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**Ritalin (and other methylphenidate preparations)**

## Pharmacology

### Mechanism of Action

Unknown; may block reuptake of norepinephrine and dopamine into presynaptic neurons; may stimulate CNS similar to amphetamines; may stimulate cerebral cortex and subcortical structures

### Absorption

Bioavailability: ~30%; large individual differences (11-52%)

Duration: 3-6 hr (IR); 3-8 hr (ER, SR); 8-12 hr (CD, LA, Concerta)

Peak plasma time: 6-8 hr (PO); 7.5-10.5 hr; (patch)

Peak plasma concentration: 3.7 ng/mL (PO); 0-114 ng/mL (patch)

Onset of action

* Immediate release: ~2hr
* Sustained-release tablet: 4-7 hr
* Extended-release tablet (Concerta): 1-2 hr
* Transdermal: ~2 hr; applied heat may expedite onset

### Distribution

Protein bound: 10-33%

VD: d-Methylphenidate (2.65 L/kg); l-methylphenidate (1.80 L/kg)

### Metabolism

Metabolized mostly to a-phenyl-2-piperidine acetic acid (PPAA)

### Elimination

Excretion: Urine (90%), mainly as PPAA

Half-life elimination

* d-Methylphenidate: 3-4 hr
* l-Methylphenidate: 1-3 hr

### Pharmacogenomics

Preliminary (and sometimes conflicting) reports have investigated whether genotypes change pharmacologic response to methylphenidate

Genes studied to determine their role in methylphenidate response include the following: SLC6A3/DAT1, DRD4, ADRA2A, and COMPT

Indications

### Attention Deficit Hyperactivity Disorder

Metadate CD: Initial, 20 mg PO qAM before breakfast; may increase in 10- to 20-mg increments, not to exceed 60 mg/day

Ritalin LA: Initial, 20 mg PO qAM; may adjust dose in weekly 10-mg increments, not to exceed 60 mg/day (patients requiring a lower initial dose may begin with 10 mg)

Concerta: Initial, 18-36 mg PO qDay; may increase by 18-mg increments at weekly intervals; maintenance dose is 18-72 mg/day

Metadate ER, Methylin ER, and Ritalin SR: Duration of action is approximately 8 hr; may use in place of methylphenidate IR tablets when 8-hr dosage of methylphenidate ER and SR tablets corresponds to the titrated 8-hour dosage of methylphenidate IR; not to exceed 60 mg/day

Methylin, Ritalin (immediate-release tablets, chewable tablets, and oral solution): 20-30 mg/day PO divided q8-12hr, 30-45 minutes before meals; may gradually increase dose at weekly intervals; some patients may require 40-60 mg/day; in others, 10-15 mg/day may be adequate

Aptensio XR: 10 mg PO qDay in AM; may increase weekly by 10-mg increments; not to exceed 60 mg/day

QuilliChew ER (chewable extended-release tablets): 20 mg PO qAM initially; may be titrated up or down weekly in increments of 10 mg, 15 mg or 20 mg, not to exceed 60 mg/day

### Narcolepsy

Methylin, Ritalin (immediate-release tablets, chewable tablets, and oral solution): 20-30 mg/day PO divided q8-12hr, 30-45 minutes before meals; some patients may require 40-60 mg/day; in others, 10-15 mg/day may be adequate

Metadate ER, Methylin ER, and Ritalin SR: Duration of action is approximately 8 hr; may use in place of methylphenidate IR tablets when 8-hr dosage of methylphenidate ER and SR tablets corresponds to the titrated 8-hr dosage of methylphenidate IR

### ADVERSE REACTIONS

Headache

Hypertension

Nausea

Nervousness

Toxic psychosis

Seizures

Tachycardia

Angina

Cardiac arrhythmia

Cerebral occlusion

Increased/decreased pulse

Cerebral arteritis

Cerebral hemorrhage

Raynaud's phenomenom

Vasculitis

Anxiety

Anger

Agitation

Irritability

Vertigo

Fatigue

Erythema multiform

Hyperhidrosis

Rash

Urticaria

Exfoliative dermatitis

Dysmenorrhea

Constipation

Xerostomia

Vomiting

Weight loss

Erectile dysfunction

Muscle tightness

Paresthesia

Blurred vision

Necrotizing vasculitis

Increased cough

Dyspnea

Sinusitis

Upper respiratory tract infection

## Warnings

### Black Box Warnings

Chronic abuse can lead to a marked tolerance and psychological dependence, with varying degrees of abnormal behavior

Frank psychotic episodes can occur, especially with parenteral abuse

Withdrawal from abusive use may result in depression

Give cautiously to patients with a history of drug dependence or alcoholism

Potential for drug dependency; withdrawal following chronic therapeutic use may unmask symptoms of the underlying disorder that may require follow-up

### Contraindications

Hypersensitivity

Glaucoma

Family history of Tourette's syndrome, motor tics

Marked anxiety, tension, agitation

Within 2 weeks of taking MAOIs: Risk of severe hypertensive reaction

Metadate CD and Metadate ER

* Heart failure, severe hypertension, arrhythmia, hyperthyroidism, recent MI or angina concomitant use of halogenated anesthetics

### Cautions

Use caution in hypertension

Stimulants used to treat ADHD are associated with serious cardiovascular events including sudden death, stroke, and MI; avoid in patients with structural cardiac abnormalities or other serious heart problems

Stimulants used to treat ADHD are associated with peripheral vasculopathy, including Raynaud phenomenon; may improve with dose reduction or discontinuation

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

Sudden deaths, stroke, and myocardial infarction reported in patients with structural cardiac abnormalities or other serious heart problems taking stimulants at usual doses

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

Particular care should be taken in using stimulants to treat ADHD patients with comorbid bipolar disorder because of concern for possible induction of mixed/manic episode in such patients

Aggressive behavior or hostility is often observed in children and adolescents with ADHD; monitor for the appearance of or worsening of aggressive behavior or hostility

Monitor growth during treatment of children with stimulants; may need to interrupt therapy in patients not growing or gaining weight as expected

Stimulants may lower convulsive threshold in patients with prior history of seizure, patients with prior EEG abnormalities in absence of seizures, and very rarely, patients without a history of seizures and no prior EEG evidence of seizures; discontinue therapy in the presence of seizures

Use with caution in patients who use other sympathomimetic drugs

Amphetamines may exacerbate motor and phonic tics and Tourette’s syndrome; perform clinical evaluation for tics and Tourette’s syndrome in children and their families prior to treating with stimulant medications

Rare instances of prolonged and sometimes painful erections (priapism), sometimes requiring surgical intervention, reported with methylphenidate products; typically not reported during initiation, but often subsequent to an increase in dose; seek immediate medical attention for abnormally sustained or frequent and painful erections

Carefully supervise during withdrawal

Possibility of tolerance, psychologic dependence, and strange behavior

Monitor blood pressure and pulse; consider benefits and risks in patients for whom increase in blood pressure or heart rate would be problem

CNS stimulants may cause psychotic or manic symptoms in patients with no prior history, or exacerbation of symptoms in patients with pre-existing psychiatric illness; evaluate for bipolar disorder prior to initiating therapy

Do not use Concerta with pre-existing severe gastrointestinal narrowing conditions, including esophageal motility disorders, cystic fibrosis, history of peritonitis, small bowel disease, or chronic intestinal pseudo-obstruction, or Meckel's diverticulum

Transdermal patch

* Chemical leukoderma (permanent loss of skin pigmentation) may occur at and around application site; loss of pigmentation, in some cases, has been reported at other sites distant from the application site; patients or their caregivers should watch for new areas of lighter skin, especially under the drug patch, and immediately report these changes to their health care professional; discontinue therapy if it occurs
* Acts faster on inflamed skin
* Use of transdermal methylphenidate may lead to contact sensitization; discontinue treatment if contact sensitization is suspected; erythema is commonly seen with use of transdermal methylphenidate and is not by itself an indication of sensitization; suspect sensitization if erythema is accompanied by evidence of a more intense local reaction, like edema, papules, and vesicles and do not significantly improve within 48 hr or spreads beyond patch site
* Avoid exposing application site to direct external heat sources; heat applied after patch application, increases both the rate and extent of absorption
* Perform periodic CBC, differential, and platelet counts during prolonged therapy

PREGNANCY AND LACTATION:

Pregnancy category: C

Lactation: Unknown; avoid during breastfeeding; use caution

**Patient Education
methylphenidate oral**

IMPORTANT: HOW TO USE THIS INFORMATION: This is a summary and does NOT have all possible information about this product. This information does not assure that this product is safe, effective, or appropriate for you. This information is not individual medical advice and does not substitute for the advice of your health care professional. Always ask your health care professional for complete information about this product and your specific health needs.

METHYLPHENIDATE - ORAL

(METH-il-FEN-i-date)

COMMON BRAND NAME(S): Ritalin

WARNING: Misuse or abuse of methylphenidate can result in serious (possibly fatal) heart and blood pressure problems.

This medication can be habit-forming and should be used cautiously by people who have mental/mood disorders or a history of alcohol/drug abuse. Before taking this medication, tell your doctor if you have abused or been dependent on drugs or alcohol. Do not increase your dose, take it more often, or take it for a longer time or in a different way than prescribed. Doing so may result in a decrease in the effect of this drug, drug dependence, or abnormal thoughts/behavior.

Your doctor may monitor you for a while after the medication is stopped, especially if you have taken this drug for a long time or in high doses. (See also How to Use section.)

USES: This medication is used to treat attention deficit hyperactivity disorder - ADHD. It works by changing the amounts of certain natural substances in the brain. Methylphenidate belongs to a class of drugs known as stimulants. It can help increase your ability to pay attention, stay focused on an activity, and control behavior problems. It may also help you to organize your tasks and improve listening skills.

This medication is also used to treat a certain sleep disorder (narcolepsy).

HOW TO USE: Read the Medication Guide provided by your pharmacist before you start taking methylphenidate and each time you get a refill. If you have any questions, ask your doctor or pharmacist.

Take this medication by mouth as directed by your doctor, usually 2 or 3 times a day. This medication is best taken 30 to 45 minutes before a meal. However, if you have stomach upset, you may take this medication with or after a meal or snack. Taking this medication late in the day may cause trouble sleeping (insomnia).

Take this medication regularly to get the most benefit from it. To help you remember, take it at the same times each day.

The dosage is based on your medical condition and response to treatment. Your doctor may direct you to gradually increase or decrease your dose. Also, if you have used it for a long time, do not suddenly stop using this drug without consulting your doctor.

This medication may cause withdrawal reactions, especially if it has been used regularly for a long time or in high doses. In such cases, withdrawal symptoms (such as depression, suicidal thoughts, or other mental/mood changes) may occur if you suddenly stop using this medication. To prevent withdrawal reactions, your doctor may reduce your dose gradually. Consult your doctor or pharmacist for more details, and report any withdrawal reactions right away.

When used for a long time, this medication may not work as well. Talk with your doctor if this medication stops working well.

Along with its benefits, this medication may rarely cause abnormal drug-seeking behavior (addiction). This risk may be increased if you have abused alcohol or drugs in the past. Take this medication exactly as prescribed to lessen the risk of addiction.

Tell your doctor if your condition does not improve or if it worsens.

SIDE EFFECTS: Nervousness, trouble sleeping, loss of appetite, weight loss, dizziness, nausea, vomiting, or headache may occur. If any of these effects persist or worsen, tell your doctor or pharmacist promptly.

Remember that your doctor has prescribed this medication because he or she has judged that the benefit to you is greater than the risk of side effects. Many people using this medication do not have serious side effects.

This medication may raise your blood pressure. Check your blood pressure regularly and tell your doctor if the results are high.

Tell your doctor right away if you have any serious side effects, including: signs of blood flow problems in the fingers or toes (such as coldness, numbness, pain, or skin color changes), unusual wounds on the fingers or toes, fast/pounding/irregular heartbeat, mental/mood/behavior changes (such as agitation, aggression, mood swings, abnormal thoughts, thoughts of suicide), uncontrolled muscle movements (such as twitching, shaking), sudden outbursts of words/sounds that are hard to control, vision changes (such as blurred vision).

Get medical help right away if you have any very serious side effects, including: fainting, seizure, symptoms of a heart attack (such as chest/jaw/left arm pain, shortness of breath, unusual sweating), symptoms of a stroke (such as weakness on one side of the body, slurred speech, sudden vision changes, confusion).

Rarely, males (including young boys and teens) may have a painful or prolonged erection lasting 4 or more hours while using this medication. Caregivers/parents should also be watchful for this serious side effect in boys. If a painful or prolonged erection occurs, stop using this drug and get medical help right away, or permanent problems could occur. Ask your doctor or pharmacist for more details.

A very serious allergic reaction to this drug is rare. However, get medical help right away if you notice any symptoms of a serious allergic reaction, including: rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.

This is not a complete list of possible side effects. If you notice other effects not listed above, contact your doctor or pharmacist.

In the US -

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or at www.fda.gov/medwatch.

In Canada - Call your doctor for medical advice about side effects. You may report side effects to Health Canada at 1-866-234-2345.

PRECAUTIONS: Before taking methylphenidate, tell your doctor or pharmacist if you are allergic to it; or to dexmethylphenidate; or if you have any other allergies. This product may contain inactive ingredients, which can cause allergic reactions or other problems. Talk to your pharmacist for more details.

Before using this medication, tell your doctor or pharmacist your medical history, especially of: high blood pressure, blood circulation problems (such as Raynaud's disease), glaucoma, heart problems (such as irregular heartbeat, heart failure, previous heart attack, problems with heart structure), family history of heart problems (such as sudden cardiac death, irregular heartbeat), mental/mood conditions (especially anxiety, tension, agitation), personal/family history of mental/mood disorders (such as bipolar disorder, depression, psychosis, suicidal thoughts), personal/family history of uncontrolled muscle movements (motor tics, Tourette's syndrome), overactive thyroid (hyperthyroidism), seizure disorder.

This drug may make you dizzy. Do not drive, use machinery, or do any activity that requires alertness until you are sure you can perform such activities safely. Limit alcoholic beverages.

Before having surgery, tell your doctor or dentist about all the products you use (including prescription drugs, nonprescription drugs, and herbal products).

If used for a long time, this drug may affect a child's growth rate, weight, and final adult height. To reduce the risk, the doctor may recommend briefly stopping the medication from time to time. Check the child's weight and height regularly, and consult your doctor or pharmacist for more details.

Older adults may be more sensitive to the side effects of this drug, especially trouble sleeping, weight loss, or chest pain.

During pregnancy, methylphenidate should be used only when clearly needed. Discuss the risks and benefits with your doctor.

This medication passes into breast milk. Consult your doctor before breast-feeding.

DRUG INTERACTIONS: Drug interactions may change how your medications work or increase your risk for serious side effects. This document does not contain all possible drug interactions. Keep a list of all the products you use (including prescription/nonprescription drugs and herbal products) and share it with your doctor and pharmacist. Do not start, stop, or change the dosage of any medicines without your doctor's approval.

Taking MAO inhibitors with this medication may cause a serious (possibly fatal) drug interaction. Avoid taking MAO inhibitors (isocarboxazid, linezolid, methylene blue, moclobemide, phenelzine, procarbazine, rasagiline, selegiline, tranylcypromine) during treatment with this medication. Most MAO inhibitors should also not be taken for two weeks before treatment with this medication. Ask your doctor when to start or stop taking this medication.

Methylphenidate is very similar to dexmethylphenidate. Do not use medications containing dexmethylphenidate while using methylphenidate.

This medication may interfere with certain medical/laboratory tests (including brain scan for Parkinson's disease), possibly causing false test results. Make sure laboratory personnel and all your doctors know you use this drug.

OVERDOSE: If someone has overdosed and has serious symptoms such as passing out or trouble breathing, call 911. Otherwise, call a poison control center right away. US residents can call their local poison control center at 1-800-222-1222. Canada residents can call a provincial poison control center. Symptoms of overdose may include: vomiting, agitation, confusion, sweating, flushing, muscle twitching, hallucinations, seizures, loss of consciousness.