ACT Methylphenidate ER®

A generic alternative to Concerta®

Indications[1]

ACT Methylphenidate ER (Methylphenidate Hydrochloride Extended-Release Tablets) is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in:

- Children (6 – 12 years of age)
- Adolescents (13 – 18 years of age)
- Adults (>18 years of age)

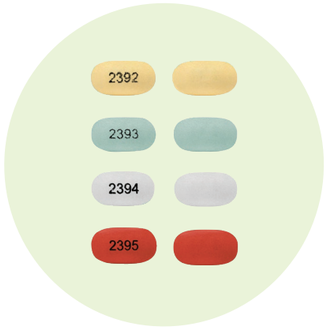
teva

ACT Methylphenidate ER®

For representation purposes only.

Refer to the Product Monograph for indications, contraindications, warnings, precautions, drug interactions, and dosing.

To place an order or to obtain additional information, contact your local Teva Canada Sales Representative or Customer Care at **1.800.268.4129**.



Strength	Size	DIN	UPC	Item Code
18 mg	Bottle 100	02441934	830790005981	107-555
27 mg	Bottle 100	02441942	830790005998	107-556
36 mg	Bottle 100	02441950	830790006001	107-557
54 mg	Bottle 100	02441969	830790006018	107-558

Format

Extended-release tablets

Active Ingredient

Methylphenidate hydrochloride

Non-medicinal Ingredients

Colloidal anhydrous, copolymers of methacrylic acid, fumaric acid, hypromellose 2208, hypromellose 2910, lactose monohydrate, magnesium stearate, methyl methacrylate, silica, talc, and triethyl citrate.

The coating of the 18 mg tablet contains: iron oxide red, iron oxide yellow, polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide.

The coating of the 27 mg tablet contains: FD&C Blue #2, iron oxide black, iron oxide yellow, polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide.

The coating of the 36 mg tablet contains: hypromellose 2910, lactose monohydrate, titanium dioxide, and triacetin/glycerol triacetate.

The coating of the 54 mg tablet contains: iron oxide red, polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide.

Product Characteristics

18 mg Yellow film coated, capsule shaped tablets imprinted with “2392” on one side

27 mg Gray film coated, capsule shaped tablets imprinted with “2393” on one side

36 mg White film coated, capsule shaped tablets imprinted with “2394” on one side

54 mg Red-brown film coated, capsule shaped tablets imprinted with “2395” on one side

Storage and Stability Recommendations

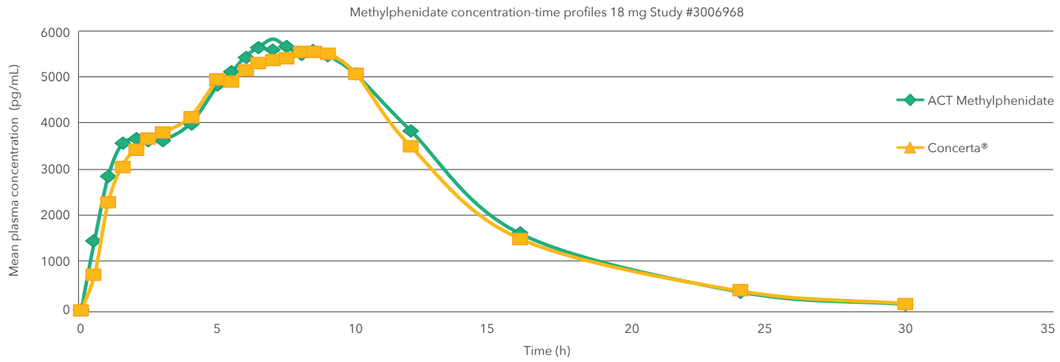
Store between 15°C – 30°C. Protect from moisture.

To view the Product Monograph, visit TevaCanada.com

Comparative bioavailability study

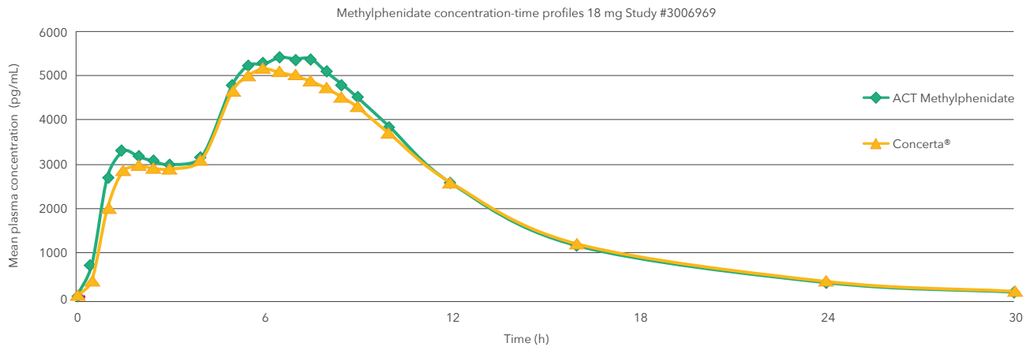
Single oral dose (1 x 18 mg) comparative bioavailability study under fed conditions

Mean methylphenidate concentration-time profiles after administration of the test formulation (treatment A) and the reference product (treatment B)[1,2,†]



Single oral dose (1 x 18 mg) comparative bioavailability study under fasting conditions

Mean methylphenidate concentration-time profiles after administration of the test formulation (treatment A) and the reference product (treatment B)[1,3,‡]

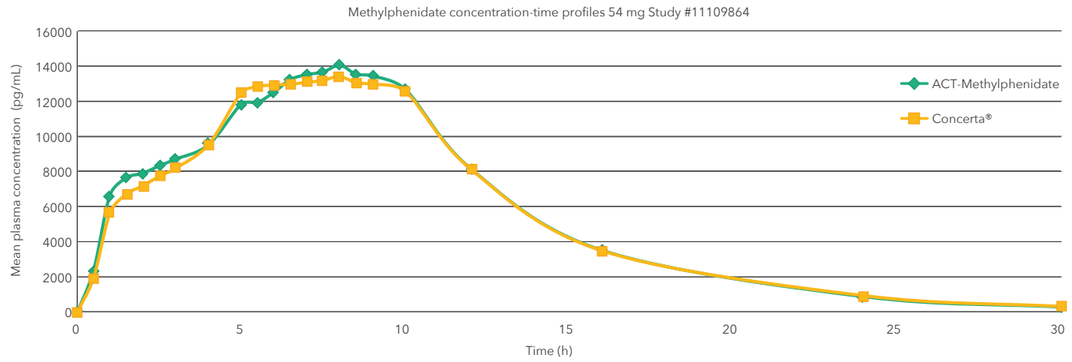


†A single-dose, two-period, two-treatment, two-way crossover bioequivalence study of methylphenidate hydrochloride 18 mg extended-release tablets (Teva Canada Limited) and Concerta® (methylphenidate hydrochloride) 18 mg extended-release tablets by Janssen Inc., Canada was conducted in healthy adult subjects under fed conditions.

‡A single-dose, two-period, two-treatment, two-way crossover bioequivalence study of methylphenidate hydrochloride 18 mg extended-release tablets (Teva Canada Limited) and Concerta® (methylphenidate hydrochloride) 18 mg extended-release tablets by Janssen Inc., Canada was conducted in healthy adult subjects under fasting conditions.

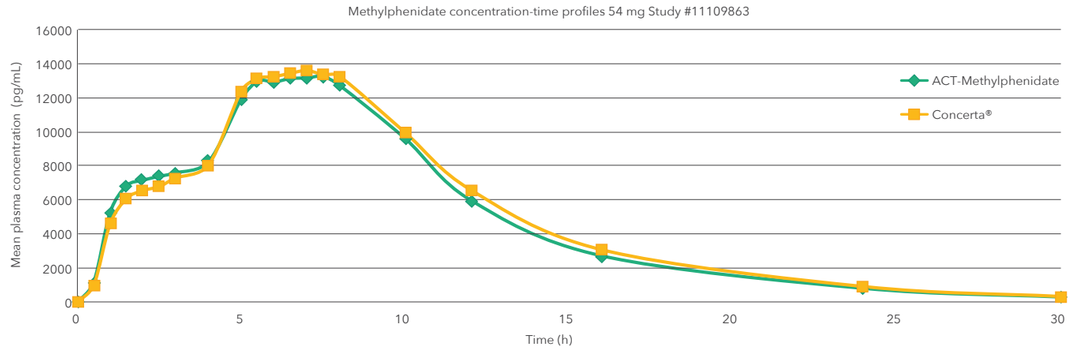
Single oral dose (1 x 54 mg) comparative bioavailability study under fed conditions

Mean methylphenidate concentration-time profiles after administration of the test formulation (treatment A) and the reference product (treatment B)[1,4,§]



Single oral dose (1 x 54 mg) comparative bioavailability study under fasting conditions

Mean methylphenidate concentration-time profiles after administration of the test formulation (treatment A) and the reference product (treatment B)[1,5,#]



§A single-dose, two-period, two-treatment, two-way crossover bioequivalence study of methylphenidate hydrochloride 18 mg extended-release tablets (Teva Canada Limited) and Concerta® (methylphenidate hydrochloride) 54 mg extended-release tablets by Janssen Inc., Canada was conducted in healthy adult subjects under fed conditions.

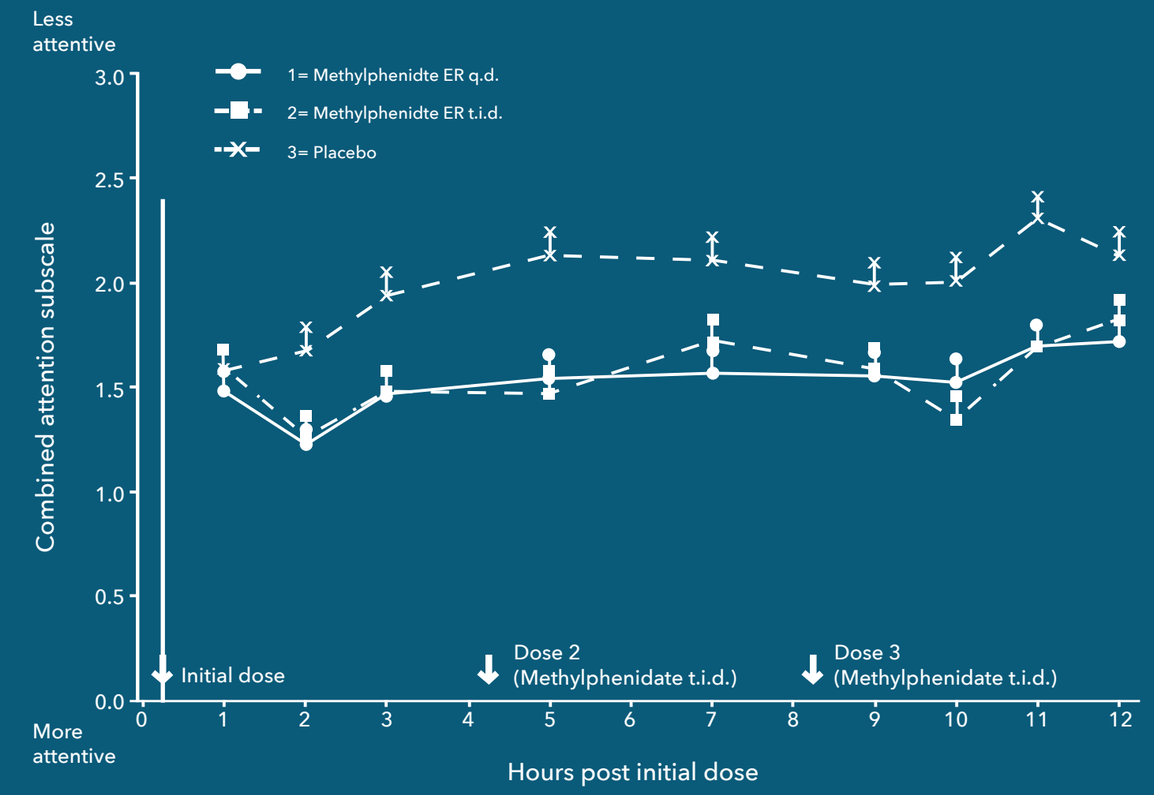
#A single-dose, two-period, two-treatment, two-way crossover bioequivalence study of methylphenidate hydrochloride 18 mg extended-release tablets (Teva Canada Limited) and Concerta® (methylphenidate hydrochloride) 54 mg extended-release tablets by Janssen Inc., Canada was conducted in healthy adult subjects under fasting conditions.

Proven bioequivalence to Concerta®

The ACT Methylphenidate ER modified release dosage formulation has been developed to offer a comparable methylphenidate release profile to Concerta®.

Significant improvement in attention and behaviour with sustained beneficial effects has been shown in children versus placebo[II]

- In the two placebo-controlled crossover studies (Studies 1 and 2), symptoms of ADHD were evaluated by laboratory school teachers using the SKAMP (Swanson, Kotkin, Agler, M-Flynn, and Pelham) laboratory school rating scale
- Significant improvement in attention and behaviour versus placebo was shown consistently across the two studies ($p < 0.005$)
- Efficacy was maintained through 12 hours after dosing
- Sustained beneficial effects of methylphenidate hydrochloride extended-release tablets q.d. therapy seen throughout the laboratory classroom day were comparable in duration to those with methylphenidate hydrochloride t.i.d.



Adapted from the ACT-Methylphenidate ER Product Monograph

Mean laboratory school teacher SKAMP Ratings of Combined Attention (Study 1) with methylphenidate hydrochloride extended-release tablets q.d. (18, 36, or 54 mg), methylphenidate hydrochloride t.i.d. over 12 hours (15, 30, or 45 mg total daily dose), and placebo. Error bars represent mean plus standard error of the mean. The sample sizes for methylphenidate hydrochloride extended-release tablets, methylphenidate hydrochloride t.i.d., and placebo groups were 60, 62, and 60, respectively.

q.d. = once a day; t.i.d. = three times a day

[II]Three double-blind, active- and placebo-controlled studies were conducted in 416 children aged six to twelve. The controlled studies compared methylphenidate hydrochloride extended-release tablets q.d. (18, 36, or 54 mg), methylphenidate hydrochloride t.i.d. over 12 hours (15, 30, or 45 mg total daily dose), and placebo in two single-centre, 3-week, crossover studies (Study 1 and Study 2), and in a multicentre, 4-week, parallel-group comparison (Study 3). The primary comparison of interest in all three trials was methylphenidate hydrochloride extended-release tablets versus placebo.

Demonstrated to be effective in the treatment of ADHD and well-tolerated in adolescents at doses up to 72 mg/day (1.4 mg/kg/day)¶

In a randomized, double-blind, multicentre, placebo-controlled trial (Study 4) involving 177 patients, methylphenidate hydrochloride extended-release tablets was demonstrated to be:

- Effective in the treatment of ADHD
  - Mean scores for the investigator rating on the ADHD Rating Scale for methylphenidate hydrochloride extended-release tablets were significantly improved relative to placebo (CON –14.93; PLA –9.58; p=0.001)
  - Mean scores for methylphenidate hydrochloride extended-release tablets and placebo, respectively, at the end of the double-blind phase were 16.62 and 21.40, compared to 31.55 and 30.99 at baseline
- Generally well tolerated in adolescents aged 13 to 18 at doses up to 72 mg/day (1.4 mg/kg/day)

Demonstrated statistically significant superiority in improving the investigator-rated Connors' Adult ADHD Rating Scale (CAARS) total scores compared to placebo[Δ]

- All doses of methylphenidate hydrochloride extended-release tablets (18 mg, 36 mg, and 72 mg/day) were statistically significantly superior to placebo in improving the CAARS total scores at double-blind endpoint compared to baseline (mean change of -7.6 for placebo, -10.6 (p=0.0146) for methylphenidate hydrochloride extended-release tablets 18 mg, -11.5 (p=0.0131) for methylphenidate hydrochloride extended-release tablets 36 mg, and -13.7 (p<0.0001) for the methylphenidate hydrochloride extended-release tablets 72 mg
- Statistically significant differences compared to placebo were first observed at Week 1

¶Of 220 patients who entered an open 4-week titration phase, 177 adolescent patients aged 13 to 18 who met the DSM-IV criteria for ADHD were titrated to an individualized dose (maximum 72 mg/day) based on meeting specific improvement criteria on the ADHD Rating Scale and the Global Assessment of Effectiveness with acceptable tolerability. Patients who met these criteria were then randomized to receive either their individualized dose of methylphenidate hydrochloride extended-release tablets (18 – 72 mg/day, n = 87) or placebo (n = 90) during a 2-week double-blind phase.

[Δ]5-week, randomized, double-blind, multicentre, placebo-controlled, dose-response trial (Study 5) was conducted in 401 adults with ADHD aged 18 to 65 years using once daily methylphenidate hydrochloride extended-release tablets fixed doses of 18 mg, 36 mg, and 72 mg. Efficacy was evaluated by the mean change from baseline to double-blind endpoint in the investigator-rated Connors' Adult ADHD Rating Scale (CAARS) total score.

Clinical use

Pediatrics (<6 – 18 years of age)

Based on the data submitted and reviewed by Health Canada, the safety and efficacy of methylphenidate hydrochloride extended-release tablets in pediatric patients from 6 to 18 years of age has been established. Therefore, Health Canada has authorized an indication for pediatric use.

Pediatrics (<6 years of age)

Methylphenidate hydrochloride extended-release tablets should not be used in children under six years of age.

Geriatrics (>65 years of age)

No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use.

A diagnosis of ADHD (DSM-IV) implies the presence of hyperactive-impulsive or inattentive symptoms that caused impairment and that were present before age 7 years. The symptoms must be persistent, must be more severe than is typically observed in individuals at a comparable level of development, must cause clinically significant impairment, e.g., in social, academic, or occupational functioning, and must be present in 2 or more settings, e.g., school (or work) and at home. The symptoms must not be better accounted for by another mental disorder. For the Inattentive Type, at least 6 of the following symptoms must have persisted for at least 6 months: lack of attention to details/careless mistakes, lack of sustained attention, poor listener, failure to follow through on tasks, poor organization, avoids tasks requiring sustained mental effort, loses things, easily distracted, forgetful. For the Hyperactive-Impulsive Type, at least 6 of the following symptoms must have persisted for at least 6 months: fidgeting/squirming, leaving seat, inappropriate running/climbing, difficulty with quiet activities, "on the go," excessive talking, blurting answers, can't wait turn, intrusive.

Need for comprehensive treatment program

ACT Methylphenidate ER is indicated as an integral part of a total treatment program for ADHD that may include other measures (psychological, educational, social) for patients with this syndrome. Drug treatment may not be indicated for all patients with this syndrome. Drug treatment is not intended for use in the patient who exhibits symptoms secondary to environmental factors and/or other primary psychiatric disorders, including psychosis. Appropriate educational placement is essential in children and adolescents with this diagnosis and psychosocial intervention is often helpful. When remedial measures alone are insufficient, the decision to prescribe drug treatment medication will depend upon the physician's assessment of the chronicity and severity of the patient's symptoms.

Long-term use

The effectiveness of methylphenidate hydrochloride extended-release tablets for long-term use, i.e., for more than 4 weeks in children and adolescents or 7 weeks in adults, has not been systematically evaluated in placebo-controlled trials. Therefore, the physician who elects to use ACT Methylphenidate ER for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

Contraindications

ACT Methylphenidate ER is contraindicated in:

- Patients who are hypersensitive to methylphenidate or to any ingredient in the formulation or component of the container
- Thyrotoxicosis
- Advanced arteriosclerosis
- Symptomatic cardiovascular disease
- Moderate to severe hypertension
- Glaucoma
- During treatment with monoamine oxidase inhibitors, and also within a minimum of 14 days following discontinuation of a monoamine oxidase inhibitor

Most serious warnings and precautions

Drug dependence – Like other stimulants, ACT Methylphenidate ER has the potential to be abused, leading to dependence and tolerance.

Other relevant warnings and precautions

General – ACT Methylphenidate ER is intended for oral use only. In dogs, the intravenous injection of the pulverized methylphenidate hydrochloride extended-release tablets resulted in death.

Fatigue – ACT Methylphenidate ER should not be used for the prevention or treatment of normal fatigue states.

Information for patients – Patients should be informed that ACT Methylphenidate ER should be swallowed whole with the aid of liquids. Tablets should not be chewed, divided, or crushed.

Hypertension and other cardiovascular conditions – ACT Methylphenidate ER is contraindicated in moderate to severe hypertension and should be used cautiously in patients with mild hypertension and other cardiovascular conditions. Blood pressure should be monitored at appropriate intervals in patients receiving ACT Methylphenidate ER, especially in patients with hypertension. Caution is advised in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate, e.g., those with pre-existing hypertension, heart failure or recent myocardial infarction.

Pre-existing cardiovascular and cerebral vascular conditions – ACT Methylphenidate ER is contraindicated in advanced arteriosclerosis and symptomatic cardiovascular disease. CNS stimulants should be used with caution in patients with a pre-existing cardiovascular or cerebrovascular condition, taking into account risk predictors for these conditions. Patients should be screened for pre-existing or underlying cardiovascular or cerebrovascular conditions before initiation of treatment with ACT Methylphenidate ER and monitored for new conditions of the heart or brain during the course of treatment.

Sudden death and pre-existing structural cardiac abnormalities or other serious heart problems – Children and adolescents: Sudden death has been reported in association with stimulant drugs used for ADHD treatment at usual doses in children and adolescents with structural cardiac abnormalities or other serious cardiac problems. Although some serious heart problems alone carry an increased risk of sudden death, ACT Methylphenidate ER generally should not be used in children, adolescents, or adults with known structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, or other serious cardiac problems that may place them at increased vulnerability to the sympathomimetic effects of a stimulant drug. Adults: Sudden deaths, stroke, and myocardial infarction have been reported in adults taking stimulant drugs at usual doses for ADHD. Although the role of stimulants in these adult cases is also unknown, adults have a greater likelihood than children of having serious structural cardiac abnormalities, cardiomyopathy, serious heart rhythm abnormalities, coronary artery disease, or other serious cardiac problems. Adults with such abnormalities should also generally not be treated with stimulant drugs. General: All drugs with sympathomimetic effects prescribed in the management of ADHD should be used with caution in patients who: a) are involved in strenuous exercise or activities, b) use other sympathomimetic ADHD drugs, or c) have a family history of sudden/cardiac death. Prior to the initiation of treatment with sympathomimetic medications, a personal and family history (including assessment for a family history of sudden death or ventricular arrhythmia) and physical exam should be obtained to assess for the presence of cardiac disease. In patients with relevant risk factors and based on the clinician's judgment, further cardiovascular evaluation may be considered (e.g., electrocardiogram and echocardiogram). Patients who develop symptoms such as exertional chest pain, unexplained syncope, or other symptoms suggestive of cardiac disease during ADHD treatment should undergo a prompt cardiac evaluation.

Peripheral vasculopathy, including Raynaud's phenomenon – Stimulants used to treat ADHD, such as methylphenidate hydrochloride extended-release tablets, are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; however, very rare sequelae include digital ulceration and/or soft tissue breakdown. Careful observation for digital changes is necessary during treatment with ADHD stimulants. Further clinical evaluation (e.g., rheumatology referral) may be appropriate for certain patients.

Drug dependence – ACT Methylphenidate ER contains methylphenidate, a Schedule III Controlled Substance. ACT Methylphenidate ER should be given cautiously to patients with a history of drug dependence or alcoholism. Chronic abusive use can lead to marked tolerance and psychological dependence with varying degrees of abnormal behaviour. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during withdrawal from abuse since severe depression may occur. Withdrawal following chronic therapeutic use may unmask symptoms of an underlying disorder that may require follow-up.

Driving and operating machinery – Because methylphenidate may affect performance, due caution should be exercised when driving or operating a vehicle or potentially dangerous machinery. Patients should be cautioned accordingly until they are reasonably certain that ACT Methylphenidate ER does not adversely affect their ability to engage in such activities.

Thyrotoxicosis – ACT Methylphenidate ER is contraindicated in patients with thyrotoxicosis.

Long-term suppression of growth – Suppression of growth (i.e., weight gain and/or height) has been reported with the long-term use of stimulants in children. Therefore, patients requiring long-term therapy should be carefully monitored. Patients who are not growing or gaining weight as expected should have their treatment interrupted.

Potential for gastrointestinal obstruction – Methylphenidate hydrochloride extended-release tablets should not be administered to patients with pre-existing gastrointestinal narrowing (pathologic or iatrogenic, such as small bowel inflammatory disease, "short gut" syndrome due to adhesions or decreased transit time, past history of peritonitis, cystic fibrosis, chronic intestinal pseudo-obstruction, or Meckel's diverticulum). Due to the controlled-release design, methylphenidate hydrochloride extended-release tablets should only be used in patients who are able to swallow the tablets whole.

Monitoring and laboratory tests – Periodic laboratory tests are advised during prolonged therapy. The tests should include, but not be limited to, haematological parameters, including complete blood count, differential and platelet counts, and liver enzymes.

Cerebrovascular disorders – Consider cerebrovascular disorders as a possible diagnosis in any patient who develops new neurological symptoms that are consistent with cerebral ischemia during methylphenidate hydrochloride extended-release tablet therapy. These symptoms could include severe headache, unilateral weakness or paralysis, and impairment of coordination, vision, speech, language, or memory. If a cerebrovascular disorder is suspected during treatment, discontinue ACT Methylphenidate ER immediately. In patients with pre-existing cerebrovascular disorders (e.g., aneurysm, vascular malformations/anomalies), treatment with ACT Methylphenidate ER is not recommended.

Motor and verbal tics, and worsening of Tourette's syndrome – Central nervous system (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. It is recommended that the family history be assessed, and that the patient is clinically evaluated for tics or Tourette's syndrome before initiating methylphenidate. Regular monitoring for the emergence or worsening of tics or Tourette's syndrome during treatment with methylphenidate is recommended at every dose adjustment and every visit, and treatment discontinued if clinically appropriate.

Serotonin toxicity / serotonin syndrome – Serotonin toxicity also known as serotonin syndrome is a potentially life-threatening condition and has been reported with methylphenidate, including methylphenidate hydrochloride extended-release tablets, with concomitant use of serotonergic or dopaminergic drugs. If concomitant treatment with ACT Methylphenidate ER and other serotonergic agents is clinically warranted, careful observation of the patient is advised. If serotonin toxicity is suspected, treatment with ACT Methylphenidate ER (and serotonergic drugs) must be immediately discontinued and appropriate treatment instituted.

Increased intraocular pressure and glaucoma – There have been reports of elevation of intraocular pressure (IOP) and glaucoma associated with methylphenidate treatment. ACT Methylphenidate ER is contraindicated in patients with glaucoma.

Aggression, anxiety, and agitation – Patients beginning treatment for ADHD should be monitored for the appearance of or worsening of aggressive behaviour, marked anxiety or agitation, in which case consider discontinuing methylphenidate.

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

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

Screening patients for bipolar disorder – Particular care should be taken in using stimulants to treat ADHD in patients with comorbid bipolar disorder because of concern for possible induction of a mixed/manic episode in such patients. Prior to initiating treatment with a stimulant, patients with comorbid depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a family history of suicide, bipolar disorder, and depression.

Suicidal behaviour and ideation – It is recommended for patients treated with ADHD drugs that caregivers and physicians monitor for signs of suicide-related behaviour, including at dose initiation/optimization and drug discontinuation. Patients should be encouraged to report any distressing thoughts or feelings at any time to their healthcare professional. Patients with emergent suicidal ideation and behaviour should be evaluated immediately. The physician should initiate appropriate treatment of the underlying psychiatric condition and consider a possible change in the ADHD treatment regimen.

Priapism – Priapism can develop after some time on methylphenidate, often subsequent to an increase in dose. Priapism has also appeared during a period of methylphenidate withdrawal (drug holidays or during discontinuation). Patients who develop abnormally sustained erections or frequent and painful erections should seek immediate medical attention.

Pregnant women – ACT Methylphenidate ER should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Breast-feeding – A decision should be made whether nursing women should abstain from breast-feeding or to abstain from ACT Methylphenidate ER therapy, taking into account the benefit of breast-feeding to the child and the benefit of therapy to the mother.

For more information

Please consult the ACT Methylphenidate ER Product Monograph at https://health-products.canada.ca/dpd-bdpp/index-eng.jsp for important information relating to adverse reactions, drug interactions, and dosing, which has not been discussed in this piece. The Product Monograph is also available by calling Teva Canada Limited at 1-800-268-4127 option 3 or emailing druginfo@tevacanada.com.

References

1. Teva Canada Limited. ACT Methylphenidate ER Product Monograph. April 11, 2023.
2. Data on File Study #3006968.
3. Data on File Study #3006969.
4. Data on file Study #11109864.
5. Data on file Study #11109863.

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