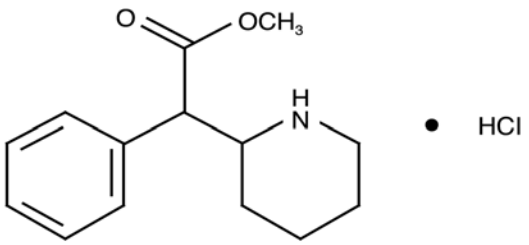
Methylin™ Oral Solution
methylphenidate HCl oral solution, 5 mg/5 mL
methylphenidate HCl oral solution, 10 mg/5 mL
Rx only

C II

DESCRIPTION

Methylin™ methylphenidate HCl oral solution, is a mild central nervous system (CNS) stimulant, available as 5 mg/5 mL and 10 mg/5 mL oral solutions for oral administration. Methylphenidate hydrochloride is methyl α-phenyl-2-piperidineacetate hydrochloride, and its structural formula is



Methylphenidate Hydrochloride

$C_{14}H_{19}NO_2$ • HCl **MW = 269.77**

Methylphenidate hydrochloride USP is a white, odorless, fine crystalline powder. Its solutions are acid to litmus. It is freely soluble in water and in methanol, soluble in alcohol, and slightly soluble in chloroform and in acetone.

Each mL of Methylin™ Oral Solution 5 mg/5 mL contains 1 mg of methylphenidate hydrochloride USP.

Each mL of Methylin™ Oral Solution 10 mg/5 mL contains 2 mg of methylphenidate hydrochloride USP.

In addition, Methylin™ Oral Solution also contains the following inactive ingredients: citric acid anhydrous, glycerin, N&A grape flavor, PEG 1450, and purified water.

CLINICAL PHARMACOLOGY

Methylphenidate is a racemic mixture comprised of the *d*- and *l-threo* enantiomers. The *d-threo* enantiomer is more pharmacologically active than the *l-threo* enantiomer.

Methylphenidate HCl is a central nervous system (CNS) stimulant.

The mode of therapeutic action in humans is not completely understood, but methylphenidate presumably activates the brain stem arousal system and cortex to produce its stimulant effect. Methylphenidate is thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

There is neither specific evidence which clearly establishes the mechanism whereby Methylin produces its mental and behavioral effects in children, nor conclusive evidence regarding how these effects relate to the condition of the central nervous system.

Pharmacokinetics

Absorption

Methylin Oral Solution is readily absorbed. Following oral administration of Methylin Oral Solution, peak plasma methylphenidate concentrations are achieved at 1 to 2 hours. Methylin Oral Solution has been shown to be bioequivalent to Ritalin® tablet. The mean C_{max} following a 20 mg dose is approximately 9 ng/mL.

Food Effect

In a study in adult volunteers to investigate the effects of a high-fat meal on the bioavailability of Methylin Oral Solution at a dose of 20 mg, the presence of food delayed the peak by approximately 1 hour (1.7 hours, fasted and 2.7 hours, fed). Overall, a high-fat meal increased the C_{max} of Methylin Oral Solution by about 13% and the AUC by about 25%, on average. Through a cross-study comparison, the magnitude of increase in C_{max} and AUC is found to be comparable between the Methylin Oral Solution and Ritalin®, the immediate release tablet.

Metabolism and Excretion

In humans, methylphenidate is metabolized primarily via deesterification to alpha-phenylpiperidine acetic acid (PPA, ritalinic acid). The metabolite has little or no pharmacologic activity.

After oral dosing of radiolabeled methylphenidate in humans, about 90% of the radioactivity was recovered in urine. The main urinary metabolite was PPA, accounting for approximately 80% of the dose.

The pharmacokinetics of the Methylin Oral Solution have been studied in healthy adult volunteers. The mean terminal half-life ($t_{½}$) of methylphenidate following administration of 20 mg Methylin ($t_{½}$ = 2.7 hours) is comparable to the mean terminal $t_{½}$ following administration of Ritalin® (methylphenidate hydrochloride immediate-release tablets) ($t_{½}$ = 2.8h) in healthy adult volunteers.

Special Populations

Gender – The effect of gender on the pharmacokinetics of methylphenidate after Methylin Oral Solution administration has not been studied.

Race – The influence of race on the pharmacokinetics of methylphenidate after Methylin Oral Solution administration has not been studied.

Age – The pharmacokinetics of methylphenidate after Methylin Oral Solution administration have not been studied in pediatrics.

Renal Insufficiency

There is no experience with the use of Methylin Oral Solution 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 ritalinic acid. Since renal clearance is not an important route of methylphenidate clearance, renal insufficiency is expected to have little effect on the pharmacokinetics of Methylin Oral Solution.

Hepatic Insufficiency

There is no experience with the use of Methylin Oral Solution in patients with hepatic insufficiency.

INDICATIONS AND USAGE

Attention Deficit Disorders, Narcolepsy

Attention Deficit Disorders (previously known as Minimal Brain Dysfunction in Children). Other terms being used to describe the behavioral syndrome below include: Hyperkinetic Child Syndrome, Minimal Brain Damage, Minimal Cerebral Dysfunction, Minor Cerebral Dysfunction.

Methylin™ is indicated as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate-to-severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity. The diagnosis of this syndrome should not be made with finality when these symptoms are only of comparatively recent origin. Nonlocalizing (soft) neurological signs, learning disability, and abnormal EEG may or may not be present, and a diagnosis of central nervous system dysfunction may or may not be warranted.

Special Diagnostic Considerations

Specific etiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of special psychological, educational, and social resources.

Characteristics commonly reported include: chronic history of short attention span, distractibility, emotional lability, impulsivity, and moderate-to-severe hyperactivity; minor neurological signs and abnormal EEG. Learning may or may not be impaired. The diagnosis must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these characteristics.

Drug treatment is not indicated for all children with this syndrome. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or primary psychiatric disorders, including psychosis. Appropriate educational placement is essential and psychosocial intervention is generally necessary. 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 child's symptoms.

CONTRAINDICATIONS

Marked anxiety, tension, and agitation are contraindications to Methylin, since the drug may aggravate these symptoms. Methylin is contraindicated also in patients known to be hypersensitive to the drug, in patients with glaucoma, and in patients with motor tics or with a family history or diagnosis of Tourette's syndrome.

Methylin is contraindicated 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).

WARNINGS

Serious Cardiovascular Events

Sudden Death and Pre-Existing Structural Cardiac Abnormalities or Other Serious Heart Problems

Children and Adolescents – Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Although some serious heart problems alone carry an increased risk of sudden death, stimulant products generally should not be used in children or adolescents with known serious 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 drug.

Adults – Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs.

Hypertension and other Cardiovascular Conditions

Stimulant medications cause a modest increase in average blood pressure (about 2 to 4 mmHg) and average heart rate (about 3 to 6 bpm), and individuals may have larger increases. While the mean changes alone would not be expected to have short-term consequences, all patients should be monitored for larger changes in heart rate and blood pressure. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g., those with pre-existing hypertension, heart failure, recent myocardial infarction, or ventricular arrhythmia.

Assessing Cardiovascular Status in Patients being Treated with Stimulant Medications

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

Psychiatric Adverse Events

Pre-Existing Psychosis – Administration of stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder.

Bipolar Illness – Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, 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.

Emergence of New Psychotic or Manic Symptoms – Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in children and adolescents 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. In a pooled analysis of multiple short-term, placebo-controlled studies, such symptoms occurred in about 0.1% (4 patients with events out of 3482 exposed to methylphenidate or amphetamine for several weeks at usual doses) of stimulant-treated patients compared to 0 in placebo-treated patients.

Aggression – Aggressive behavior or hostility is often observed in children and adolescents with ADHD, and has been reported in clinical trials and the postmarketing experience of some medications indicated for the treatment of ADHD. Although there is no systematic evidence that stimulants cause aggressive behavior or hostility, patients beginning treatment for ADHD should be monitored for the appearance of or worsening of aggressive behavior or hostility.

Long-Term Suppression of Growth

Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated children over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e., treatment for 7 days per week throughout the year) have a temporary slowing in growth rate (on average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during this period of development.

Published data are inadequate to determine whether chronic use of amphetamines may cause a similar suppression of growth, however, it is anticipated that they likely have this effect as well. Therefore, growth should be monitored during treatment with stimulants, and patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

Seizures

There is some clinical evidence that stimulants may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

Visual Disturbance

Difficulties with accommodation and blurring of vision have been reported with stimulant treatment.

USE IN CHILDREN LESS THAN SIX YEARS OF AGE

Methylin should not be used in children under six years, since safety and efficacy in this age group have not been established.

DRUG ABUSE AND DEPENDENCE

Methylin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative.

Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbances.

PRECAUTIONS

General

Patients with an element of agitation may react adversely; discontinue therapy if necessary.

Periodic CBC, differential, and platelet counts are advised during prolonged therapy.

Drug treatment is not indicated in all cases of this behavioral syndrome and should be considered only in light of the complete history and evaluation of the child. The decision to prescribe Methylin should depend on the physician's assessment of the chronicity and severity of the child's symptoms and their appropriateness for his/her age. Prescription should not depend solely on the presence of one or more of the behavioral characteristics.

When these symptoms are associated with acute stress reactions, treatment with Methylin is usually not indicated.

Long-term effects of Methylin in children have not been well established.

Information for Patients

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with methylphenidate and should counsel them in its appropriate use. A patient Medication Guide is available for Methylin Oral Solution. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

Drug Interactions

Methylin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents.

Human pharmacologic studies have shown that Methylin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, diphenylhydantoin, primidone), phenylbutazone, and tricyclic drugs (imipramine, clomipramine, desipramine). Downward dosage adjustments of these drugs may be required when given concomitantly with Methylin.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a lifetime carcinogenicity study carried out in B6C3F1 mice, methylphenidate caused an increase in hepatocellular adenomas and, in males only, an increase in hepatoblastomas, at a daily dose of approximately 60 mg/kg/day. This dose is approximately 30 times and 2.5 times the maximum recommended human dose on a mg/kg and mg/m^2 basis, respectively. Hepatoblastoma is a relatively rare rodent malignant tumor type. There was no increase in total malignant hepatic tumors. The mouse strain used is sensitive to the development of hepatic tumors, and the significance of these results to humans is unknown.

Methylphenidate did not cause any increase in tumors in a lifetime carcinogenicity study carried out in F344 rats; the highest dose used was approximately 45 mg/kg/day, which is approximately 22 times and 4 times the maximum recommended human dose on a mg/kg and mg/m^2 basis, respectively.

Methylphenidate was not mutagenic in the in vitro Ames reverse mutation assay or in the in vitro mouse lymphoma cell forward mutation assay. Sister chromatid exchanges and chromosome aberrations were increased, indicative of a weak clastogenic response, in an in vitro assay in cultured Chinese Hamster Ovary (CHO) cells. The genotoxic potential of methylphenidate has not been evaluated in an in vivo assay.

Usage in Pregnancy

Adequate animal reproduction studies to establish safe use of Methylin during pregnancy have not been conducted. However, in a recently conducted study, methylphenidate has been shown to have teratogenic effects in rabbits when given in doses of 200 mg/kg/day, which is approximately 167 times and 78 times the maximum recommended human dose on a mg/kg and a mg/m^2 basis, respectively. In rats, teratogenic effects were not seen when the drug was given in doses of 75 mg/kg/day, which is approximately 62.5 and 13.5 times the maximum recommended human dose on a mg/kg and a mg/m^2 basis, respectively. Therefore, until more information is available, methylphenidate should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

ADVERSE REACTIONS

Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include hypersensitivity (including skin rash, urticaria, fever, arthralgia, exfoliative dermatitis, erythema multiforme with histopathological findings of necrotizing vasculitis, and thrombocytopenic purpura); anorexia; nausea; dizziness; palpitations; headache; dyskinesia; drowsiness; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmia; abdominal pain; weight loss during prolonged therapy. There have been rare reports of Tourette's syndrome. Toxic psychosis has been reported. Although a definite causal relationship has not been established, the following have been reported in patients taking this drug: instances of abdominal liver function, ranging from transaminase elevation to hepatic coma; isolated cases of cerebral arteritis and/or occlusion; leukopenia and/or anemia; transient depressed mood; a few instances of scalp hair loss. Very rare reports of neuroleptic malignant syndrome (NMS) have been received, and, in most of these, patients were concurrently receiving therapies associated with NMS. In a single report, a ten year old boy who had been taking methylphenidate for approximately 18 months experienced an NMS-like event within 45 minutes of ingesting his first dose of venlafaxine. It is uncertain whether this case represented a drug-drug interaction, a response to either drug alone, or some other cause.

In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently; however, any of the other adverse reactions listed above may also occur.

OVERDOSAGE

Signs and symptoms of acute overdosage, resulting principally from overstimulation of the central nervous system and from excessive sympathomimetic effects, may include the following: vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, mydriasis, and dryness of mucous membranes.

Consult with a Certified Poison Control Center regarding treatment for up-to-date guidance and advice.

Treatment consists of appropriate supportive measures. The patient must be protected against self-injury and against external stimuli that would aggravate overstimulation already present. Gastric contents may be evacuated by gastric lavage. In the presence of severe intoxication, use a carefully titrated dosage of a *short-acting* barbiturate before performing gastric lavage. Other measures to detoxify the gut include administration of activated charcoal and a cathartic.

Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for hyperpyrexia.

Efficacy of peritoneal dialysis or extracorporeal hemodialysis for methylphenidate overdosage has not been established.

DOSAGE AND ADMINISTRATION

Dosage should be individualized according to the needs and responses of the patient.

Adults

Administer in divided doses 2 or 3 times daily, preferably 30 to 45 minutes before meals. Average dosage is 20 to 30 mg daily. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. Patients who are unable to sleep if medication is taken late in the day should take the last dose before 6 p.m.

Children (6 years and over)

Methylin should be initiated in small doses, with gradual weekly increments. Daily dosage above 60 mg is not recommended.

If improvement is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued.

Start with 5 mg twice daily (before breakfast and lunch) with gradual increments of 5 to 10 mg weekly.

If paradoxical aggravation of symptoms or other adverse effects occur, reduce dosage, or, if necessary, discontinue the drug.

Methylin should be periodically discontinued to assess the child's condition. Improvement may be sustained when the drug is either temporarily or permanently discontinued.

Drug treatment should not and need not be indefinite and usually may be discontinued after puberty.

HOW SUPPLIED

Methylin™ Oral Solution 5 mg per 5 mL is available as a colorless, grape flavored liquid.

Bottles of 500 mL .....NDC 59630-750-50

Methylin™ Oral Solution 10 mg per 5 mL is available as a colorless, grape flavored liquid.

Bottles of 500 mL .....NDC 59630-755-50

Dispense in tight container with child-resistant closure.

Storage: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Methylin is a trademark of Mallinckrodt Inc.

Ritalin is a registered trademark of Novartis Corporation.

Manufactured for:
Shionogi Pharma, Inc.
Atlanta, GA 30328

Manufactured by:
Mallinckrodt Inc.
Hazelwood, MO 63042 USA

Rev 09/2010

MEDICATION GUIDE
Methylin™ Oral Solution
(methylphenidate HCl oral solution) 5 mg/5 mL and 10 mg/5 mL

CII

Read the Medication Guide that comes with Methylin Oral Solution before you or your child starts taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your doctor about your or your child's treatment with Methylin Oral Solution.

What is the most important information I should know about Methylin Oral Solution?

The following have been reported with use of methylphenidate HCl oral solution and other stimulant medicines.

1. Heart-related problems:

- **sudden death in patients who have heart problems or heart defects**
- **stroke and heart attack in adults**
- **increased blood pressure and heart rate**

Tell your doctor if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems.

Your doctor should check you or your child carefully for heart problems before starting Methylin Oral Solution.

Your doctor should check you or your child's blood pressure and heart rate regularly during treatment with Methylin Oral Solution.

Call your doctor right away if you or your child has any signs of heart problems such as chest pain, shortness of breath, or fainting while taking Methylin Oral Solution.

2. Mental (Psychiatric) problems:

All Patients

- **new or worse behavior and thought problems**
- **new or worse bipolar illness**
- **new or worse aggressive behavior or hostility**

Children and Teenagers

- **new psychotic symptoms (such as hearing voices, believing things that are not true, are suspicious) or new manic symptoms**

Tell your doctor about any mental problems you or your child have, or about a family history of suicide, bipolar illness, or depression.

Call your doctor right away if you or your child have any new or worsening mental symptoms or problems while taking Methylin Oral Solution, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.

What Is Methylin Oral Solution?

Methylin Oral Solution is a central nervous system stimulant prescription medicine. Methylin Oral Solution is a liquid form of medication that you take by mouth. **It is used for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD).** Methylin Oral Solution may help increase attention and decrease impulsiveness and hyperactivity in patients with ADHD.

Methylin Oral Solution should be used as a part of a total treatment program for ADHD that may include counseling or other therapies.

Methylin Oral Solution is also used in the treatment of a sleep disorder called narcolepsy.

Methylin Oral Solution is a federally controlled substance (CII) because it can be abused or lead to dependence. Keep Methylin Oral Solution in a safe place to prevent misuse and abuse. Selling or giving away Methylin Oral Solution may harm others, and is against the law.

Tell your doctor if you or your child have (or have a family history of) ever abused or been dependent on alcohol, prescription medicines or street drugs.

Who should not take Methylin Oral Solution?

Methylin Oral Solution should not be taken if you or your child:

- are very anxious, tense, or agitated
- have an eye problem called glaucoma
- have tics or Tourette's syndrome, or a family history of Tourette's syndrome. Tics are hard to control repeated movements or sounds.
- are taking or have taken within the past 14 days an antidepression medicine called a mono-amine oxidase inhibitor or MAOI.
- are allergic to anything in Methylin Oral Solution. See the end of this Medication Guide for a complete list of ingredients.

Methylin Oral Solution should not be used in children less than 6 years old because it has not been studied in this age group.

Methylin Oral Solution may not be right for you or your child. Before starting Methylin Oral Solution tell your or your child's doctor about all health conditions (or a family history of) including:

- heart problems, heart defects, high blood pressure
- mental problems including psychosis, mania, bipolar illness, or depression
- tics or Tourette's syndrome
- seizures or have had an abnormal brain wave test (EEG)

Tell your doctor if you or your child is pregnant, planning to become pregnant, or breastfeeding.

Can Methylin Oral Solution be taken with other medicines?

Tell your doctor about all of the medicines that you or your child take including prescription and nonprescription medicines, vitamins, and herbal supplements. Methylin Oral Solution and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be adjusted while taking Methylin Oral Solution.

Your doctor will decide whether Methylin Oral Solution can be taken with other medicines.

Especially tell your doctor if you or your child takes:

- antidepression medicines including MAOIs
- seizure medicines
- blood thinner medicines
- blood pressure medicines
- cold or allergy medicines that contain decongestants

Know the medicines that you or your child takes. Keep a list of your medicines with you to show your doctor and pharmacist.

Do not start any new medicine while taking Methylin Oral Solution without talking to your doctor first.

How should Methylin Oral Solution be taken?

- **Take Methylin Oral Solution exactly as prescribed.** Your doctor may adjust the dose until it is right for you or your child.
- Methylin Oral Solution is usually taken 2 to 3 times a day.
- Take Methylin Oral Solution 30 to 45 minutes before meals.
- From time to time, your doctor may stop Methylin Oral Solution treatment for awhile to check ADHD symptoms.
- Your doctor may do regular checks of the blood, heart, and blood pressure while taking Methylin Oral Solution. Children should have their height and weight checked often while taking Methylin Oral Solution. Methylin Oral Solution treatment may be stopped if a problem is found during these check-ups.
- **If you or your child takes too much Methylin Oral Solution or overdoses, call your doctor or poison control center right away, or get emergency treatment.**

What are possible side effects of Methylin Oral Solution?

See **"What is the most important information I should know about Methylin Oral Solution?"** for information on reported heart and mental problems.

Other serious side effects include:

- slowing of growth (height and weight) in children
- seizures, mainly in patients with a history of seizures
- eyesight changes or blurred vision

Common side effects include:

- nervousness
- trouble sleeping
- headache
- stomach ache
- fast heart beat
- nausea
- decreased appetite
- dizziness
- weight loss

Talk to your doctor if you or your child has side effects that are bothersome or do not go away.

This is not a complete list of possible side effects. Ask your doctor or pharmacist for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Methylin Oral Solution?

- Store Methylin Oral Solution in a safe place at room temperature, 68° to 77°F (20° to 25°C).
- **Keep Methylin Oral Solution and all medicines out of the reach of children.**

General information about Methylin Oral Solution

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Methylin Oral Solution for a condition for which it was not prescribed. Do not give Methylin Oral Solution to other people, even if they have the same condition. It may harm them and it is against the law.

This Medication Guide summarizes the most important information about Methylin Oral Solution. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about Methylin Oral Solution that was written for healthcare professionals. For more information, please contact Shionogi Pharma, Inc. at 1-800-849-9707 or visit the website at www.methylinrx.com.

What are the ingredients in Methylin Oral Solution?

Active Ingredient: methylphenidate hydrochloride USP

Inactive Ingredients: citric acid anhydrous, glycerin, N&A grape flavor, PEG 1450, and purified water.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured for:
Shionogi Pharma, Inc.
Atlanta, GA 30328

Manufactured by:
Mallinckrodt Inc.
Hazelwood, MO 63042 USA

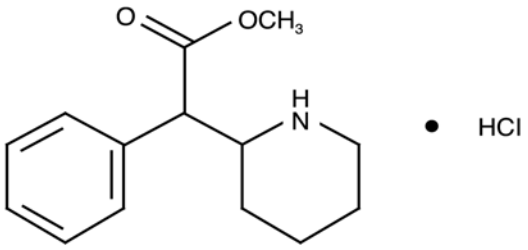
Rev 09/2010

Methylin™ Chewable Tablets
(methylphenidate HCl chewable tablets)
2.5 mg, 5 mg and 10 mg
Rx only

C II

DESCRIPTION

Methylin™ (methylphenidate HCl) is a mild central nervous system (CNS) stimulant, available as 2.5 mg, 5 mg and 10 mg chewable tablets for oral administration. Methylphenidate hydrochloride is methyl α-phenyl-2-piperidineacetate hydrochloride, and its structural formula is



Methylphenidate Hydrochloride

$C_{14}H_{19}NO_2$ • HCl **MW = 269.77**

Methylphenidate hydrochloride USP is a white, odorless, fine crystalline powder. Its solutions are acid to litmus. It is freely soluble in water and in methanol, soluble in alcohol, and slightly soluble in chloroform and in acetone.

Each Methylin™ Chewable Tablet, for oral administration, contains 2.5 mg, 5 mg or 10 mg of methylphenidate hydrochloride USP. In addition, Methylin™ Chewable Tablets also contain the following inactive ingredients: aspartame, maltose, microcrystalline cellulose, guar gum, grape flavor, pregelatinized starch, and stearic acid.

CLINICAL PHARMACOLOGY

Methylphenidate is a racemic mixture comprised of the *d*- and *l-threo* enantiomers. The *d-threo* enantiomer is more pharmacologically active than the *l-threo* enantiomer.

Methylphenidate HCl is a central nervous system (CNS) stimulant.

The mode of therapeutic action in humans is not completely understood, but methylphenidate presumably activates the brain stem arousal system and cortex to produce its stimulant effect. Methylphenidate is thought to block the reuptake of norepinephrine and dopamine into the presynaptic neuron and increase the release of these monoamines into the extraneuronal space.

There is neither specific evidence which clearly establishes the mechanism whereby Methylin produces its mental and behavioral effects in children, nor conclusive evidence regarding how these effects relate to the condition of the central nervous system.

Pharmacokinetics

Absorption

Methylin Chewable Tablets are readily absorbed. Following oral administration of Methylin Chewable Tablets, peak plasma methylphenidate concentrations are achieved at about 1 to 2 hours. Methylin Chewable Tablets have been shown to be bioequivalent to Ritalin® tablet. The mean C_{max} following a 20 mg dose is approximately 10 ng/mL.

Food Effect

In a study in adult volunteers investigating the effects of a high-fat meal on the bioavailability of Methylin Chewable Tablets at a dose of 20 mg, the presence of food delayed the peak concentrations by approximately 1 hour (1.5 hours, fasted and 2.4 hours, fed). Overall, a high-fat meal increased the AUC of Methylin Chewable Tablets by about 20%, on average. Through a cross-study comparison, the magnitude of food effect is found to be comparable between the Methylin Chewable Tablets and Ritalin®, the immediate release tablet.

Metabolism and Excretion

In humans, methylphenidate is metabolized primarily via deesterification to alpha-phenylpiperidine acetic acid (PPA, ritalinic acid). The metabolite has little or no pharmacologic activity.

After oral dosing of radiolabeled methylphenidate in humans, about 90% of the radioactivity was recovered in urine. The main urinary metabolite was PPA, accounting for approximately 80% of the dose.

The pharmacokinetics of the Methylin Chewable Tablets have been studied in healthy adult volunteers. The mean terminal half-life ($t_{½}$) of methylphenidate following administration of 20 mg Methylin Chewable Tablets ($t_{½}$ = 3 hours) is comparable to the mean terminal $t_{½}$ following administration of Ritalin® (methylphenidate hydrochloride immediate-release tablets) ($t_{½}$ = 2.8 hours) in healthy adult volunteers.

Special Populations

Gender – The effect of gender on the pharmacokinetics of methylphenidate after Methylin Chewable Tablets administration has not been studied.

Race – The influence of race on the pharmacokinetics of methylphenidate after Methylin Chewable Tablets administration has not been studied.

Age – The pharmacokinetics of methylphenidate after Methylin Chewable Tablets administration have not been studied in pediatrics.

Renal Insufficiency

There is no experience with the use of Methylin Chewable 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 ritalinic acid. Since renal clearance is not an important route of methylphenidate clearance, renal insufficiency is expected to have little effect on the pharmacokinetics of Methylin Chewable Tablets.

Hepatic Insufficiency

There is no experience with the use of Methylin Chewable Tablets in patients with hepatic insufficiency.

INDICATIONS AND USAGE

Attention Deficit Disorders, Narcolepsy

Attention Deficit Disorders (previously known as Minimal Brain Dysfunction in Children). Other terms being used to describe the behavioral syndrome below include: Hyperkinetic Child Syndrome, Minimal Brain Damage, Minimal Cerebral Dysfunction, Minor Cerebral Dysfunction.

Methylin™ is indicated as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate-to-severe distractibility, short attention span, hyperactivity, emotional lability, and impulsivity. The diagnosis of this syndrome should not be made with finality when these symptoms are only of comparatively recent origin. Nonlocalizing (soft) neurological signs, learning disability, and abnormal EEG may or may not be present, and a diagnosis of central nervous system dysfunction may or may not be warranted.

Special Diagnostic Considerations

Specific etiology of this syndrome is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of special psychological, educational, and social resources.

Characteristics commonly reported include: chronic history of short attention span, distractibility, emotional lability, impulsivity, and moderate-to-severe hyperactivity; minor neurological signs and abnormal EEG. Learning may or may not be impaired. The diagnosis must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these characteristics.

Drug treatment is not indicated for all children with this syndrome. Stimulants are not intended for use in the child who exhibits symptoms secondary to environmental factors and/or primary psychiatric disorders, including psychosis. Appropriate educational placement is essential and psychosocial intervention is generally necessary. 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 child's symptoms.

CONTRAINDICATIONS

Marked anxiety, tension, and agitation are contraindications to Methylin, since the drug may aggravate these symptoms. Methylin is contraindicated also in patients known to be hypersensitive to the drug, in patients with glaucoma, and in patients with motor tics or with a family history or diagnosis of Tourette's syndrome.

Methylin is contraindicated 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).

WARNINGS

Serious Cardiovascular Events

Sudden Death and Pre-Existing Structural Cardiac Abnormalities or Other Serious Heart Problems

Children and Adolescents – Sudden death has been reported in association with CNS stimulant treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious heart problems. Although some serious heart problems alone carry an increased risk of sudden death, stimulant products generally should not be used in children or adolescents with known serious 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 drug.

Adults – Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs.

Hypertension and other Cardiovascular Conditions

Stimulant medications cause a modest increase in average blood pressure (about 2 to 4 mmHg) and average heart rate (about 3 to 6 bpm), and individuals may have larger increases. While the mean changes alone would not be expected to have short-term consequences, all patients should be monitored for larger changes in heart rate and blood pressure. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g., those with pre-existing hypertension, heart failure, recent myocardial infarction, or ventricular arrhythmia.

Assessing Cardiovascular Status in Patients being Treated with Stimulant Medications

Children, adolescents, or adults who are being considered for treatment with stimulant medications should have a careful history (including assessment for a family history of sudden

death or ventricular arrhythmia) and physical exam to assess for the presence of cardiac disease, and should receive further cardiac evaluation if findings suggest such disease (e.g., electrocardiogram and echocardiogram). Patients who develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during stimulant treatment should undergo a prompt cardiac evaluation.

Psychiatric Adverse Events

Pre-Existing Psychosis – Administration of stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder.

Bipolar Illness – Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, 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.

Emergence of New Psychotic or Manic Symptoms – Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, or mania in children and adolescents 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. In a pooled analysis of multiple short-term, placebo-controlled studies, such symptoms occurred in about 0.1% (4 patients with events out of 3482 exposed to methylphenidate or amphetamine for several weeks at usual doses) of stimulant-treated patients compared to 0 in placebo-treated patients.

Aggression – Aggressive behavior or hostility is often observed in children and adolescents with ADHD, and has been reported in clinical trials and the postmarketing experience of some medications indicated for the treatment of ADHD. Although there is no systematic evidence that stimulants cause aggressive behavior or hostility, patients beginning treatment for ADHD should be monitored for the appearance of or worsening of aggressive behavior or hostility.

Long-Term Suppression of Growth

Careful follow-up of weight and height in children ages 7 to 10 years who were randomized to either methylphenidate or non-medication treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and non-medication treated children over 36 months (to the ages of 10 to 13 years), suggests that consistently medicated children (i.e., treatment for 7 days per week throughout the year) have a temporary slowing in growth rate (on average, a total of about 2 cm less growth in height and 2.7 kg less growth in weight over 3 years), without evidence of growth rebound during this period of development.

Published data are inadequate to determine whether chronic use of amphetamines may cause a similar suppression of growth, however, it is anticipated that they likely have this effect as well.

Therefore, growth should be monitored during treatment with stimulants, and patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

Seizures

There is some clinical evidence that stimulants may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and, very rarely, in patients without a history of seizures and no prior EEG evidence of seizures. In the presence of seizures, the drug should be discontinued.

Visual Disturbance

Difficulties with accommodation and blurring of vision have been reported with stimulant treatment.

USE IN CHILDREN LESS THAN SIX YEARS OF AGE

Methylin should not be used in children under six years, since safety and efficacy in this age group have not been established.

DRUG ABUSE AND DEPENDENCE

Methylin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative.

Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbances.

PRECAUTIONS

General

Patients with an element of agitation may react adversely; discontinue therapy if necessary.

Periodic CBC, differential, and platelet counts are advised during prolonged therapy.

Drug treatment is not indicated in all cases of this behavioral syndrome and should be considered only in light of the complete history and evaluation of the child. The decision to prescribe Methylin should depend on the physician's assessment of the chronicity and severity of the child's symptoms and their appropriateness for his/her age. Prescription should not depend solely on the presence of one or more of the behavioral characteristics.

When these symptoms are associated with acute stress reactions, treatment with Methylin is usually not indicated.

Long-term effects of Methylin in children have not been well established.

Information for Patients

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with methylphenidate and should counsel them in its appropriate use. A patient Medication Guide is available for Methylin Chewable Tablets. The prescriber or health professional should instruct patients, their families, and their caregivers to read the Medication Guide and should assist them in understanding its contents. Patients should be given the opportunity to discuss the contents of the Medication Guide and to obtain answers to any questions they may have. The complete text of the Medication Guide is reprinted at the end of this document.

Physicians are advised to discuss the following issues with patients for whom they prescribe Methylin:

Choking – Taking this product without adequate fluid may cause it to swell and block your throat or esophagus and may cause choking. Do not take this product if you have difficulty in swallowing. If you experience chest pain, vomiting, or difficulty in swallowing or breathing after taking this product, seek immediate medical attention.

Directions – Take this product (child or adult dose) with at least 8 ounces (a full glass) of water or other fluid. Taking this product without enough liquid may cause choking. See choking warning.

Phenylketonurics – Phenylalanine is a component of aspartame. Each 2.5 mg Methylin Chewable Tablet contains 0.42 mg of phenylalanine; each 5.0 mg Methylin Chewable Tablet contains 0.84 mg of phenylalanine and each 10.0 mg Methylin Chewable Tablet contains 1.68 mg of phenylalanine.

Drug Interactions

Methylin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents.

Human pharmacologic studies have shown that Methylin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, diphenylhydantoin, primidone), phenylbutazone, and tricyclic drugs (imipramine, clomipramine, desipramine). Downward dosage adjustments of these drugs may be required when given concomitantly with Methylin.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a lifetime carcinogenicity study carried out in B6C3F1 mice, methylphenidate caused an increase in hepatocellular adenomas and, in males only, an increase in hepatoblastomas, at a daily dose of approximately 60 mg/kg/day. This dose is approximately 30 times and 2.5 times the maximum recommended human dose on a mg/kg and mg/m^2 basis, respectively. Hepatoblastoma is a relatively rare rodent malignant tumor type. There was no increase in total

malignant hepatic tumors. The mouse strain used is sensitive to the development of hepatic tumors, and the significance of these results to humans is unknown.

Methylphenidate did not cause any increase in tumors in a lifetime carcinogenicity study carried out in F344 rats; the highest dose used was approximately 45 mg/kg/day, which is approximately 22 times and 4 times the maximum recommended human dose on a mg/kg and mg/m^2 basis, respectively.

Methylphenidate was not mutagenic in the in vitro Ames reverse mutation assay or in the in vitro mouse lymphoma cell forward mutation assay. Sister chromatid exchanges and chromosome aberrations were increased, indicative of a weak clastogenic response, in an in vitro assay in cultured Chinese Hamster Ovary (CHO) cells. The genotoxic potential of methylphenidate has not been evaluated in an in vivo assay.

Usage in Pregnancy

Adequate animal reproduction studies to establish safe use of Methylin during pregnancy have not been conducted. However, in a recently conducted study, methylphenidate has been shown to have teratogenic effects in rabbits when given in doses of 200 mg/kg/day, which is approximately 167 times and 78 times the maximum recommended human dose on a mg/kg and a mg/m^2 basis, respectively. In rats, teratogenic effects were not seen when the drug was given in doses of 75 mg/kg/day, which is approximately 62.5 and 13.5 times the maximum recommended human dose on a mg/kg and a mg/m^2 basis, respectively. Therefore, until more information is available, methylphenidate should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

ADVERSE REACTIONS

Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include hypersensitivity (including skin rash, urticaria, fever, arthralgia, exfoliative dermatitis, erythema multiforme with histopathological findings of necrotizing vasculitis, and thrombocytopenic purpura); anorexia; nausea; dizziness; palpitations; headache; dyskinesia; drowsiness; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmia; abdominal pain; weight loss during prolonged therapy. There have been rare reports of Tourette's syndrome. Toxic psychosis has been reported. Although a definite causal relationship has not been established, the following have been reported in patients taking this drug: instances of abdominal liver function, ranging from transaminase elevation to hepatic coma; isolated cases of cerebral arteritis and/or occlusion; leukopenia and/or anemia; transient depressed mood; a few instances of scalp hair loss. Very rare reports of neuroleptic malignant syndrome (NMS) have been received, and, in most of these, patients were concurrently receiving therapies associated with NMS. In a single report, a ten year old boy who had been taking methylphenidate for approximately 18 months experienced an NMS-like event within 45 minutes of ingesting his first dose of venlafaxine. It is uncertain whether this case represented a drug-drug interaction, a response to either drug alone, or some other cause.

In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently; however, any of the other adverse reactions listed above may also occur.

OVERDOSAGE

Signs and symptoms of acute overdosage, resulting principally from overstimulation of the central nervous system and from excessive sympathomimetic effects, may include the following: vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac arrhythmias, hypertension, mydriasis, and dryness of mucous membranes.

Consult with a Certified Poison Control Center regarding treatment for up-to-date guidance and advice.

Treatment consists of appropriate supportive measures. The patient must be protected against self-injury and against external stimuli that would aggravate overstimulation already present. Gastric contents may be evacuated by gastric lavage. In the presence of severe intoxication, use a carefully titrated dosage of a *short-acting* barbiturate before performing gastric lavage. Other measures to detoxify the gut include administration of activated charcoal and a cathartic.

Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required for hyperpyrexia.

Efficacy of peritoneal dialysis or extracorporeal hemodialysis for methylphenidate overdosage has not been established.

DOSAGE AND ADMINISTRATION

Dosage should be individualized according to the needs and responses of the patient.

Directions – Take this product (child or adult dose) with at least 8 ounces (a full glass) of water or other fluid. Taking this product without enough liquid may cause choking. See choking warning.

Adults

Administer in divided doses 2 or 3 times daily, preferably 30 to 45 minutes before meals. Average dosage is 20 to 30 mg daily. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. Patients who are unable to sleep if medication is taken late in the day should take the last dose before 6 p.m.

Children (6 years and over)

Methylin should be initiated in small doses, with gradual weekly increments. Daily dosage above 60 mg is not recommended.

If improvement is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued.

Chewable Tablets: Start with 5 mg twice daily (before breakfast and lunch) with gradual increments of 5 to 10 mg weekly.

If paradoxical aggravation of symptoms or other adverse effects occur, reduce dosage, or, if necessary, discontinue the drug.

Methylin should be periodically discontinued to assess the child's condition. Improvement may be sustained when the drug is either temporarily or permanently discontinued.

Drug treatment should not and need not be indefinite and usually may be discontinued after puberty.

HOW SUPPLIED

Each Methylin™ Chewable Tablet 2.5 mg is available as a white to cream colored, grape flavored, rounded square tablet with a convex surface, debossed with a "2.5" and "CHEW" below it on one side, and a debossed 人 on the other side.

Bottles of 100…….NDC 59630-760-10

Each Methylin™ Chewable Tablet 5 mg is available as a white to cream colored, grape flavored, rounded square tablet with a convex surface, debossed with a "5" and "CHEW" below it on one side, and a debossed 人 on the other side.

Bottles of 100…….NDC 59630-761-10

Each Methylin™ Chewable Tablet 10 mg is available as a white to cream colored, grape flavored, scored rounded square tablet with a convex surface, debossed with a "10" and "CHEW" below it on one side, and a debossed 人 on the other side.

Bottles of 100…….NDC 59630-762-10

Protect from moisture. Dispense in tight container with child-resistant closure.

Storage: Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Methylin is a trademark of Mallinckrodt Inc.

Ritalin is a registered trademark of Novartis Corporation.

Manufactured for:
Shionogi Pharma, Inc.
Atlanta, GA 30328

Manufactured by:
Mallinckrodt Inc.
Hazelwood, MO 63042 USA

Rev 09/2010

MEDICATION GUIDE
Methylin™ Chewable Tablets
(methylphenidate HCl chewable tablets) 2.5 mg, 5 mg, and 10 mg

Read the Medication Guide that comes with Methylin Chewable Tablets before you or your child starts taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your doctor about your or your child's treatment with Methylin Chewable Tablets.

What is the most important information I should know about Methylin Chewable Tablets?

The following have been reported with use of methylphenidate HCl and other stimulant medicines.

1. Heart-related problems:

- **sudden death in patients who have heart problems or heart defects**
- **stroke and heart attack in adults**
- **increased blood pressure and heart rate**

Tell your doctor if you or your child have any heart problems, heart defects, high blood pressure, or a family history of these problems.

Your doctor should check you or your child carefully for heart problems before starting Methylin Chewable Tablets.

Your doctor should check you or your child's blood pressure and heart rate regularly during treatment with Methylin Chewable Tablets.

Call your doctor right away if you or your child has any signs of heart problems such as chest pain, shortness of breath, or fainting while taking Methylin Chewable Tablets.

2. Mental (Psychiatric) problems:

All Patients

- **new or worse behavior and thought problems**
- **new or worse bipolar illness**
- **new or worse aggressive behavior or hostility**

Children and Teenagers

- **new psychotic symptoms (such as hearing voices, believing things that are not true, are suspicious) or new manic symptoms**

Tell your doctor about any mental problems you or your child have, or about a family history of suicide, bipolar illness, or depression.

Call your doctor right away if you or your child have any new or worsening mental symptoms or problems while taking Methylin Chewable Tablets, especially seeing or hearing things that are not real, believing things that are not real, or are suspicious.

What Is Methylin Chewable Tablets?

Methylin Chewable Tablets is a central nervous system stimulant prescription medicine. Methylin Chewable Tablets are tablets that are made to be chewed and swallowed. **It is used for the treatment of attention deficit and hyperactivity disorder (ADHD).** Methylin Chewable Tablets may help increase attention and decrease impulsiveness and hyperactivity in patients with ADHD.

Methylin Chewable Tablets should be used as a part of a total treatment program for ADHD that may include counseling or other therapies.

Methylin Chewable Tablets is also used in the treatment of a sleep disorder called narcolepsy.

Methylin Chewable Tablets is a federally controlled substance (CII) because it can be abused or lead to dependence. Keep Methylin Chewable Tablets in a safe place to prevent misuse and abuse. Selling or giving away Methylin Chewable Tablets may harm others, and is against the law.

Tell your doctor if you or your child have (or have a family history of) ever abused or been dependent on alcohol, prescription medicines or street drugs.

Who should not take Methylin Chewable Tablets?

Methylin Chewable Tablets should not be taken if you or your child:

- are very anxious, tense, or agitated
- have an eye problem called glaucoma
- have tics or Tourette's syndrome, or a family history of Tourette's syndrome. Tics are hard to control repeated movements or sounds.
- are taking or have taken within the past 14 days an antidepression medicine called a monoamine oxidase inhibitor or MAOI.
- are allergic to anything in Methylin Chewable Tablets. See the end of this Medication Guide for a complete list of ingredients.

Methylin Chewable Tablets should not be used in children less than 6 years old because it has not been studied in this age group.

Methylin Chewable Tablets may not be right for you or your child. Before starting Methylin Chewable Tablets tell your or your child's doctor about all health conditions (or a family history of) including:

- heart problems, heart defects, high blood pressure
- mental problems including psychosis, mania, bipolar illness, or depression
- tics or Tourette's syndrome
- seizures or have had an abnormal brain wave test (EEG)

Tell your doctor if you or your child is pregnant, planning to become pregnant, or breastfeeding.

Can Methylin Chewable Tablets be taken with other medicines?

Tell your doctor about all of the medicines that you or your child take including prescription and nonprescription medicines, vitamins, and herbal supplements.

Methylin Chewable Tablets and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be adjusted while taking Methylin Chewable Tablets.

Your doctor will decide whether Methylin Chewable Tablets can be taken with other medicines.

Especially tell your doctor if you or your child takes:

- anti-depression medicines including MAOIs
- seizure medicines
- blood thinner medicines
- blood pressure medicines
- cold or allergy medicines that contain decongestants

Know the medicines that you or your child takes. Keep a list of your medicines with you to show your doctor and pharmacist.

Do not start any new medicine while taking Methylin Chewable Tablets without talking to your doctor first.

How should Methylin Chewable Tablets be taken?

- **Take Methylin Chewable Tablets exactly as prescribed.** Your doctor may adjust the dose until it is right for you or your child.
- Methylin Chewable Tablets are usually taken 2 to 3 times a day.
- Take Methylin Chewable Tablets 30 to 45 minutes before a meal.
- **Chew Methylin Chewable Tablets well and swallow with at least 8 ounces (a full glass) of water or other liquid. Methylin Chewable Tablets can swell and cause choking if enough liquid is not taken with them. Get emergency medical care if you have chest pain, vomiting, or trouble swallowing, or breathing after taking a Methylin Chewable Tablet.**
- From time to time, your doctor may stop Methylin Chewable Tablets treatment for awhile to check ADHD symptoms.
- Your doctor may do regular checks of the blood, heart, and blood pressure while taking Methylin Chewable Tablets. Children should have their height and weight checked often while taking Methylin Chewable Tablets. Methylin Chewable Tablets treatment may be stopped if a problem is found during these check-ups.
- **If you or your child takes too much Methylin Chewable Tablets or overdoses, call your doctor or poison control center right away, or get emergency treatment.**

What are possible side effects of Methylin Chewable Tablets?

See **"What is the most important information I should know about Methylin Chewable Tablets?"** for information on reported heart and mental problems.

Other serious side effects include:

- slowing of growth (height and weight) in children
- seizures, mainly in patients with a history of seizures
- eyesight changes or blurred vision

Common side effects include:

- nervousness
- trouble sleeping
- headache
- stomach ache
- fast heart beat
- nausea
- decreased appetite
- dizziness
- weight loss

Talk to your doctor if you or your child has side effects that are bothersome or do not go away.

This is not a complete list of possible side effects. Ask your doctor or pharmacist for more information.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Methylin Chewable Tablets?

- Store Methylin Chewable Tablets in a safe place at room temperature, 68° to 77°F (20° to 25°C). Protect from moisture.
- **Keep Methylin Chewable Tablets and all medicines out of the reach of children.**

General information about Methylin Chewable Tablets

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Methylin Chewable Tablets for a condition for which it was not prescribed. Do not give Methylin Chewable Tablets to other people, even if they have the same condition. It may harm them and it is against the law.

This Medication Guide summarizes the most important information about Methylin Chewable Tablets. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about Methylin Chewable Tablets that was written for healthcare professionals. For more information, please contact Shionogi Pharma, Inc. at 1-800-849-9707 or visit the website at www.methylinrx.com.

What are the ingredients in Methylin Chewable Tablets?

CAUTION PHENYLKETONURICS: Methylin Chewable Tablets contain phenylalanine.

Active Ingredient: methylphenidate HCl

Inactive Ingredients: aspartame, maltose, microcrystalline cellulose, guar gum, grape flavor, pregelatinized starch, and stearic acid.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured for:
Shionogi Pharma, Inc.
Atlanta, GA 30328

Manufactured by:
Mallinckrodt Inc.
Hazelwood, MO 63042 USA

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