloride modified-release tablets at endpoint vs. a mean change of roughly -2 to 3 bpm with placebo. Mean changes in blood pressure at endpoint ranged from about -1 to 1 mm Hg (systolic) and 0 to 1 mm Hg (diastolic) for methylphenidate hydrochloride modified-release tablets and from -1 to 1 mm Hg (systolic) and -2 to 0 mm Hg (diastolic) for placebo. Therefore, caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate.

Cardiovascular status should be carefully monitored. Blood pressure and pulse should be recorded on a centile chart at each adjustment of dose and then at least every 6 months.

The use of methylphenidate is contraindicated in certain pre-existing cardiovascular disorders unless specialist paediatric cardiac advice has been obtained.

Misuse and Cardiovascular Events

Misuse of stimulants of the central nervous system may be associated with sudden death and other serious cardiovascular adverse events.

Cerebrovascular disorders

See section 4.3 Contraindications for cerebrovascular conditions in which methylphenidate treatment in contraindicated. Patients with additional risk factors (such as a history of cardiovascular disease, concomitant medications that elevate blood pressure) should be assessed at every visit for neurological signs and symptoms after initiating treatment with methylphenidate.

Cerebral vasculitis appears to be a very rare idiosyncratic reaction to methylphenidate exposure. There is little evidence to suggest that patients at higher risk can be identified and the initial onset of symptoms may be the first indication of an underlying clinical problem. Early diagnosis, based on a high index of suspicion, may allow the prompt withdrawal of methylphenidate and early treatment. The diagnosis should therefore be considered in any patient who develops new neurological symptoms that are consistent with cerebral ischemia during methylphenidate therapy. These symptoms could include severe headache, numbness, weakness, paralysis, and impairment of coordination, vision, speech, language or memory.

Treatment with methylphenidate is not contraindicated in patients with hemiplegic cerebral palsy.

Priapism

Prolonged and painful erections requiring immediate medical attention (sometimes including surgical intervention, have been reported with methylphenidate products, including methylphenidate hydrochloride modified-release tablets, in both paediatric and adult patients (see section 4.8 Undesirable effects). Priapism can develop after some time on methylphenidate, often subsequent to an increase in dose. Priapism has also appeared during a period of methylphenidate withdrawal (drug holidays or during discontinuation). Patients who develop abnormally sustained erections or frequent and painful erections should seek immediate medical attention.

Cerebrovascular disorders

Cerebrovascular disorders (including cerebral vasculitis and cerebral hemorrhage) have been reported with the use of methylphenidate hydrochloride modified-release tablets (see section

4.8 Undesirable effects). Consider cerebrovascular disorders as a possible diagnosis in any patient who develops new neurological symptoms that are consistent with cerebral ischemia during METHYLPHENIDATE SANDOZ XR therapy. These symptoms could include severe headache, unilateral weakness or paralysis, and impairment of coordination, vision, speech, language, or memory. If a cerebrovascular disorder is suspected during treatment, discontinue METHYLPHENIDATE SANDOZ XR immediately. Early diagnosis may guide subsequent treatment. In patients with pre-existing cerebrovascular disorders (e.g., aneurysm, vascular malformations/anomalies), treatment with METHYLPHENIDATE SANDOZ XR is not recommended.

Aggression, anxiety and agitation

Aggressive behaviour, marked anxiety, or agitation are often observed in patients with ADHD, and have been reported in patients treated with methylphenidate hydrochloride modified-release tablets (see section 4.8 Undesirable effects). Anxiety led to discontinuation of methylphenidate hydrochloride modified-release tablets in some patients. It is recommended to monitor patients beginning treatment with METHYLPHENIDATE SANDOZ XR for the appearance of, or worsening of, aggressive behaviour, marked anxiety, or agitation.

Haematologic Monitoring

Periodic full blood count, differential and platelet counts are advised during prolonged therapy.

Increased intraocular pressure and glaucoma

There have been reports of a transient elevation of intraocular pressure (IOP) associated with methylphenidate treatment. It is recommended to prescribe METHYLPHENIDATE SANDOZ XR to patients with open-angle glaucoma or abnormally increased IOP only if the benefit of treatment is considered to outweigh the risk. Patients with a history of abnormally increased IOP or open-angle glaucoma, and patients at risk for acute angle-closure glaucoma (e.g., patients with significant hyperopia) must be closely monitored.

METHYLPHENIDATE SANDOZ XR is not recommended in patients with acute angle-closure glaucoma.

Use in patients with renal impairment

There is no experience with the use of methylphenidate hydrochloride modified-release tablets in patients with renal insufficiency. After oral administration of radiolabeled methylphenidate in humans, methylphenidate was extensively metabolized and approximately 80% of the radioactivity was excreted in the urine in the form of PPAA. Since renal clearance is not an important route of methylphenidate clearance, renal insufficiency is expected to have little effect on the pharmacokinetics of METHYLPHENIDATE SANDOZ XR.

Use in patients with hepatic impairment

There is no experience with the use of methylphenidate hydrochloride modified-release tablets in patients with hepatic insufficiency.

Use in children

The safety and efficacy of methylphenidate hydrochloride modified-release tablets in children under 6 years old have not been established.

Long-term use (more than 12 months) in children and adolescents: The safety and efficacy of long term use of methylphenidate has not been systematically evaluated in controlled trials.

Methylphenidate treatment should not and need not, be indefinite. Methylphenidate treatment is usually discontinued during or after puberty. Patients on long-term therapy (i.e. over 12 months) must have careful ongoing monitoring according to the guidance under section 4.2 Dose and method of administration and section 4.4 Special warnings and precautions for use for hypertension and cardiovascular conditions, growth, appetite, development of *de novo* or worsening of pre-existing psychiatric disorders. Psychiatric disorders to monitor for are described below, and include (but are not limited to) motor or vocal tics, aggressive or hostile behaviour, agitation, anxiety, depression, psychosis, mania, delusions, irritability, lack of spontaneity, withdrawal and excessive perseveration.

The physician who elects to use methylphenidate for extended periods (over 12 months) in children and adolescents with ADHD should periodically re-evaluate the long term usefulness of the drug for the individual patient with trial periods off medication to assess the patient's functioning without pharmacotherapy. It is recommended that methylphenidate is de-challenged at least once yearly to assess the child's condition (preferably during times of school holidays). Improvement may be sustained when the drug is either temporarily or permanently discontinued.

Growth: Moderately reduced weight gain and growth retardation have been reported with the long-term use of methylphenidate in children.

The effects of methylphenidate on final height and final weight are currently unknown and being studied.

Growth should be monitored during methylphenidate treatment: height, weight and appetite should be recorded at least 6 monthly with maintenance of a growth chart. Patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

Use in the elderly

Methylphenidate should not be used in the elderly. Safety and efficacy has not been established in this age group.

4.5. INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Pharmacokinetic interaction:

It is not known how methylphenidate may effect plasma concentrations of concomitantly administered drugs. Therefore, caution is recommended at combining methylphenidate with other drugs, especially those with a narrow therapeutic window.

Methylphenidate is not metabolised by cytochrome P450 to a clinically relevant extent. Inducers or inhibitors of cytochrome P450 are not expected to have any relevant impact on methylphenidate pharmacokinetics. Conversely, the d- and l- enantiomers of methylphenidate do not relevantly inhibit cytochrome P450 1A2, 2C8, 2C9, 2C19, 2D6, 2E1 or 3A.

Pharmacodynamic interactions:

Use with drugs that elevate blood pressure

Caution is advised in patients being treated with methylphenidate with any other drug that can also elevate blood pressure (see also sections on cardiovascular and cerebrovascular conditions in section 4.4 Special warnings and precautions for use).

Because of possible hypertensive crisis, methylphenidate is contraindicated in patients being treated (currently or within the preceding 2 weeks) with non-selective, irreversible MAO-inhibitors (see section 4.3 Contraindications).

Anti-hypertensive drugs

Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. It is recommended to monitor blood pressure and adjust the dosage of the antihypertensive drug as needed (see section 4.4 Special warnings and precautions for use).

Use with alcohol

Alcohol may exacerbate the adverse CNS effects of psychoactive drugs, including methylphenidate. It is therefore advisable for patients to abstain from alcohol during treatment.

Use with halogenated anaesthetics

Concomitant use of halogenated anaesthetics and methylphenidate hydrochloride modified-release tablets may increase the risk of sudden blood pressure and heart rate increase during surgery. It is recommended to avoid use of METHYLPHENIDATE SANDOZ XR in patients being treated with anaesthetics on the day of surgery.

Use with dopaminergic drugs

Caution is recommended when administering methylphenidate with dopaminergic drugs, including antipsychotics. Because a predominant action of methylphenidate is to increase extracelluar dopamine levels, methylphenidate may be associated with pharmacodynamic interactions when co-administered with direct and indirect dopamine agonists (including DOPA and tricyclic antidepressants) or with dopamine antagonists including antipsychotics.

Use with serotonergic drugs

There have been reports of serotonin syndrome following coadministration of methylphenidate with serotonergic drugs. If concomitant use of METHYLPHENIDATE SANDOZ XR with a serotonergic drug is warranted, prompt recognition of the symptoms of serotonin syndrome is important. METHYLPHENIDATE SANDOZ XR must be discontinued as soon as possible if serotonin syndrome is suspected.

Use with antipsychotic drugs

Because a predominant action of methylphenidate is to increase extracellular dopamine levels, methylphenidate hydrochloride modified-release tablets may be associated with pharmacodynamic interactions when co-administered with some antipsychotics. Caution is warranted in patients receiving both METHYLPHENIDATE SANDOZ XR and an antipsychotic, as extrapyramidal symptoms could emerge when these drugs are administered concomitantly or when adjusting the dosage of one or both drugs.

4.6. FERTILITY, PREGNANCY AND LACTATION

Use in pregnancy – Category B3

The safety of methylphenidate for use during human pregnancy has not been established, and no studies are available on the use of methylphenidate hydrochloride modified-release tablets in pregnant women. There is a limited amount of data from the use of methylphenidate in pregnant women.

Medicines should only be prescribed in pregnancy when the expected benefits to the mother outweigh any potential risks to the mother and foetus. If possible, medicines should be used at the lowest effective dose for the shortest possible duration. Careful consideration and discussion of the risks and benefits of the medicines should be taken in the management of pregnant women or women intending to become pregnant. Women of child-bearing potential should be fully informed of the risks and benefits of the use of methylphenidate during pregnancy.

Cases of neonatal cardiorespiratory toxicity, specifically fetal tachycardia and respiratory distress have been reported in spontaneous case reports.

Oral administration of methylphenidate to rabbits during the period of organogenesis has produced teratogenic effects at doses of 200 mg/kg/day, associated with systemic exposure (plasma AUC) approximately 5-6 fold that in humans receiving the maximal recommended dose. The exposure at the no-effect dose in rabbits (60 mg/kg/day) was less than human exposure. Teratogenic effects were not seen in rats at oral methylphenidate doses up to 75 mg/kg/day, associated with systemic exposure of 21-25 fold that in humans receiving the maximal dose. Oral administration of methylphenidate to rats from early pregnancy until weaning was associated with maternal toxicity, reduced offspring weight and marginal alterations in neuromotor performance in offspring at a maternal dose of 30 mg/kg/day, approximately 3-6 fold the maximum recommended clinical dose on a mg/m^2 basis.

Breast-feeding

Methylphenidate has been detected in human milk. Based on breast milk sampling from five mothers, methylphenidate concentrations in human milk resulted in infant doses of 0.16% to 0.7% of the maternal weight-adjusted dosage, and a milk to maternal plasma ratio ranging between 1.1 and 2.7. Caution should be exercised if METHYLPHENIDATE SANDOZ XR is administered to a breast-feeding woman.

There is one case report of an infant who experienced an unspecified decrease in weight during the period of exposure but recovered and gained weight after the mother discontinued treatment with methylphenidate. A risk to the suckling child cannot be excluded.

Oral administration of methylphenidate to rats from early pregnancy until weaning was associated with maternal toxicity, reduced offspring weight and marginal alterations in neuromotor performance in offspring at a maternal dose of 30 mg/kg/day, approximately 3-6 fold the maximum recommended clinical dose on a mg/m^2 basis.

A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from methylphenidate therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Methylphenidate can cause dizziness, drowsiness and visual disturbances including difficulties with accommodation, diplopia and blurred vision and may impair the ability of the patient to operate potentially hazardous machinery or vehicles. Patients should be cautioned accordingly until they are reasonably certain that METHYLPHENIDATE SANDOZ XR does not adversely affect their ability to engage in such activities.

4.8. UNDESIRABLE EFFECTS

Throughout this section, adverse reactions are presented. Adverse reactions are adverse events that were considered to be reasonably associated with the use of methylphenidate based on the comprehensive assessment of the available adverse event information. A causal relationship with methylphenidate cannot be reliably established in individual cases. Further, because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Clinical Trial Data

Double-Blind Data – Adverse Drug Reactions Reported at ≥1% Frequency

Adverse Drug Reactions (ADRs) in either the paediatric or adult double-blind studies (Table 2 and Table 3) may be relevant for both patient populations.

Paediatric Patients

The safety of methylphenidate hydrochloride modified-release tablets was evaluated in 639 paediatric patients (children and adolescents) with ADHD who participated in 4 placebo-controlled, double-blind clinical trials. The information presented in this section was derived from pooled data.

Adverse Drug Reactions (ADRs) reported by ≥1% of methylphenidate hydrochloride modified-release tablets-treated children and adolescent subjects and more frequently than placebo in these trials are shown in Table 2.

Table 2: Adverse Drug Reactions Reported by ≥1% of Methylphenidate Hydrochloride Modified-Release Tablets-Treated Children and Adolescent Subjects and More Frequently than Placebo in 4 Placebo-Controlled, Double-Blind Clinical Trials

System/Organ Class Adverse Drug Reaction	**Methylphenidate Hydrochloride Modified-Release Tablets (n=321) %**	**Placebo (n=318) %**
Infections and Infestations		
Nasopharyngitis	2.8	2.2
Psychiatric Disorders		
Insomnia	2.8	0.3
Nervous System Disorders		
Headache	10.6	11.9
Dizziness	1.9	0
Respiratory, Thoracic and Mediastinal Disorders		
Cough	1.9	0.9
Oropharyngeal Pain	1.2	0.9
Gastrointestinal Disorders		
Abdominal Pain upper	6.2	3.8
Vomiting	2.8	1.6
General Disorders and Administration Site Conditions		
Pyrexia	2.2	0.9

*Terms of Initial insomnia (Methylphenidate hydrochloride modified-release tablets=0.6%) and Insomnia (Methylphenidate hydrochloride modified-release tablets=2.2%) are combined into Insomnia.

The majority of ADRs were mild to moderate in severity.

Adult Patients

The safety of methylphenidate hydrochloride modified-release tablets was evaluated in 905 adult subjects with ADHD who participated in 3 placebo-controlled, double-blind clinical trials. The information presented in this section was derived from pooled data.

Adverse Drug Reactions (ADRs) reported by ≥1% of methylphenidate hydrochloride modified-release tablets-treated adult subjects in these trials are shown in Table 3.

Table 3: Adverse Drug Reactions Reported by ≥1% of Methylphenidate Hydrochloride Modified-Release Tablets-Treated Adult Subjects in 3 Placebo-Controlled, Double-Blind Clinical Trials

System/Organ Class Adverse Drug Reaction	**Methylphenidate Hydrochloride Modified-Release Tablets (n=596) %**	**Placebo (n=309) %**
Infections and Infestations		
Upper respiratory tract infection	1.7	1.0
Sinusitis	1.3	1.0
Metabolism and Nutrition Disorders		
Decreased appetite	24.8	6.1
Anorexia	4.2	1.3
Psychiatric Disorders		
Insomnia	13.3	7.8
Anxiety	8.4	2.9
Initial insomnia	5.7	2.6
Depressed mood	4.4	2.6
Restlessness	4.0	0
Agitation	3.2	0.6
Nervousness	2.3	0.6
Bruxism	1.5	0.6
Depression	1.5	0.6
Affect lability	1.3	0.6
Libido decreased*	1.5	0.6
Panic attack	1.3	0.3
Tension	1.3	0.3
Aggression	1.2	0.6
Confusional state	1.0	0.3
Nervous System Disorders		
Headache	24.2	18.8
Dizziness	7.4	5.5
Tremor	3.4	0.6
Paraesthesia	1.2	0
Tension headache	1.0	0.3
Eye Disorders		
Accommodation disorder	1.3	0
Vision blurred	1.3	1.0
Ear and Labyrinth Disorders		
Vertigo	2.0	0.3

System/Organ Class Adverse Drug Reaction	Methylphenidate Hydrochloride Modified-Release Tablets (n=596) %	Placebo (n=309) %
Cardiac Disorders		
Tachycardia	6.0	0
Palpitations	4.5	0.6
Vascular Disorders		
Hypertension	2.2	1.6
Hot flush	1.3	0.6
Respiratory, Thoracic and Mediastinal Disorders		
Oropharyngeal pain	1.5	1.3
Cough	1.2	1.0
Dyspnoea	1.2	0.6
Gastrointestinal Disorders		
Dry mouth	15.1	3.6
Nausea	14.3	4.9
Dyspepsia	2.0	1.9
Vomiting	1.8	0.6
Constipation	1.5	0.6
Skin and Subcutaneous Tissue Disorders		
Hyperhidrosis	5.7	1.3
Musculoskeletal and Connective Tissue Disorders		
Muscle tightness	1.3	0
Muscle spasms	1.0	0.3
Reproductive System and Breast Disorders		
Erectile dysfunction	1.0	0.3
General Disorders and Administration Site Conditions		
Irritability	5.2	2.9
Fatigue	4.7	4.2
Thirst	1.8	0.6
Asthenia	1.2	0
Investigations		
Weight decreased	8.7	3.6
Heart rate increased	3.0	1.9
Blood pressure increased	2.5	1.9
Alanine aminotransferase increased	1.0	0

*The adverse reaction libido decreased includes the preferred term loss of libido.

The majority of ADRs were mild to moderate in severity.

Open-Label Data – Adverse Drug Reactions Reported at ≥1% Frequency

The safety of methylphenidate hydrochloride modified-release tablets was evaluated in 3782 paediatric and adult subjects with ADHD who participated in 12 open-label clinical trials. The information presented in this section was derived from pooled data. Adverse Drug Reactions (ADRs) reported by ≥1% of methylphenidate hydrochloride modified-release tablets-treated subjects in these trials and not listed in Table 2 and Table 3 are shown in Table 4.

Table 4: Adverse Drug Reactions Reported by ≥1% of Methylphenidate Hydrochloride Modified-Release Tablets-Treated Subjects in 12 Open-Label Clinical Trials

System/Organ Class Adverse Drug Reaction	**Methylphenidate Hydrochloride Modified-Release Tablets (n=3782) %**
Psychiatric Disorders	
Tic	2.0
Mood swings	1.1
Nervous System Disorders	
Somnolence	1.0
Gastrointestinal Disorders	
Diarrhea	2.4
Abdominal discomfort	1.3
Abdominal pain	1.2
Skin and Subcutaneous Tissue Disorders	
Rash	1.3
General Disorders and Administration Site Conditions	
Feeling jittery	1.4

The majority of ADRs were mild to moderate in severity.

Double Blind and Open-Label Data – Adverse Drug Reactions Reported at <1% Frequency

Additional ADRs that occurred in <1% of methylphenidate hydrochloride modified-release tablets-treated paediatric and adult subjects in the double-blind and open-label clinical datasets are listed in Table 5.

Table 5: Adverse Drug Reactions Reported by <1% of Methylphenidate Hydrochloride Modified-Release Tablets-Treated Pediatric and Adult Subjects in Either Double-Blind or Open-Label Clinical Trials

Blood and Lymphatic System Disorders Leukopenia
Psychiatric Disorders Anger, Sleep disorder, Hypervigilance, Tearfulness, Mood altered
Nervous System Disorders Psychomotor hyperactivity, Sedation, Lethargy
Eye Disorders Dry eye
Skin and Subcutaneous Tissue Disorders Rash macular
Investigations Cardiac murmur

The majority of ADRs were mild to moderate in severity.

Postmarketing Data

ADRs identified during postmarketing experience with methylphenidate hydrochloride modified-release tablets are included in Table 6. The frequencies are provided according to the following convention:

Very common	≥1/10
Common	≥1/100 and <1/10
Uncommon	≥1/1000 and <1/100
Rare	≥1/10000 and <1/1000
Very rare	<1/10000, including isolated reports

Table 6: Adverse Drug Reactions Identified During Postmarketing Experience with Methylphenidate Hydrochloride Modified-Release Tablets by Frequency Category Estimated from Spontaneous Reporting Rates

Blood and Lymphatic System Disorders	
Very rare	Pancytopenia, Thrombocytopenia, Thrombocytopenic, Purpura
Immune System Disorders	
Rare	Hypersensitivity reactions such as Angioedema, Anaphylactic reactions, Auricular swelling, Bullous conditions, Exfoliative conditions, Urticarias, Pruritus NEC, Rashes, Eruptions and Exanthemas NEC
Psychiatric Disorders	
Very rare	Disorientation, Hallucination, Hallucination Auditory, Hallucination Visual, Mania, Logorrhoea, libido disorder*, Obsessive-compulsive disorders and symptoms (including trichotillomania, obsessive thoughts, compulsions)
Nervous System Disorders	
Very rare	Convulsion, Grand Mal Convulsion, Dyskinesia, Cerebrovascular disorder (including cerebral vasculitis, cerebral haemorrhage, cerebral arteritis, cerebral vascular occlusion)
Eye Disorders	
Very rare	Diplopia, Mydriasis, Visual Impairment, Glaucoma, Intraocular Pressure increased
Cardiac Disorders	
Very rare	Angina Pectoris, Bradycardia, Extrasystoles, Supraventricular Tachycardia, Ventricular Extrasystoles
Vascular Disorders	
Very rare	Raynaud's Phenomenon
Respiratory, thoracic and mediastinal disorders	
Very rare	Epistaxis
Skin and Subcutaneous Tissue Disorders	
Very rare	Alopecia, Erythema, Hyperhidrosis
Hepatobiliary Disorders	
Very rare	Hepatocellular injury, Acute hepatic failure
Musculoskeletal, and Connective Tissue Disorders	
Very rare	Arthralgia, Myalgia, Muscle Twitching
Reproductive System and Breast Disorders	
Very rare	Priapism
Very rare	Gynecomastia
General Disorders and Administration Site Conditions	
Rare	Therapeutic Response Decreased
Very rare	Chest Pain, Chest Discomfort, Drug Effect Decreased, Hyperpyrexia
Investigations	
Very rare	Blood Alkaline Phosphatase Increased, Blood Bilirubin Increased, Hepatic Enzyme Increased, Platelet Count Decreased, White Blood Cell Count Abnormal

NEC = not elsewhere classified

*The adverse reaction libido disorder includes terms apart from those associated with decreases in libido

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://pophealth.my.site.com/carmreportnz/s/

4.9. OVERDOSE

The prolonged release of methylphenidate from methylphenidate hydrochloride modified-release tablets should be considered when treating patients with overdose.

Signs and Symptoms

Signs and symptoms of methylphenidate hydrochloride modified-release tablets overdosage, resulting principally from overstimulation of the CNS and from excessive sympathomimetic effects, may include the following: vomiting, agitation, muscle twitching, convulsion, grand mal convulsion, confusional state, hallucination (auditory and/or visual), hyperhidrosis, headache, pyrexia, tachycardia, palpitations, heart rate increased, sinus arrhythmia, hypertension, mydriasis, and dry mouth.

Treatment

Treatment consists of appropriate supportive measures. The patient must be protected against self-injury and against external stimuli that would aggravate overstimulation already present. The efficacy of activated charcoal has not been established. Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for pyrexia. Efficacy of peritoneal dialysis or extracorporeal haemodialysis for methylphenidate hydrochloride modified-release tablets overdosage has not been established.

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

5. PHARMACOLOGICAL PROPERTIES

5.1. PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: centrally acting sympathomimetics: ACT code: N06BA04

Methylphenidate is a central nervous system stimulant. The mode of therapeutic action in Attention Deficit Hyperactivity Disorder (ADHD) is not known. Methylphenidate is thought to block the reuptake of noradrenaline and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

Methylphenidate hydrochloride is the racemic mixture of d,l methyl α-phenyl-2-piperidineacetate hydrochloride. The d-isomer is pharmacologically more active than the l-isomer.

Clinical trials

Children

Methylphenidate hydrochloride modified-release tablets was demonstrated to be effective in the treatment of ADHD, in children aged 6 to 12 years, in three pivotal studies. Studies 1 and 2 were single-centre, double-blind, double-dummy, randomised, placebo and active-controlled, crossover comparisons (n = 64 and 70). Study 3 was a multicentre, 4 week, double-blind, double-dummy, randomised, placebo and active-controlled, parallel study (n = 282).

The primary comparison of interest in all three trials was methylphenidate hydrochloride modified-release tablets versus placebo. The primary efficacy parameter for methylphenidate hydrochloride modified-release tablets was the Inattention/Overactivity with Aggression (IOWA) Conners I/O subscale rated by the community school teacher. Statistically significant ($p < 0.001$) reduction in the Inattention/Overactivity subscale versus placebo was shown consistently across all three controlled studies for methylphenidate hydrochloride modified-release tablets once daily.

Onset and duration of efficacy were assessed by the laboratory school teacher using the SKAMP (Swanson, Kotkin, Agler, M-Fynn and Pelham) combined attention ratings for studies 1 and 2. The onset of efficacy was estimated to be 1.5 hours and duration continued through to 12 hours. Patients demonstrated higher productivity and greater accuracy during methylphenidate hydrochloride modified-release tablets treatment.

Adults

Two double-blind, placebo-controlled studies were conducted in 627 adults aged 18 to 65 years. The controlled studies compared methylphenidate hydrochloride modified-release tablets administered once daily and placebo in a multi-centre, parallel group, 5-week, fixed-dose study (Study 4) (18, 36, and 72 mg/day) and in a multi-centre, parallel group, 7-week dose-titration study (Study 5) (36 to 108 mg/day).

Study 4 was a multi-centre, double-blind, randomized, placebo-controlled, parallel group, dose-response study (5-week duration) with 3 fixed dose groups (18, 36, and 72 mg). Patients were randomized to receive methylphenidate hydrochloride modified-release tablets administered at doses of 18 mg (n=101), 36 mg (n=102), 72 mg/day (n=102), or placebo (n=96). All three doses of methylphenidate hydrochloride modified-release tablets were significantly more effective than placebo in improving CAARS (Conners' Adult ADHD Rating Scale) total scores at double-blind end point in adult subjects with ADHD.

Study 5 demonstrated the effectiveness of methylphenidate hydrochloride modified-release tablets in the treatment of ADHD in adults aged 18 to 65 years at doses from 36 mg/day to 108 mg/day based on the change from baseline to final study visit on the Adult ADHD Investigator Rating Scale (AISRS). Of 226 patients who entered the 7-week trial, 110 were randomized to methylphenidate hydrochloride modified-release tablets and 116 were randomized to placebo. Treatment was initiated at 36 mg/day and patients continued with incremental increases of 18 mg/day (36 to 108 mg/day) based on meeting specific improvement criteria with acceptable tolerability. At the final study visit, mean change scores (LS Mean, SEM) for the investigator rating on the AISRS demonstrated that methylphenidate hydrochloride modified-release tablets was significantly superior to placebo.

5.2. PHARMACOKINETIC PROPERTIES

Absorption

Methylphenidate is readily absorbed. Following oral administration of methylphenidate hydrochloride modified-release tablets to adults, the drug overcoat dissolves and plasma methylphenidate concentrations increase rapidly reaching an initial maximum at about 1 to 2 hours. The methylphenidate contained in two internal drug layers is gradually released over the next few hours. Peak plasma concentrations are achieved at about 6 to 8 hours after which plasma levels of methylphenidate gradually decrease. methylphenidate hydrochloride modified-release tablets once daily minimises the fluctuations between peak and trough concentrations associated with immediate-release methylphenidate three times daily. The

extent of absorption of methylphenidate hydrochloride modified-release tablets once daily is generally comparable to conventional immediate release preparations given three times daily.

Following the administration of methylphenidate hydrochloride modified-release tablets 18 mg once daily in 36 adults, the mean pharmacokinetic parameters were C_{max} 3.7 ± 1.0 ng/mL, T_{max} 6.8 ± 1.8 h, AUC_{∞} 41.8 ± 13.9 ngh/mL and $t_{1/2}$ 3.5 ± 0.4 h. No differences in the pharmacokinetics of methylphenidate hydrochloride modified-release tablets were noted following single and repeated once daily dosing indicating no significant drug accumulation. The AUC and $t_{1/2}$ following repeated once daily dosing are similar to those following the first dose of methylphenidate hydrochloride modified-release tablets 18 mg.

Following administration of methylphenidate hydrochloride modified-release tablets in single doses of 18, 36 and 54 mg/day to adults, C_{max} and $AUC_{0-\infty}$ of d-methylphenidate were proportional to dose, whereas l-methylphenidate C_{max} and $AUC_{0-\infty}$ increased disproportionately with respect to dose. Following administration of methylphenidate hydrochloride modified-release tablets, plasma concentrations of the l-isomer were approximately 1/40th the plasma concentrations of the d-isomer.

In healthy adults, single and multiple dosing of once daily methylphenidate hydrochloride modified-release tablet doses from 54 to 144 mg/day resulted in linear and dose proportional increases in C_{max} and AUC_{inf} for total methylphenidate (MPH) and its major metabolite, (alpha)-phenyl-piperidine acetic acid (PPAA). The single dose and steady state (Day 4) clearance and half-life parameters were similar, indicating that there was no time dependency in the pharmacokinetics of methylphenidate. The ratio of metabolite (PPAA) to parent drug (MPH) was constant across doses from 54 to 144 mg/day, both after single dose and upon multiple dosing.

Pharmacokinetic equivalence has been demonstrated for two 27-mg methylphenidate hydrochloride modified-release tablets with three 18-mg methylphenidate hydrochloride modified-release tablets. The mean values of the treatment ratio (2 x 27 mg fasted/3 x 18 mg fasted) of the log-transformed pharmacokinetic values for C_{max}, T_{max} and AUC_{inf} were 101.1%, 104.3% and 100.3% respectively. The 90% CIs for the treatment ratios were within the pre-specified 80% - 125% range.

In a multiple dose study in adolescent ADHD patients aged 13 to 16 administered their prescribed dose (18 to 72 mg/day) of methylphenidate hydrochloride modified-release tablets, mean C_{max} and AUC_{TAU} of methylphenidate increased proportionally with respect to dose.

Studies on the effects of dosing after overnight fasting, after consumption of a normal breakfast and a high-fat breakfast showed no differences in pharmacokinetics or pharmacodynamics of methylphenidate hydrochloride modified-release tablets. There is no evidence of dose dumping in the presence or absence of food.

Distribution

Plasma methylphenidate concentrations in adults decline biexponentially following oral administration. The terminal plasma half-life of methylphenidate in adults following oral administration of methylphenidate hydrochloride modified-release tablets was approximately 3.5 hours.

Metabolism

In humans, methylphenidate is metabolised primarily by de-esterification to α-phenyl-piperidine acetic acid (PPAA) which has little or no pharmacologic activity. In adults the

metabolism of methylphenidate hydrochloride modified-release tablets once daily, as evaluated by metabolism to PPAA, is similar to that of methylphenidate three times daily. The metabolism of single and repeated once daily doses of methylphenidate hydrochloride modified-release tablets is similar.

Excretion

After oral dosing of radiolabelled methylphenidate in humans, about 90% of the radioactivity was recovered in urine. The main urinary metabolite was PPAA, accounting for approximately 80% of the dose. Since renal clearance is not an important route of methylphenidate clearance, renal insufficiency is not expected to have a significant effect on the pharmacokinetics of methylphenidate hydrochloride modified-release tablets.

5.3. PRECLINICAL SAFETY DATA

Carcinogenicity

In a lifetime dietary carcinogenicity study carried out in mice, methylphenidate caused an increase in hepatocellular adenomas at a dose of 60–80 mg/kg/day, and in males only, an increase in hepatoblastomas (a relatively rare rodent malignant tumour type) at 60 mg/kg/day. These dose levels are approximately 3–8 fold the maximal recommended clinical dose on a mg/m^2 basis. There was no increase in tumours at 30-40 mg/kg/day (approximately 1-4 fold the maximal recommended clinical dose on a mg/m^2 basis). The mouse strain used is sensitive to the development of hepatic tumours, and the significance of these results to humans is not known. There was no evidence of carcinogenicity in two strains of transgenic mice administered methylphenidate in the diet for 24 weeks at doses up to 60–74 mg/kg/day (approximately 3–8 fold the maximal recommended clinical dose on a mg/m^2 basis) or in a lifetime dietary study in rats at doses up to 50 mg/kg/day (approximately 4–10 fold the maximal recommended clinical dose on a mg/m^2 basis).

Mutagenicity

Methylphenidate was not mutagenic in the *in vitro* assays (Ames reverse mutation assay, mouse lymphoma cell forward mutation assay). Methylphenidate was weakly clastogenic *in vitro* (Chinese Hamster ovary cells) but was negative *in vivo* (mouse bone marrow micronucleus assay). Sister chromatid exchange assay results were positive only at high (cytotoxic) concentrations.

Impairment of fertility

Dietary administration of methylphenidate to male and female mice at doses up to 150–160 mg/kg/day did not impair fertility in an 18–week continuous breeding study in which both parents and offspring were treated. This dose was approximately 7–16 fold the maximal recommended human dose on a mg/m^2 basis.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS

- hypromellose
- polyethylene oxide
- succinic acid
- magnesium stearate

- sodium chloride
- colloidal silicon dioxide
- iron oxide black
- macrogol 3350
- cellulose acetate
- OPADRY complete film coating system YS-3-7413 Clear
- OPADRY II complete film coating system 32K92800 Yellow (18 mg tabs only)
- OPADRY II complete film coating system 32K275013 Grey (27 mg tabs only)
- OPADRY II complete film coating system Y-30-18037 White (36 mg tabs only)
- OPADRY II complete film coating system 32K240063 Pink (54 mg tabs only)

6.2. INCOMPATIBILITIES

Not applicable.

6.3. SHELF LIFE

2 years.

6.4. SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Keep container tightly closed.

6.5. NATURE AND CONTENTS OF CONTAINER

METHYLPHENIDATE SANDOZ XR tablets are supplied in HDPE bottles with child-resistant closure and silica gel desiccant.

Pack size of 30 tablets.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL

No special requirements.

7. MEDICINE SCHEDULE

Controlled Drug – B2

8. SPONSOR

Sandoz New Zealand Limited
12 Madden Street
Auckland 1010
New Zealand

Tel: 0800 726 369

9. DATE OF FIRST APPROVAL

16/09/2025

10. DATE OF REVISION OF THE TEXT

31/03/2026

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.1	Minor editorial change
4.8	Addition of Glaucoma, Intraocular Pressure increased, Hyperhidrosis to ADR table