serdexmethylphenidate–dexmethylphenidate
Azstarys

Pharmaceutical company: Corium, Inc.
Pharmacologic classification: Norepinephrine and dopamine reuptake inhibitors
Therapeutic classification: CNS stimulants
Controlled substance schedule: CII

AVAILABLE FORMS
Capsules: serdexmethylphenidate–dexmethylphenidate: 26.1 mg/5.2 mg; 39.2 mg/7.8 mg; 52.3 mg/10.4 mg

INDICATIONS AND DOSAGES
Attention deficit hyperactivity disorder (ADHD)
Adults and children age 13 and older: Initially, serdexmethylphenidate–dexmethylphenidate 39.2 mg/7.8 mg PO once daily in the morning. Increase after 1 week to the maximum recommended dosage of serdexmethylphenidate–dexmethylphenidate 52.3 mg/10.4 mg PO daily.
Children ages 6 to 12 years: Initially, serdexmethylphenidate–dexmethylphenidate 39.2 mg/7.8 mg PO once daily in the morning. Dose may be increased after 1 week to serdexmethylphenidate–dexmethylphenidate 52.3 mg/10.4 mg PO once daily or decreased to serdexmethylphenidate–dexmethylphenidate 26.1 mg/5.2 mg PO daily depending on response and tolerability. Maximum dosage is serdexmethylphenidate–dexmethylphenidate 52.3 mg/10.4 mg PO daily.
Adjust-a-dose: Reduce the dose or discontinue the drug if paradoxical aggravation of ADHD symptoms or other adverse reactions occur. Periodically discontinue the drug to assess a pediatric patient’s condition. If improvement is not observed after appropriate dosage adjustment over 1 month, discontinue the drug.

CONTRAINDICATIONS AND CAUTIONS
- Black Box Warning: This product and other CNS stimulants (methylphenidate-containing products, amphetamines) have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing, and monitor for signs of abuse and dependence while on therapy.
- Contraindicated in patients with hypersensitivity to serdexmethylphenidate, methylphenidate, or other components of this product. Bronchospasm, rash, and pruritus have been reported. Hypersensitivity reactions (angioedema, anaphylactic reactions) have been reported in patients treated with other methylphenidate products.
- Avoid use in patients with structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious heart problems. Assess for cardiac disease (cardiac history, family history of sudden death or ventricular arrhythmia, and physical exam). Sudden death, stroke, and MI have been reported with CNS stimulants at recommended doses. Evaluate patients who develop exertional chest pain, unexplained syncope, or arrhythmias during treatment.
- CNS stimulants cause an increase in blood pressure and heart rate. Monitor for hypertension and tachycardia.
- CNS stimulants are associated with peripheral vasculopathy, including Raynaud phenomenon. Signs and symptoms generally improve after dose reduction or drug discontinuation.
- CNS stimulants may exacerbate symptoms of behavior disturbance and thought disorder in patients with a preexisting psychotic disorder.
- CNS stimulants may induce a manic or mixed mood episode in patients with bipolar disorder. Prior to initiating treatment, screen patients for risk factors for
developing a manic episode (comorbid or history of depressive symptoms or a
cFamily history of suicide, bipolar disorder, or depression).

- In patients without a prior history of psychotic illness or mania, CNS stimulants
  at recommended doses, may cause psychotic or manic symptoms (hallucinations,
delusional thinking, or mania). If such symptoms occur, consider discontinuing
  the stimulant.

- Prolonged and painful erections, sometimes requiring surgical intervention, have
  been reported with methylphenidate products. Priapism developed after some
time on the drug, often during a drug holiday, or after a dosage increase or drug
  discontinuation.

- CNS stimulants have been associated with weight loss and slowing of growth rate
  in pediatric patients. Closely monitor growth in children. Pediatric patients not
growing or gaining weight as expected may need to have therapy interrupted or
discontinued.

- Do not substitute this product for other methylphenidate products on a mg-per-mg
  basis since these have different pharmacokinetic profiles and may have different
  methylphenidate base composition.

- The long-term efficacy of methylphenidate in pediatric patients has not been
  established.

- The safety and effectiveness of the product in patients younger than age 6 have
  not been established.

- Use in patients age 65 and older has not been studied.

**Dialyzable drug:** Unknown.

**PREGNANCY-LACTATION-REPRODUCTION**

- There are no available data on use in pregnant women to evaluate for a drug-
  associated risk of major birth defects, miscarriage, or other adverse maternal or
  fetal outcomes.

- The use of CNS stimulants during pregnancy can cause vasoconstriction and
decrease placental perfusion. No fetal 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.

- Health care providers are encouraged to register female patients in the National
  Pregnancy Registry for Psychostimulants at 1-866-961-2388.

- There are no available data on the presence of serdexmethylphenidate in human
  milk, effects on the breastfed infant, or 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 the product and any potential adverse effects
  on the breastfed infant or from the underlying maternal condition.

- Monitor breastfeeding infants for adverse reactions (agitation, anorexia, and
  reduced weight gain).

**INTERACTIONS**

**Drug-drug. MAO inhibitors (selegiline, tranlycypromine, isocarboxazid, phenelzine,
linezolid, methylene blue):** May cause hypertensive crisis. Do not administer
concomitantly with or within 14 days of discontinuing MAO inhibitor.

**Antihypertensive drugs (potassium-sparing and thiazide diuretics, calcium channel
blockers, ACE inhibitors, ARBs, beta blockers, centrally acting alpha-2 receptor
agonists):** May decrease effectiveness of drugs used to treat hypertension. Monitor
blood pressure and adjust the dosage of the antihypertensive drug as needed.

**Halogenated anesthetics (halothane, isoflurane, enflurane, desflurane, sevoflurane):**
May increase the risk of sudden blood pressure and heart rate increase during surgery.
Avoid concomitant use on the day of surgery.

**Risperidone:** May increase the risk of extrapyramidal symptoms (EPS) when there is an
increase or decrease in dosage of either or both medications. Monitor for signs of EPS.
Serotonergic drugs (SSRIs, SNRIs, tricyclic antidepressants, opioids): May increase risk of serotonin syndrome. Use cautiously together.

ADVERSE REACTIONS
CNS: insomnia, anxiety, affect lability, irritability, dizziness, fever, seizure, dyskinesia, serotonin syndrome, nervousness, headache, tremor, drowsiness, vertigo, disorientation, hallucination, auditory hallucination, visual hallucination, logorrhea, mania, restlessness, agitation.
CV: increased blood pressure, tachycardia, angina pectoris, bradycardia, extrasystole, supraventricular tachycardia, ventricular extrasystole, palpitations, increased heart rate, chest pain, chest discomfort, Raynaud phenomenon.
EENT: diplopia, mydriasis, visual impairment, blurred vision, dry mouth.
GI: nausea, abdominal pain, dyspepsia, vomiting, decreased appetite.
GU: change in libido, priapism.
Hematologic: pancytopenia, thrombocytopenia, thrombocytopenic purpura.
Hepatic: hepatocellular injury, acute hepatic failure.
Metabolic: decreased weight.
Musculoskeletal: arthralgia, myalgia, muscle twitching, rhabdomyolysis, muscle cramps.
Skin: alopecia, erythema, hyperhidrosis.
Other: hypersensitivity reactions (angioedema, anaphylactic reactions, auricular swelling, bullous conditions, exfoliative conditions, urticarias, pruritus necrotizing enterocolitis [NEC], rashes, eruptions, and exanthems NEC).

Reactions in bold italics are life-threatening.

Released: May 2021
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**tepotinib**

Pharmacological classification: Kinase inhibitor

**Therapeutic classification:** Antineoplastic

**AVAILABLE FORMS**

*Tablets:* 225 mg

**INDICATIONS AND DOSAGES**

**Metastatic non–small-cell lung cancer harboring mesenchymal-epithelial transition exon 14 skipping alterations**

*Adults:* 450 mg PO daily until disease progression or unacceptable toxicity.

*Adjust-a-dose:* Refer to the manufacturer’s instructions for toxicity-related dosage adjustments. Permanently discontinue the drug in those who are unable to tolerate 225 mg orally once daily.

**CONTRAINDICATIONS AND CAUTIONS**

- Use cautiously in those with severe renal or hepatic impairment.
- This drug may cause interstitial lung disease (ILD)/pneumonitis. Immediately withhold therapy in patients with suspected ILD/pneumonitis. Permanently discontinue therapy in patients with a confirmed diagnosis with ILD/pneumonitis of any severity.
- This drug may cause hepatotoxicity. Monitor liver function tests. Withhold, reduce dose, or permanently discontinue therapy based on severity.
- Safety and effectiveness in children have not been established.

**Dialyzable drug:** Unknown.

**PREGNANCY-LACTATION-REPRODUCTION**

- This drug can cause fetal harm. Advise pregnant women of the potential harm to a fetus.
- Verify pregnancy status in females of reproductive potential prior to initiating.
- Advise females of reproductive potential or males with female partners of reproductive potential to use effective contraception during treatment and for 1 week after the final dose.
- Advise women not to breastfeed during treatment and for 1 week after the final dose.

**INTERACTIONS**

**Drug-drug.** *P-glycoprotein (P-gp) substrates (dabigatran, digoxin, morphine, cyclosporine, sirolimus):* May increase the concentration of P-gp substrate levels and increase the incidence and severity of adverse reactions. Avoid concomitant use where minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, reduce the P-gp substrate dosage if recommended in its approved product labeling.

*Strong CYP3A inducers (phenytoin, rifampin):* May decrease tepotinib level. Avoid concomitant use.

*Strong CYP3A inhibitors (ketoconazole, nefazodone, ritonavir) and P-gp inhibitors:* May increase tepotinib level and the incidence and severity of adverse reactions. Avoid concomitant use.

**ADVERSE REACTIONS**
CNS: fatigue, asthenia, fever, dizziness, headache.
CV: edema, *pulmonary embolism*.
GI: nausea, diarrhea, abdominal pain, constipation, vomiting, decreased appetite.
**Hematologic:** *lymphocytopenia,* decreased albumin, decreased hemoglobin.
**Hepatic:** *hepatotoxicity,* hepatic pain.
**Metabolic:** decreased sodium, increased liver function tests.
**Musculoskeletal:** musculoskeletal pain.
**Respiratory:** ILD/pneumonitis, pleural effusion, pneumonia, dyspnea, cough.
**Skin:** rash, pruritus.
**Other:** general health deterioration.

Reactions in bold italics are *life-threatening.*

Released: May 2021
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**trilaciclib**
Cosela

*Pharmaceutical company:* G1 Therapeutics

*Pharmacologic classification:* Kinase inhibitor

*Therapeutic classification:* Antineoplastic

**AVAILABLE FORMS**
Injection: 300-mg single-dose vial

**INDICATIONS AND DOSAGES**
Decrease the incidence of chemotherapy-induced myelosuppression when administered prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small-cell lung cancer

*Adults:* 240 mg/m²-IV infusion over 30 minutes completed within 4 hours prior to start of chemotherapy on each day of chemotherapy. If given on sequential days, the interval between doses of trilaciclib should not be greater than 28 hours.

*Adjust-a-dose:* Refer to the manufacturer’s instructions for toxicity-related dosage adjustments.

**CONTRAINDICATIONS AND CAUTIONS**
- Contraindicated in patients with a history of serious hypersensitivity reactions to this drug. Reactions have included anaphylaxis.
- Use is not recommended in patients with moderate or severe hepatic impairment (total bilirubin greater than 1.5 times the upper limit of normal, irrespective of AST)
- Severe, life-threatening, or fatal interstitial lung disease (ILD) or pneumonitis can occur.
- Safety and effectiveness in children have not been established.
- *Dialyzable drug:* Unknown.

**PREGNANCY-LACTATION-REPRODUCTION**
- This drug can cause fetal harm. Advise pregnant women of the risk.
- For females of reproductive potential, a pregnancy test is recommended prior to treatment.
- There are no data on the presence of this drug in human milk, effects on the breastfed child, or effects on milk production. Because of the potential for serious adverse reactions in breastfed children, advise lactating females to not breastfeed while taking this drug and for at least 3 weeks after the last dose.
- Females of reproductive potential should use an effective method of contraception during treatment with this drug and for at least 3 weeks after the last dose.
- This drug may impair female fertility.

**INTERACTIONS**

**Drug-drug. Cisplatin:** May increase risk of cisplatin-related nephrotoxicity. Closely monitor renal function.

*Dalfampridine:* May increase dalfampridine blood levels and the risk of seizures. Use together cautiously.

*Dofetilide:* May increase dofetilide blood levels and the risk of serious ventricular arrhythmias associated with QT interval prolongation, including torsades de pointes. Use cautiously together.

*OCT2, MATE1, and MATE-2K substrates (metformin):* May increase substrate level. Avoid concomitant use with certain substrates where minimal concentration changes may lead to serious or life-threatening toxicities.
ADVERSE REACTIONS
CNS: asthenia, fatigue, headache.
CV: thrombosis, hemorrhage, peripheral edema.
GI: upper abdominal pain.
Hematologic: neutropenia, febrile neutropenia, anemia, thrombocytopenia, leukopenia.
Hepatic: increased AST.
Metabolic: hypocalcemia, hypokalemia, hypophosphatemia, hyperglycemia.
Respiratory: respiratory failure, pneumonia.
Skin: injection-site reaction, rash.
Other: hypersensitivity reaction.

Reactions in bold italics are life-threatening.