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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use COTEMPLA XR-ODT safely and effectively. See full prescribing information for COTEMPLA XR-ODT.

COTEMPLA XR-ODT (methylphenidate extended-release orally disintegrating tablets), CII
Initial U.S. Approval: 1955

WARNING: ABUSE, MISUSE, AND ADDICTION

See full prescribing information for complete boxed warning.

COTEMPLA XR-ODT has a high potential for abuse and misuse, which can lead to the development of a substance use disorder, including addiction. Misuse and abuse of CNS stimulants, including COTEMPLA XR-ODT, can result in overdose and death (5.1, 9.2, 10):

- **Before prescribing COTEMPLA XR-ODT, assess each patient's risk for abuse, misuse, and addiction.**
- **Educate patients and their families about these risks, proper storage of the drug, and proper disposal of any unused drug.**
- **Throughout treatment, reassess each patient's risk and frequently monitor for signs and symptoms of abuse, misuse, and addiction.**

---------- RECENT MAJOR CHANGES ----------

Boxed Warning	10/2023
Dosage and Administration (2.1, 2.2, 2.3)	10/2023
Warnings and Precautions (5.1, 5.2, 5.8, 5.9, 5.10)	10/2023

---------- INDICATIONS AND USAGE ----------

COTEMPLA XR-ODT is a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 17 years of age. (1)

---------- DOSAGE AND ADMINISTRATION ----------

- Recommended starting dose for pediatric patients 6 to 17 years of age is 17.3 mg given orally once daily in the morning. Dosage may be increased weekly in increments of 8.6 mg to 17.3 mg per day. Daily dosage above 51.8 mg is not recommended. (2.2)
- Patients are advised to take COTEMPLA XR-ODT consistently either with food or without food. (2.2)

---------- DOSAGE FORMS AND STRENGTHS ----------

Extended-release orally disintegrating tablets: 8.6 mg, 17.3 mg, 25.9 mg (3)

---------- CONTRAINDICATIONS ----------

- Known hypersensitivity to methylphenidate or product components. (4)
- Concurrent treatment with a monoamine oxidase inhibitor (MAOI), or use of an MAOI within the preceding 14 days. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- *Risks to Patients with Serious Cardiac Disease:* Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmias, coronary artery disease, or other serious cardiac disease. (5.2)
- *Increased Blood Pressure and Heart Rate:* Monitor blood pressure and pulse. (5.3)
- *Psychiatric Adverse Reactions:* Prior to initiating COTEMPLA XR-ODT, screen patients for risk factors for developing a manic episode. If new psychotic or manic symptoms occur, consider discontinuing COTEMPLA XR-ODT. (5.4)
- *Priapism:* If abnormally sustained or frequent and painful erections occur, patient should seek immediate medical attention. (5.5)
- *Peripheral Vasculopathy, including Raynaud's Phenomenon:* Careful observation for digital changes is necessary during COTEMPLA XR-ODT treatment. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for patients who develop signs or symptoms of peripheral vasculopathy. (5.6)
- *Long-term Suppression of Growth in Pediatric Patients:* Closely monitor growth (height and weight) in pediatric patients. Pediatric patients not growing or gaining height or weight as expected may need to have their treatment interrupted. (5.7)
- *Acute Angle Closure Glaucoma:* COTEMPLA XR-ODT-treated patients considered at risk for acute angle closure glaucoma (e.g., patients with significant hyperopia) should be evaluated by an ophthalmologist. (5.8)
- *Increased Intraocular Pressure (IOP) and Glaucoma:* Prescribe COTEMPLA XR-ODT to patients with open-angle glaucoma or abnormally increased IOP only if the benefit of treatment is considered to outweigh the risk. Closely monitor patients with a history of increased IOP or open angle glaucoma. (5.9)
- *Motor and Verbal Tics and Worsening of Tourette's Syndrome:* Before initiating COTEMPLA XR-ODT, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor patients for the emergence or worsening of tics or Tourette's syndrome. Discontinue treatment if clinically appropriate. (5.10)

---------- ADVERSE REACTIONS ----------

Based on accumulated data from other methylphenidate products, the most common (>5% and twice the rate of placebo) adverse reactions are appetite decreased, insomnia, nausea, vomiting, dyspepsia, abdominal pain, weight decreased, anxiety, dizziness, irritability, affect lability, tachycardia, and blood pressure increased. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Neos Therapeutics, Inc. at 1-888-319-1789 or http://www.COTEMPLAXRODT.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

- Antihypertensive Drugs: Monitor blood pressure. Adjust dosage of antihypertensive drug as needed. (7)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 10/2023

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FULL PRESCRIBING INFORMATION

WARNING: ABUSE, MISUSE, AND ADDICTION

COTEMPLA XR-ODT has a high potential for abuse and misuse, which can lead to the development of a substance use disorder, including addiction. Misuse and abuse of CNS stimulants, including COTEMPLA XR-ODT, can result in overdose and death [*see Overdosage (10)*], and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.

Before prescribing COTEMPLA XR-ODT, assess each patient's risk for abuse, misuse, and addiction. Educate patients and their families about these risks, proper storage of the drug, and proper disposal of any unused drug. Throughout COTEMPLA XR-ODT treatment, reassess each patient's risk of abuse, misuse, and addiction and frequently monitor for signs and symptoms of abuse, misuse, and addiction [*see Warnings and Precautions (5.1) and Drug Abuse and Dependence (9.2)*].

1 INDICATIONS AND USAGE

COTEMPLA XR-ODT is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients 6 to 17 years of age *[see Clinical Studies (14)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Pretreatment Screening

Prior to treating patients with COTEMPLA XR-ODT, assess:

- for the presence of cardiac disease (i.e., perform a careful history, family history of sudden death or ventricular arrhythmia, and physical exam) *[see Warnings and Precautions (5.2)]*.
- the family history and clinically evaluate patients for motor or verbal tics or Tourette's syndrome before initiating COTEMPLA XR-ODT *[see Warnings and Precautions (5.10)].*

2.2 General Dosing Information

COTEMPLA XR-ODT is given orally once daily in the morning.

Advise patients to take COTEMPLA XR-ODT consistently either with food or without food *[see Clinical Pharmacology (12.3)]*.

The recommended starting dose of COTEMPLA XR-ODT for patients 6 to 17 years of age is 17.3 mg once daily in the morning. The dose may be titrated weekly in increments of 8.6 mg to 17.3 mg. Daily doses above 51.8 mg have not been studied and are not recommended.

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

2.3 Dosage Reduction and Discontinuation

If paradoxical aggravation of symptoms or other adverse reactions occur, reduce dosage, or, if necessary, discontinue COTEMPLA XR-ODT. If improvement is not observed after appropriate dosage adjustment over a one-month period, discontinue COTEMPLA XR-ODT.

2.4 COTEMPLA XR-ODT Administration

Instruct the patient or caregiver on the following administration instructions:

- Do not remove the tablet from the blister pack until just prior to dosing. Take the tablet immediately after opening the blister pack. Do not store the tablet for future use.
- Use dry hands when opening the blister pack.
- Remove the tablet by peeling back the foil on the blister pack. Do not push the tablet through the foil.
- As soon as the blister is opened, remove the tablet and place on the patient's tongue.
- Place the whole tablet on the tongue and allow it to disintegrate without chewing or crushing.
- The tablet will disintegrate in saliva so that it can be swallowed. No liquid is needed to take the tablet.

3 DOSAGE FORMS AND STRENGTHS

- 8.6 mg Extended-Release Orally Disintegrating Tablet: round, purple to light purple mottled (debossed "T1" on one side and plain on the other)
- 17.3 mg Extended-Release Orally Disintegrating Tablet: round, purple to light purple mottled (debossed "T2" on one side and plain on the other)
- 25.9 mg Extended-Release Orally Disintegrating Tablet: round, purple to light purple mottled (debossed "T3" on one side and plain on the other)

4 CONTRAINDICATIONS

COTEMPLA XR-ODT is contraindicated in patients with:

- Known hypersensitivity to methylphenidate or other components of COTEMPLA XR-ODT. Hypersensitivity reactions such as angioedema and anaphylactic reactions have been reported in patients treated with methylphenidate products *[see Adverse Reactions (6.2)]*.
- Concomitant treatment with monoamine oxidase inhibitors (MAOIs), and also within a minimum of 14 days following discontinuation of treatment with a monoamine oxidase inhibitor because of the risk of hypertensive crisis *[see Drug Interactions (7.1)]*.

5 WARNINGS AND PRECAUTIONS

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5.1 Abuse, Misuse, and Addiction

COTEMPLA XR-ODT has a high potential for abuse and misuse. The use of COTEMPLA XR-ODT exposes individuals to the risks of abuse and misuse, which can lead to the development of a substance use disorder, including addiction. COTEMPLA XR-ODT can be diverted for non-medical use into illicit channels or distribution [*see Drug Abuse and Dependence (9.2)*]. Misuse and abuse of CNS stimulants, including COTEMPLA XR-ODT, can result in overdose and death [*see Overdosage (10)*], and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.

Before prescribing COTEMPLA XR-ODT, assess each patient's risk for abuse, misuse, and addiction. Educate patients and their families about these risks and proper disposal of any unused drug. Advise patients to store COTEMPLA XR-ODT in a safe place, preferably locked, and instruct patients to not give COTEMPLA XR-ODT to anyone else. Throughout COTEMPLA XR-ODT treatment, reassess each patient's risk of abuse, misuse, and addiction and frequently monitor for signs and symptoms of abuse, misuse, and addiction.

5.2 Risks to Patients with Serious Cardiac Disease

Sudden death has occurred in patients with structural cardiac abnormalities or other serious cardiac disease who were treated with CNS stimulants at the recommended ADHD dosages.

Avoid COTEMPLA XR-ODT use in patients with known structural cardiac abnormalities, cardiomyopathy, serious cardiac arrhythmia, coronary artery disease, or other serious cardiac disease.

5.3 Increased Blood Pressure and Heart Rate

CNS stimulants cause an increase in blood pressure (mean increase approximately 2 to 4 mm Hg) and heart rate (mean increase approximately 3 to 6 bpm). Some patients may have larger increases.

Monitor all COTEMPLA XR-ODT-treated patients for hypertension and tachycardia.

5.4 Psychiatric Adverse Reactions

Exacerbation of Pre-Existing Psychosis

CNS stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder.

Induction of a Manic Episode in Patients with Bipolar Disorder

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CNS stimulants may induce a manic or mixed episode in patients. Prior to initiating COTEMPLA XR-ODT treatment, screen patients for risk factors for developing a manic episode (e.g., comorbid or history of depressive symptoms or a family history of suicide, bipolar disorder, or depression).

New Psychotic or Manic Symptoms

CNS stimulants, at the recommended dosage, may cause psychotic or manic symptoms (e.g., hallucinations, delusional thinking or mania) in patients without a prior history of psychotic illness or mania. In a pooled analysis of multiple short-term, placebo-controlled studies of CNS stimulants, psychotic or manic symptoms occurred in approximately 0.1% of CNS stimulant-treated patients, compared to 0% of placebo-treated patients. If such symptoms occur, consider discontinuing COTEMPLA XR-ODT.

5.5 Priapism

Prolonged and painful erections, sometimes requiring surgical intervention, have been reported with methylphenidate use in both adult and pediatric male patients. Although priapism was not reported with methylphenidate initiation, it developed after some time on methylphenidate, often subsequent to an increase in dosage. Priapism also occurred during methylphenidate withdrawal (drug holidays or during discontinuation).

COTEMPLA XR-ODT-treated patients who develop abnormally sustained or frequent and painful erections should seek immediate medical attention.

5.6 Peripheral Vasculopathy, including Raynaud's Phenomenon

CNS stimulants, including COTEMPLA XR-ODT, used to treat ADHD are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; however, sequelae have included digital ulceration and/or soft tissue breakdown. Effects of peripheral vasculopathy, including Raynaud's phenomenon, were observed in post-marketing reports and at the therapeutic dosages of CNS stimulants in all age groups throughout the course of treatment. Signs and symptoms generally improved after dosage reduction or discontinuation of the CNS stimulant.

Careful observation for digital changes is necessary during COTEMPLA XR-ODT treatment. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for COTEMPLA XR-ODT-treated patients who develop signs or symptoms of peripheral vasculopathy.

5.7 Long-Term Suppression of Growth in Pediatric Patients

CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients.

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Careful follow-up of weight and height in pediatric patients ages 7 to 10 years who were randomized to either methylphenidate or nonmedication-treatment groups over 14 months, as well as in naturalistic subgroups of newly methylphenidate-treated and nonmedication-treated pediatric patients over 36 months (to the ages of 10 to 13 years), suggests that pediatric patients who received methylphenidate for 7 days per week throughout the year had 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 development period.

Closely monitor growth (weight and height) in COTEMPLA XR-ODT-treated pediatric patients. Pediatric patients who are not growing or gaining height or weight as expected may need to have their treatment interrupted.

5.8 Acute Angle Closure Glaucoma

There have been reports of angle closure glaucoma associated with methylphenidate treatment.

Although the mechanism is not clear, COTEMPLA XR-ODT-treated patients considered at risk for acute angle closure glaucoma (e.g., patients with significant hyperopia) should be evaluated by an ophthalmologist.

5.9 Increased Intraocular Pressure and Glaucoma

There have been reports of an elevation of intraocular pressure (IOP) associated with methylphenidate treatment *[see Adverse Reactions (6.2)]*.

Prescribe COTEMPLA XR-ODT to patients with open-angle glaucoma or abnormally increased IOP only if the benefit of treatment is considered to outweigh the risk. Closely monitor COTEMPLA XR-ODT-treated patients with a history of abnormally increased IOP or open angle glaucoma.

5.10 Motor and Verbal Tics, and Worsening of Tourette's Syndrome

CNS stimulants, including methylphenidate, have been associated with the onset or exacerbation of motor and verbal tics. Worsening of Tourette's syndrome has also been reported *[see Adverse Reactions (6.2)]*.

Before initiating COTEMPLA XR-ODT, assess the family history and clinically evaluate patients for tics or Tourette's syndrome. Regularly monitor COTEMPLA XR-ODT-treated patients for the emergence or worsening of tics or Tourette's syndrome, and discontinue treatment if clinically appropriate.

6 ADVERSE REACTIONS

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The following are discussed in more detail in other sections of the labeling:

- Known hypersensitivity to methylphenidate or other ingredients of Cotempla XR-ODT *[see Contraindications (4)]*
- Hypertensive crisis when used concomitantly with monoamine oxidase inhibitors *[see Contraindications (4) and Drug Interactions (7.1)]*
- Abuse, Misuse, and Addiction *[see Boxed Warning, Warnings and Precautions (5.1), and Drug Abuse and Dependence (9.2, 9.3)]*
- Risks to patients with serious cardiac disease *[see Warnings and Precautions (5.2)]*
- Increased blood pressure and heart rate *[see Warnings and Precautions (5.3)]*
- Psychiatric adverse reactions *[see Warnings and Precautions (5.4)]*
- Priapism *[see Warnings and Precautions (5.5)]*
- Peripheral vasculopathy, including Raynaud's phenomenon *[see Warnings and Precautions (5.6)]*
- Long-term suppression of growth in pediatric patients *[see Warnings and Precautions (5.7)]*
- Acute Angle Closure Glaucoma *[see Warnings and Precautions (5.8)]*
- Increased Intraocular Pressure and Glaucoma *[see Warnings and Precautions (5.9)]*
- Motor and Verbal Tics, and Worsening of Tourette's Syndrome *[see Warnings and Precautions (5.10)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the 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.

Adverse Reactions in Studies with Other Methylphenidate Products in Children, Adolescents, and Adults with ADHD

Commonly reported (≥2% of the methylphenidate group and at least twice the rate of the placebo group) adverse reactions from placebo-controlled trials of methylphenidate products include: appetite decreased, weight decreased, nausea, abdominal pain, dyspepsia, dry mouth, vomiting, insomnia, anxiety, nervousness, restlessness, affect lability, agitation, irritability, dizziness, vertigo, tremor, blurred vision, blood pressure increased, heart rate increased, tachycardia, palpitations, hyperhidrosis, and pyrexia.

Adverse Reactions in Studies with COTEMPLA XR-ODT in Children with ADHD

There is limited experience with COTEMPLA XR-ODT in controlled trials. Based on this limited experience, the adverse reaction profile of COTEMPLA XR-ODT appears similar to other methylphenidate extended release-products.

6.2 Postmarketing Experience

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The following adverse reactions have been identified during post approval use of methylphenidate products. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure. These adverse reactions are as follows:

Blood and Lymphatic System Disorders: Pancytopenia, Thrombocytopenia, Thrombocytopenic purpura
Cardiac Disorders: Angina pectoris, Bradycardia, Extrasystole, Supraventricular tachycardia, Ventricular extrasystole
Eye Disorders: Diplopia, Increased intraocular pressure, Mydriasis, Visual impairment
General Disorders: Chest pain, Chest discomfort, Hyperpyrexia
Immune System Disorders: Hypersensitivity reactions such as Angioedema, Anaphylactic reactions, Auricular swelling, Bullous conditions, Exfoliative conditions, Urticarias, Pruritis NEC, Rashes, Eruptions, and Exanthemas NEC
Investigations: Alkaline phosphatase increased, Bilirubin increased, Hepatic enzyme increased, Platelet count decreased, White blood cell count abnormal
Musculoskeletal, Connective Tissue and Bone Disorders: Arthralgia, Myalgia, Muscle twitching, Rhabdomyolysis
Nervous System Disorders: Convulsion, Grand mal convulsion, Dyskinesia, Serotonin syndrome in combination with serotonergic drugs, Motor and Verbal Tics
Psychiatric Disorders: Disorientation, Hallucination, Hallucination auditory, Hallucination visual, Libido changes, Mania
Urogenital System: Priapism
Skin and Subcutaneous Tissue Disorders: Alopecia, Erythema
Vascular Disorders: Raynaud's phenomenon

7 DRUG INTERACTIONS

7.1 Clinically Important Interactions with COTEMPLA XR-ODT

Table 1: Drugs Having Clinically Important Interactions with Methylphenidate

Monoamine Oxidase Inhibitors (MAOI)	
Clinical Impact:	Concomitant use of MAOIs and CNS stimulants can cause hypertensive crisis. Potential outcomes include death, stroke, myocardial infarction, aortic dissection, ophthalmological complications, eclampsia, pulmonary edema, and renal failure *[see Contraindications (4)]*.
Intervention:	Do not administer COTEMPLA-XR ODT concomitantly with MAOIs or within 14 days after discontinuing MAOI treatment.
Gastric pH Modulators	
Clinical Impact:	May change the release profile and alter the pharmacodynamics of COTEMPLA-XR ODT.
Intervention:	Concomitant use of Cotempla XR-ODT with a gastric pH modulator (i.e., a H2-blocker or a proton pump inhibitor) is not recommended.

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Antihypertensive Drugs	
Clinical Impact:	Cotempla XR-ODT may decrease the effectiveness of drug used to treat hypertension *[see Warnings and Precautions (5.3)]*.
Intervention:	Monitor blood pressure and adjust the dosage of the antihypertensive drug as needed.
Halogenated Anesthetics	
Clinical Impact:	Concomitant use of halogenated anesthetics and COTEMPLA XR-ODT may increase the risk of sudden blood pressure and heart rate increase during surgery.
Intervention:	Avoid use of COTEMPLA XR-ODT in patients being treated with anesthetics on the day of surgery.
Risperidone	
Clinical Impact:	Combined use of methylphenidate with risperidone when there is a change, whether an increase or decrease, in dosage of either or both medications, may increase the risk of extrapyramidal symptoms (EPS).
Intervention:	Monitor for signs of EPS.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COTEMPLA XR-ODT during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Psychostimulants at 1-866-961-2388.

Risk Summary

Published studies and postmarketing reports on methylphenidate use during pregnancy are insufficient to inform a drug-associated risk of adverse pregnancy-related outcomes *[see Data]*. There are risks to the fetus associated with the use of central nervous system (CNS) stimulants during pregnancy *[see Clinical Considerations]*. No teratogenic effects were observed in embryo-fetal development studies with oral administration of methylphenidate to pregnant rats and rabbits during organogenesis at doses 4 and 18 times, respectively, the maximum recommended human dose (MRHD) of 51.8 mg (as base). However, spina bifida was observed in rabbits at a dose 60 times the MRHD *[see Data]*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

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Fetal/Neonatal adverse reactions

CNS stimulants, such as COTEMPLA XR-ODT, can cause vasoconstriction and thereby decrease placental perfusion. No fetal and/or neonatal adverse reactions have been reported with the use of therapeutic doses of methylphenidate during pregnancy; however, premature delivery and low birth weight infants have been reported in amphetamine-dependent mothers.

Data

Human Data

A limited number of pregnancies have been reported in published observational studies and postmarketing reports describing methylphenidate use during pregnancy. Due to the small number of methylphenidate-exposed pregnancies with known outcomes, these data cannot definitely establish or exclude any drug-associated risk during pregnancy. Methodological limitations of these observational studies include small sample size, concomitant use of other medications, lack of detail regarding dose and duration of exposure to methylphenidate and non-generalizability of the enrolled populations.

Animal Data

In studies conducted in rats and rabbits, methylphenidate was administered orally at doses of up to 75 and 200 mg/kg/day, respectively, during the period of organogenesis. Teratogenic effects (increased incidence of fetal spina bifida) were observed in rabbits at the highest dose, which is approximately 60 times the maximum recommended human dose (MRHD) of 51.8 mg (as base) for adolescents on a mg/m^2 basis. The no effect level for embryo-fetal development in rabbits was 60 mg/kg/day (18 times the MRHD for adolescent on a mg/m^2 basis). There was no evidence of specific teratogenic activity in rats, although increased incidences of fetal skeletal variations were seen at the highest dose level (11 times the MRHD on a mg/m^2 basis for adolescent), which was also maternally toxic. The no effect level for embryo-fetal development in rats was 25 mg/kg/day (4 times the MRHD on a mg/m^2 basis for adolescent).

8.2 Lactation

Risk Summary

Limited published literature, based on breast milk sampling from five mothers, reports that methylphenidate is present in human milk, which resulted in infant doses of 0.16% to 0.7% of the maternal weight-adjusted dosage and a milk/plasma ratio ranging between 1.1 and 2.7. There are no reports of adverse effects on the breastfed infant and no effects on milk production. Long-term neurodevelopmental effects on infants from stimulant exposure are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for COTEMPLA XR-ODT and any potential adverse effects on the breastfed child from COTEMPLA XR-ODT or from the underlying maternal condition.

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Clinical Considerations

Monitor breastfeeding infants for adverse reactions, such as agitation, insomnia, anorexia, and reduced weight gain.

8.4 Pediatric Use

The safety and effectiveness of COTEMPLA XR-ODT have been established in pediatric patients 6 to 17 years of age in one adequate and well-controlled study in pediatric patients 6 to 12 years, pharmacokinetic data in adolescents, and safety information from other methylphenidate-containing products *[see Clinical Pharmacology (12) and Clinical Studies (14)]*.

The safety and effectiveness of COTEMPLA XR-ODT in pediatric patients below 6 years of age have not been established. The long-term efficacy of methylphenidate in pediatric patients has not been established.

Long Term Suppression Growth

Growth should be monitored during treatment with stimulants, including COTEMPLA XR-ODT. Children who are not growing or gaining weight as expected may need to have their treatment interrupted *[see Warnings and Precautions (5.7)]*.

Juvenile Animal Toxicity Data

Rats treated with methylphenidate early in the postnatal period through sexual maturation demonstrated a decrease in spontaneous locomotor activity in adulthood. A deficit in acquisition of a specific learning task was observed in females only. The doses at which these findings were observed are at least 6 times the maximum recommended human dose (MRHD) of 51.8 mg (as base) for pediatric patients on a mg/m^2 basis.

In the study conducted in young rats, methylphenidate was administered orally at doses of up to 100 mg/kg/day for 9 weeks, starting early in the postnatal period (postnatal day 7) and continuing through sexual maturity (postnatal week 10). When these animals were tested as adults (postnatal weeks 13-14), decreased spontaneous locomotor activity was observed in males and females previously treated with 50 mg/kg/day [approximately 6 times the MRHD of 51.8 mg (as base) on a mg/m^2 basis] or greater, and a deficit in the acquisition of a specific learning task was observed in females exposed to the highest dose (12 times the MRHD on a mg/m^2 basis). The no effect level for juvenile neurobehavioral development in rats was 5 mg/kg/day (half the MRHD on a mg/m^2 basis). The clinical significance of the long-term behavioral effects observed in rats is unknown.

8.5 Geriatric Use

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COTEMPLA XR-ODT has not been studied in patients over the age of 65 years.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

COTEMPLA XR-ODT contains methylphenidate, a Schedule II controlled substance.

9.2 Abuse

COTEMPLA XR-ODT has a high potential for abuse and misuse which can lead to the development of a substance use disorder, including addiction *[see Warnings and Precautions (5.1)]*. COTEMPLA XR-ODT can be diverted for non-medical use into illicit channels or distribution.

Abuse is the intentional non-therapeutic use of a drug, even once, to achieve a desired psychological or physiological effect. Misuse is the intentional use, for therapeutic purposes, of a drug by an individual in a way other than prescribed by a health care provider or for whom it was not prescribed. Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use (e.g., continuing drug use despite harmful consequences, giving a higher priority to drug use than other activities and obligations), and possible tolerance or physical dependence.

Misuse and abuse of methylphenidate may cause increased heart rate, respiratory rate, or blood pressure; sweating; dilated pupils; hyperactivity; restlessness; insomnia; decreased appetite; loss of coordination; tremors; flushed skin; vomiting; and/or abdominal pain. Anxiety, psychosis, hostility, aggression, and suicidal or homicidal ideation have also been observed with CNS stimulants abuse and/or misuse. Misuse and abuse of CNS stimulants, including COTEMPLA XR-ODT, can result in overdose and death *[see Overdosage (10)]*, and this risk is increased with higher doses or unapproved methods of administration, such as snorting or injection.

9.3 Dependence

Physical Dependence

COTEMPLA XR-ODT may produce physical dependence. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug.

Withdrawal signs and symptoms after abrupt discontinuation or dose reduction following prolonged use of CNS stimulants including COTEMPLA XR-ODT include dysphoric mood; depression; fatigue; vivid, unpleasant dreams; insomnia or hypersomnia; increased appetite; and psychomotor retardation or agitation.

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Tolerance

COTEMPLA XR-ODT may produce tolerance. Tolerance is a physiological state characterized by a reduced response to a drug after repeated administration (i.e., a higher dose of a drug is required to produce the same effect that was once obtained at a lower dose).

10 OVERDOSAGE

Clinical Effects of Overdose

Overdose of CNS stimulants is characterized by the following sympathomimetic effects:

- Cardiovascular effects including tachyarrhythmias, and hypertension or hypotension. Vasospasm, myocardial infarction, or aortic dissection may precipitate sudden cardiac death. Takotsubo cardiomyopathy may develop.
- CNS effects including psychomotor agitation, confusion, and hallucinations. Serotonin syndrome, seizures, cerebral vascular accidents, and coma may occur.
- Life-threatening hyperthermia (temperatures greater than 104^{o}F) and rhabdomyolysis may develop.

Overdose Management

Consider the possibility of multiple drug ingestion. The pharmacokinetic profile of COTEMPLA XR-ODT should be considered when treating patients with overdose. Because methylphenidate has a large volume of distribution and is rapidly metabolized, dialysis is not useful. Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

11 DESCRIPTION

COTEMPLA XR-ODT contains methylphenidate, a central nervous system (CNS) stimulant. COTEMPLA XR-ODT is an extended-release orally disintegrating tablet intended for once daily administration. COTEMPLA XR-ODT contains approximately 25% immediate-release and 75% extended-release methylphenidate. Methylphenidate is ionically-bound to the sulfonate of polystyrene sulfonate particles.

COTEMPLA XR-ODT contains 8.6 mg, 17.3 mg or 25.9 mg of methylphenidate which is the same as the amount of methylphenidate (base equivalent) found, respectively, in 10 mg, 20 mg and 30 mg strength methylphenidate hydrochloride products.

The chemical name of methylphenidate is methyl α-phenyl-2-piperidineacetate, and its structural formula is shown in Figure 1.

Figure 1: Methylphenidate Structure

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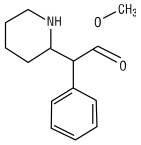

$C_{14}H_{19}NO_2$ Mol. Wt. 233.31

COTEMPLA XR-ODT also contains the following inactive ingredients: Mannitol, Fructose, Microcrystalline Cellulose, Crospovidone, Methacrylic Acid, Polystyrene Sulfonate, Citric Acid, Colloidal Silicon Dioxide, Grape Flavor, Natural Masking Type Powder, Triethyl Citrate, Magnesium Stearate, Ethylcellulose, Sucralose, Lake Blend Purple, and Polyethylene Glycol.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Methylphenidate is a central nervous system (CNS) stimulant. The mode of therapeutic action in ADHD is not known.

12.2 Pharmacodynamics

Methylphenidate is a racemic mixture comprised of the *d*- and *1*-isomers. The *d*-isomer is more pharmacologically active than the *l*-isomer. 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.

12.3 Pharmacokinetics

After oral administration of COTEMPLA XR-ODT, circulation levels of *l*- methylphenidate (MPH) were about 2% of total MPH.

Absorption

Following a single dose of 51.8 mg (2x25.9 mg daily) COTEMPLA XR-ODT in healthy adult subjects under fasted conditions, plasma methylphenidate (MPH) reached maximal concentration (C_{max}) at a median time of 5 hours after dosing. Compared to an extended release capsule formulation of methylphenidate, methylphenidate mean C_{max} and exposure (AUC_{inf}) was about 26% and 6% higher, respectively, after COTEMPLA XR-ODT administration (Figure 2).

Figure 2: Mean *d*-Methylphenidate Plasma Concentration-Time Profiles After Administration of COTEMPLA XR-ODT or Methylphenidate Hydrochloride Extended-Release Capsule in Healthy Volunteers Under Fasted Conditions

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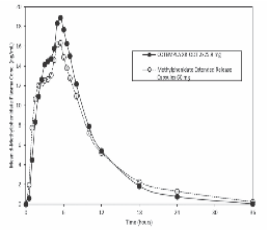

Effect of Food

Administration of 51.8 mg COTEMPLA XR-ODT with food (a high fat meal) decreased the C_{max} and increased AUC_{inf} of total MPH by approximately 24% and 16%, respectively. Food shortened the median time to peak concentration (T_{max}) by 0.5 hour (fed: 4.5 hours vs. fasted: 5.0 hours).

Effect of Alcohol

There is no in vivo study conducted for the effect of alcohol on drug exposure. An in vitro dissolution study showed alcohol-induced dose dumping potential in the presence of 40% alcohol. Dose dumping was not observed in the presence of lower alcohol concentrations.

Elimination

Plasma methylphenidate concentrations decline monophasically following oral administration of COTEMPLA XR-ODT. The mean plasma terminal elimination half-life of methylphenidate was about 4 hours in healthy volunteers following a single 51.8 mg dose administration.

Metabolism

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

Excretion

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

Specific Populations

Male and Female Patients and Ethnic Groups

There is insufficient experience with the use of COTEMPLA XR-ODT to detect gender or ethnic variations in pharmacokinetics.

Pediatric Patients

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The pharmacokinetics of methylphenidate after COTEMPLA XR-ODT administration were studied in pediatric patients (6-17 years of age) with ADHD under fasted conditions. After a single oral dose of 51.8 mg COTEMPLA XR-ODT, plasma concentrations of methylphenidate in children (6-12 years of age) were approximately twice the concentrations observed in adults. Exposure levels in adolescent patients (13 -17 years of age) were similar to those in adults. Body weight normalized clearance values were similar across the age groups (Table 2).

Table 2: PK Parameters (Mean ±SD) of *d*-MPH After 51.8 mg Oral Dosing of COTEMPLA XR-ODT Under Fasted Conditions

PK Parameter	Children (n=24)	Adolescent (n=8)	Adult (n=38)
T_{max} (hr)[†]	4.6 (2.0-8.0)	5.31 (3.5-8.0)	4.98 (2.5 - 6.5)
$T_{½}$ (hr)	4.43±1.0	3.93±0.33	4.00±0.73
C_{max} (ng/mL)	32.7±9.83	20.2±5.79	20.8±5.22
Cl (L/hr/kg)	6.21±1.48	5.54±1.19	5.48±1.46
AUC_{∞} (hr*ng/mL)	328.9±90.21	187.2±62.05	169.1±57.13

[†] data presented as median range

Patients with Renal Impairment

There is no experience with the use of COTEMPLA XR-ODT 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 COTEMPLA XR-ODT.

Patients with Hepatic Impairment

There is no experience with the use of COTEMPLA XR-ODT in patients with hepatic insufficiency.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

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. For pediatric patients, this dose is approximately 4 times the maximum recommended human dose of 51.8 (as base) on a mg/m^2 basis.

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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 5 times the maximum recommended dose of 51.8 mg (as base) for pediatric patients on a mg/m^2 basis.

Mutagenesis

Methylphenidate was not mutagenic in the *in vitro* Ames reverse mutation assay or 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. Methylphenidate was negative in an *in vivo* mouse bone marrow micronucleus assay.

Impairment of Fertility

Methylphenidate did not impair fertility in male or female mice that were fed diets containing the drug in an 18-week Continuous Breeding study. The study was conducted at doses up to 160 mg/kg/day, approximately 12-fold the maximum recommended human dose of 51.8 (as base) for adolescents on a mg/m^2 basis.

14 CLINICAL STUDIES

The efficacy of COTEMPLA XR-ODT was evaluated in a laboratory classroom study conducted in 87 pediatric patients (Aged 6 to 12 years) with ADHD. Following washout of previous methylphenidate medication, there was an open-label dose-optimization period (4 weeks) with an initial dose of 17.3 mg of COTEMPLA XR-ODT once daily in the morning. The dose could be titrated on a weekly basis from 17.3 mg, to 25.9 mg, to 34.6 mg, and up to 51.8 mg until an optimal dose or the maximum dose of 51.8 mg/day was reached. At the end of this period, subjects remained on their optimized dose for an additional week.
Subjects then entered a 1-week randomized, double-blind, parallel group treatment period with the individually optimized dose of COTEMPLA XR-ODT or placebo. At the end of this week, raters evaluated the attention and behavior of the subjects in a laboratory classroom setting, using the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) rating scale SKAMP is a validated 13-item teacher-rated scale that assesses manifestations of ADHD in a classroom setting.

The primary efficacy endpoint was the average of the SKAMP-Combined (Attention and Deportment) scores over the test day (not including the baseline score), with assessments conducted at baseline, and 1, 3, 5, 7, 10, 12, and 13 hours post-dosing. The key secondary efficacy endpoints were onset and duration of effect, defined as the first point at which active

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drug separated from placebo on SKAMP-Combined scores and the last time point at which active drug separated from placebo on SKAMP-Combined scores, respectively.

The SKAMP-Combined scores test day average was statistically significantly lower (improved) with COTEMPLA XR-ODT compared to placebo (difference of -11 (95% CI: -13.9, -8.2)) (Table 3).

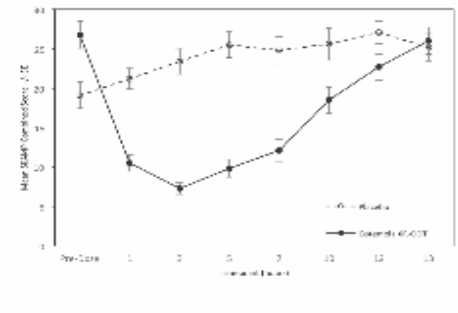
Table 3: Efficacy Analysis Results: SKAMP-Combined Scores Averaged Over Classroom Day in Patients with ADHD

Study Number	Treatment Group	Baseline Score at Randomization[a] (SD)	Pre-dose Score on Classroom Day[b] (SD)	LS Mean[c] (SE)	Placebo-subtracted Difference[d] (95% CI)
Study 1	Cotempla XR-ODT (17.3-51.8 mg/day)	21.1 (9.56)	26.8 (11.52)	14.3 (1.07)	-11.0 (-13.9, -8.2)
	Placebo	20.4 (9.09)	19.1 (11.04)	25.3 (1.16)	--

SD: standard deviation; SE: standard error; LS Mean: least-squares mean; CI: confidence interval.
[a] Visit 7 baseline score (Visit 7 occurred prior to the 1-week randomized, double-blind, parallel group treatment period).
[b] Visit 8 baseline score (Visit 8 occurred at the end of the 1-week randomized, double-blind, parallel group treatment period).
[c] Visit 8 LS mean over hours 1, 3, 5, 7, 10, 12, and 13.
[d] Difference (drug minus placebo) in least-squares means.

The SKAMP-Combined scores were also statistically significantly lower (improved) at time points (1, 3, 5, 7, 10, 12 hours) post-dosing with COTEMPLA XR-ODT compared to placebo (Figure 3).

Figure 3:LS Mean SKAMP Combined Score After Treatment with COTEMPLA XR-ODT or Placebo During Classroom Day in Patients with ADHD



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*SE = Standard Error

The database was not large enough to assess whether there were differences in effects in age, gender, or race subgroups.

16 HOW SUPPLIED/STORAGE AND HANDLING

COTEMPLA XR-ODT Extended Release Orally Disintegrating Tablets are available in three strengths:

- 8.6 mg tablets, round, purple to light purple, mottled, and debossed "T1" on one side of the tablet;
- 17.3 mg tablets, round, purple to light purple, mottled, and debossed "T2" on one side of the tablet;
- 25.9 mg tablets, round, purple to light purple, mottled, and debossed "T3" on one side of the tablet.

They are available as follows:

NDC 70165-100-30 8.6 mg tablets: carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets with a reusable travel case.

NDC 70165-200-30 17.3 mg tablets: carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets with a reusable travel case.

NDC 70165-300-30 25.9 mg tablets: carton containing 5 blister cards of 6 tablets each, for a total of 30 tablets with a reusable travel case.

Store at 20° C to 25° C (68° F to 77° F); excursions permitted from 15° C to 30° C (59° F to 86° F) [see USP Controlled Room Temperature].

Store COTEMPLA XR-ODT blister packages in the reusable travel case after removal from the carton.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

<u>Abuse, Misuse, and Addiction</u>

Educate patients and their families about the risks of abuse, misuse, and addiction of COTEMPLA XR-ODT, which can lead to overdose and death, and proper disposal of any unused drug *[see Warnings and Precautions (5.1), Drug Abuse and Dependence (9.2), Overdosage (10)].*

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Advise patients to store COTEMPLA XR-ODT in a safe place, preferably locked, and instruct patients to not give COTEMPLA XR-ODT to anyone else.

Instructions for Taking COTEMPLA XR-ODT

Instruct patients and their caregivers on the following:

- The tablet should remain in the blister pack until the patient is ready to take it.
- The tablet should be taken immediately after opening the blister pack. It should not be stored for future use.
- The patient or caregiver should use dry hands when opening the blister pack.
- The patient or caregiver should remove the tablet by peeling back the foil on the blister pack. The tablet should not be pushed through the foil.
- As soon as the blister is opened, the tablet should be removed and placed on the patient's tongue.
- The whole tablet should be placed on the tongue and allowed to disintegrate without chewing or crushing.
- The tablet will disintegrate in saliva and can be swallowed. No liquid is needed to take the tablet.

Risks to Patients with Serious Cardiac Disease

Advise patients that there are potential risks to patients with serious cardiac disease, including sudden death, with COTEMPLA XR-ODT use. Instruct patients to contact a healthcare provider immediately if they develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease *[see Warnings and Precautions (5.2)]*.

Increased Blood Pressure and Heart Rate

Advise patients and their caregivers that COTEMPLA XR-ODT can elevate blood pressure and heart rate *[see Warnings and Precautions (5.3)]*.

Psychiatric Adverse Reactions

Advise patients and their caregivers that COTEMPLA XR-ODT, at recommended doses, can cause psychotic or manic symptoms, even in patients without a prior history or psychotic symptoms or mania *[see Warnings and Precautions (5.4)]*.

Priapism

Advise patients, caregivers, and family members of the possibility of painful or prolonged penile erections (priapism). Instruct the patient to seek immediate medical attention in the event of priapism *[see Warnings and Precautions (5.5)]*.

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Circulation Problems in Fingers and Toes [Peripheral vasculopathy, including Raynaud's phenomenon]

- Instruct patients about the risk of peripheral vasculopathy, including Raynaud's phenomenon, and associated signs and symptoms: fingers or toes may feel numb, cool, painful, and/or may change color from pale, to blue, to red.
- Instruct patients to report to their physician any new numbness, pain, skin color change, or sensitivity to temperature in fingers or toes.
- Instruct patients to call their physician immediately with any signs of unexplained wounds appearing on fingers or toes while taking COTEMPLA XR-ODT.
- Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients *[see Warnings and Precautions (5.6)]*.

Long-Term Suppression of Growth in Pediatric Patients

Advise patients, families, and caregivers that COTEMPLA XR-ODT can cause slowing of growth and weight loss *[see Warnings and Precautions (5.7)]*.

Increased Intraocular Pressure (IOP) and Glaucoma

Advise patients that IOP and glaucoma may occur during treatment with COTEMPLA XR-ODT *[see Warnings and Precautions (5.9)]*.

Motor and Verbal Tics, and Worsening of Tourette's Syndrome

Advise patients that motor and verbal tics and worsening of Tourette's Syndrome may occur during treatment with COTEMPLA XR-ODT. Instruct patients to notify their healthcare provider if emergence of new tics or worsening of tics or Tourette's syndrome occurs *[see Warnings and Precautions (10)]*.

Alcohol effect

Advise patients to avoid alcohol while taking COTEMPLA XR-ODT. Consumption of alcohol while taking COTEMPLA XR-ODT may result in a more rapid release of the dose of methylphenidate *[see Clinical Pharmacology (12.3)]*.

Pregnancy Registry

Advise patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in females exposed to COTEMPLA XR-ODT during pregnancy *[see Use in Specific Populations (8.1)]*.

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For more information, call 1-(888)-319-1789

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Medication Guide
COTEMPLA XR-ODT (koh-TEM-pluh - oh dee tee)
(methylphenidate)
extended-release orally disintegrating tablets, CII

What is the most important information I should know about COTEMPLA XR-ODT?
COTEMPLA XR-ODT may cause serious side effects, including:

- **Abuse, misuse, and addiction.** COTEMPLA XR-ODT has a high chance for abuse and misuse and may lead to substance use problems, including addiction. Misuse and abuse of COTEMPLA XR-ODT, other methylphenidate containing medicines, and amphetamine containing medicines, can lead to overdose and death. The risk of overdose and death is increased with higher doses of COTEMPLA XR-ODT or when it is used in ways that are not approved, such as snorting or injection.
  - Your healthcare provider should check your child's risk for abuse, misuse, and addiction before treatment with COTEMPLA XR-ODT and will monitor your child during treatment.
  - COTEMPLA XR-ODT may lead to physical dependence after prolonged use, even if taken as directed by your healthcare provider.
  - Do not give COTEMPLA XR-ODT to anyone else. See "**What is COTEMPLA XR-ODT?**" for more information.

  Keep COTEMPLA XR-ODT in a safe place and properly dispose of any used medicine. See "**How should I store COTEMPLA XR-ODT?**" for more information.

  Tell your healthcare provider if your child has ever abused or been dependent on alcohol, prescription medicines, or street drugs.

- **Risks for people with serious heart disease.** Sudden death has happened in people who have heart defects or other serious heart disease.

  Your healthcare provider should check your child carefully for heart problems before starting COTEMPLA XR-ODT. Tell your healthcare provider if your child has any heart problems, heart disease, or heart defects.

  Call your healthcare provider or go to the nearest hospital emergency room right away if your child has any signs of heart problems such as chest pain, shortness of breath, or fainting during treatment with COTEMPLA XR-ODT.

- **Increased blood pressure and heart rate.**
  Your healthcare provider should check your child's blood pressure and heart rate regularly during treatment with COTEMPLA XR-ODT.

- **Mental (psychiatric) problems, including:**
  - new or worse behavior and thought problems
  - new or worse bipolar illness
  - new psychotic symptoms (such as hearing voices, or seeing or believing things that are not real) or new manic symptoms

  Tell your healthcare provider about any mental problems your child has, or about a family history of suicide, bipolar illness, or depression.
  Call your healthcare provider right away if your child has any new or worsening mental symptoms or problems during treatment with COTEMPLA XR-ODT, especially hearing voices, seeing or believing things that are not real, or new manic symptoms.

What is COTEMPLA XR-ODT?
COTEMPLA XR-ODT is a central nervous system (CNS) stimulant prescription medicine used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children 6 to 17 years of age. COTEMPLA XR-ODT may help increase attention and decrease impulsiveness and hyperactivity in children 6 to 17 years of age with ADHD.

It is not known if COTEMPLA XR-ODT is safe and effective in children under 6 years of age.

COTEMPLA XR-ODT is a federally controlled substance (CII) because it contains methylphenidate that can be a target for people who abuse prescription medicines or street drugs. Keep COTEMPLA XR-ODT in a safe place to protect it from theft. Never give your COTEMPLA XR-ODT to anyone else, because it may cause death or harm them. Selling or giving away COTEMPLA XR-ODT may harm others and is against the law.

Do not give COTEMPLA XR-ODT to your child if they are:

- allergic to methylphenidate or any of the ingredients in COTEMPLA XR-ODT. See the end of this Medication Guide for a complete list of ingredients in COTEMPLA XR-ODT.
- taking, or has taken within the past 14 days, a medicine used to treat depression called a monoamine oxidase inhibitor (MAOI).

Before taking COTEMPLA XR-ODT tell your child's healthcare provider about all medical conditions, including if your child:

- has heart problems, heart disease, heart defects, or high blood pressure
- has mental problems including psychosis, mania, bipolar illness, or depression
- has circulation problems in fingers and toes
- have eye problems, including increased pressure in your eye, glaucoma, or problems with your close-up vision (farsightedness)
- have or had repeated movements or sounds (tics) or Tourette's syndrome, or have a family history of tics or Tourette's syndrome
- is pregnant or plans to become pregnant. It is not known if COTEMPLA XR-ODT will harm the unborn baby.
  - There is a pregnancy registry for females who are exposed to COTEMPLA XR-ODT during pregnancy. The purpose of the registry is to collect information about the health of females exposed to COTEMPLA XR-ODT and their baby. If your child becomes pregnant during treatment with COTEMPLA XR-ODT, talk to your healthcare provider about registering with the National Pregnancy Registry for Psychostimulants. You can register by calling 1-866-961-2388.
- is breastfeeding or plans to breastfeed. COTEMPLA XR-ODT passes into breast milk. You and your healthcare provider should decide if your child will take COTEMPLA XR-ODT or breastfeed.

Tell your healthcare provider about all of the medicines that your child takes, including prescription and over-the-counter medicines, vitamins, and herbal supplements. COTEMPLA XR-ODT and some medicines may interact with each other and cause serious side effects. Sometimes the doses of other medicines will need to be adjusted during treatment with COTEMPLA XR-ODT.

Your healthcare provider will decide whether COTEMPLA XR-ODT can be taken with other medicines. **Especially tell your healthcare provider if your child takes**:

- anti-depression medicines including MAOIs

Know the medicines that your child takes. Keep a list of the medicines with you to show your healthcare provider and pharmacist. **Do not start any new medicine during treatment with COTEMPLA XR-ODT without talking to your healthcare provider first.**

How should COTEMPLA XR-ODT be taken?

- Take COTEMPLA XR-ODT exactly as prescribed by your healthcare provider.
- Your healthcare provider may change the dose if needed.
- Take COTEMPLA XR-ODT 1 time each day in the morning.
- COTEMPLA XR-ODT can be taken with or without food but take it the same way each time.

Take COTEMPLA XR-ODT as follows:

- Keep COTEMPLA XR-ODT in the blister pack until your child is ready to take it. Take COTEMPLA XR-ODT right after opening the blister pack. Do not store the tablet for future use.
- Use dry hands when opening the blister pack.
- Remove the tablet by peeling back the foil on the blister pack. **Do not push the tablet through the foil.**
- As soon as the blister is opened, remove the tablet and place it on the tongue. **Do not chew or crush the tablet.**
- The tablet will dissolve and can be swallowed with saliva. No liquid is needed to take the tablet.

If your child takes too much COTEMPLA XR-ODT, call your healthcare provider or Poison Help line 1-800-222-1222 or go to the nearest hospital emergency room right away.

What should I avoid during treatment with COTEMPLA XR-ODT?

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You should avoid drinking alcohol during treatment with COTEMPLA XR-ODT.

What are possible side effects of COTEMPLA XR-ODT?
COTEMPLA XR-ODT may cause serious side effects, including:

- See **"What is the most important information I should know about COTEMPLA XR-ODT?"**
- **Painful and prolonged erections (priapism).** Priapism has happened in males who take products that contain methylphenidate. **If your child develops priapism, get medical help right away.**
- **Circulation problems in fingers and toes (peripheral vasculopathy, including Raynaud's phenomenon).** Signs and symptoms may include:
  - fingers or toes may feel numb, cool, painful
  - fingers or toes may change color from pale, to blue, to red

  Tell your healthcare provider if your child has numbness, pain, skin color change, or sensitivity to temperature in their fingers or toes.

  Call your healthcare provider right away if your child has any signs of unexplained wounds appearing on fingers or toes during treatment with COTEMPLA XR-ODT.

- **Slowing of growth (height and weight) in children.** Children should have their height and weight checked often during treatment with COTEMPLA XR-ODT. COTEMPLA XR-ODT treatment may be stopped if your child is not gaining weight or height.
- **Eye problems (increased pressure in the eye and glaucoma).** Call your healthcare provider right away if you or your child develop changes in your vision or eye pain, swelling, or redness.
- **New or worsening tics or worsening Tourette's syndrome.** Tell your healthcare provider if you or your child get any new or worsening tics or worsening Tourette's syndrome during treatment with COTEMPLA XR-ODT.

The most common side effects of methylphenidate products include:

- decreased appetite
- trouble sleeping
- nausea
- vomiting
- indigestion
- stomach pain
- weight loss
- anxiety
- dizziness
- irritability
- mood swings
- increased heart rate
- increased blood pressure

These are not all the possible side effects of COTEMPLA XR-ODT.

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 COTEMPLA XR-ODT?

- Store COTEMPLA XR-ODT at room temperature between 68°F to 77°F (20°C to 25°C).
- Store COTEMPLA XR-ODT in a safe place, like a locked cabinet.
- Store COTEMPLA XR-ODT in the blister packaging until it is ready to be taken.
- Dispose of remaining, unused, or expired COTEMPLA XR-ODT by a medicine take-back program at a U.S. Drug Enforcement Administration (DEA) authorized collection. If no take-back program or DEA authorized collector is available, mix COTEMPLA XR-ODT with an undesirable, nontoxic substance such as dirt, cat litter, or used coffee grounds to make it less appealing to children and pets. Place the mixture in a container such as a sealed plastic bag and throw away COTEMPLA XR-ODT in the household trash. Visit www.fda.gov/drugdisposal for additional information on disposal of unused medicines.

Keep COTEMPLA XR-ODT and all medicines out of the reach of children.

General information about the safe and effective use of COTEMPLA XR-ODT
Medicines are sometimes prescribed for purposes other than those listed in the Medication Guide. Do not use COTEMPLA XR-ODT for a condition for which it was not prescribed. Do not give COTEMPLA XR-ODT to other people, even if they have the same condition. It may harm them and it is against the law. You can ask your healthcare provider or pharmacist for information about COTEMPLA XR-ODT that is written for healthcare professionals.

What are the ingredients in COTEMPLA XR-ODT?
Active Ingredient: Methylphenidate
Inactive Ingredients: Mannitol, Fructose, Microcrystalline Cellulose, Crospovidone, Methacrylic Acid, Polystyrene Sulfonate, Citric Acid, Colloidal Silicon Dioxide, Grape Flavor, Natural Masking Type Powder, Triethyl Citrate, Magnesium Stearate, Ethylcellulose, Sucralose, Lake Blend Purple, and Polyethylene Glycol

Manufactured for Neos Therapeutics Brands LLC, Grand Prairie, TX 75050
For more information go to http://www.COTEMPLA XR-ODT.com or call 1-888-319-1789
COTEMPLA XR-ODT is registered in the US Patent and Trademark Office © 2014 Neos Therapeutics, Inc.

This Medication Guide has been approved by the U.S. Food and Drug Administration. **Revised: 10/2023**