Prescribing Information for Xaggitin® XL (methylphenidate hydrochloride) prolonged-release tablets

Please refer to the Summary of Product Characteristics (SPC) before prescribing.

Presentation: Available in a range of doses. Prolonged-release tablets containing 18mg, 27mg, 36mg or 54mg of methylphenidate hydrochloride, equivalent to 15.6 mg, 23.3 mg, 31.1 mg or 46.7 mg of methylphenidate, respectively. **Indication:** Attention Deficit/ Hyperactivity Disorder (ADHD): Indicated as part of a comprehensive treatment programme for ADHD in children aged 6 years of age and over when remedial measures alone prove insufficient. Treatment must be under the supervision of a specialist in childhood behavioural disorders. Diagnosis should be made according to the current DSM criteria or ICD guidelines and should be based on a complete history and evaluation of the patient. Diagnosis cannot be made solely on the presence of one or more symptom. *Xaggitin XL treatment is not indicated in all children with ADHD and the decision to use the medicinal product must be based on a very thorough assessment of the severity and chronicity of the child's symptoms in relation to the child's age.* **Dosage and Administration: Refer to SPC for details and recommendations:** For oral use. Take once daily in the morning. The tablet must be swallowed whole with liquids and must not be chewed, broken, divided, or crushed. It may be administered with or without food. *Pre-treatment screening:* Conduct a baseline evaluation of a patient's cardiovascular status including blood pressure and heart rate prior to prescribing. A comprehensive history should document concomitant medications, past and present co-morbid medical and psychiatric disorders or symptoms, family history of sudden cardiac/unexplained death and accurate recording of pre-treatment height and weight on a growth chart. *Ongoing monitoring:* growth, psychiatric and cardiovascular status should be continuously monitored. Patients should be monitored for the risk of diversion, misuse and abuse of methylphenidate. *Dose titration:* Careful dose titration is necessary at the start of treatment. Dose titration should be started at the lowest possible dose and may be adjusted in 18 mg increments at approximately weekly intervals. The maximum daily dosage is 54 mg. *Patients New to Methylphenidate:* Lower doses of short-acting methylphenidate formulations may be considered sufficient to treat patients new to methylphenidate. Careful dose titration by the physician in charge is required. The recommended starting dose is 18 mg once daily. *Patients Currently Using Methylphenidate:* Dosing recommendations are based on current dose regimen and clinical judgement. Please refer to the SPC for dose conversion. *Long-term (more than 12 months) use in children and adolescents:* Methylphenidate treatment is usually discontinued during or after puberty. If prescribed for extended periods (over 12 months), the long-term usefulness of treatment with methylphenidate should be periodically re-evaluated with trial periods off medication to assess the patient's functioning without pharmacotherapy. It is recommended that methylphenidate is de-challenged at least once yearly to assess the child's condition. *Dose reduction and discontinuation:* Treatment must be stopped if the symptoms do not improve after appropriate dosage adjustment over a one-month period. If paradoxical aggravation of symptoms or other serious adverse events occur, the dosage should be reduced or discontinued. *Adults:* In adolescents, whose symptoms persist into adulthood and who have shown clear benefit from treatment, it may be appropriate to continue treatment into adulthood. Initiation of treatment with Xaggitin XL in adults is not appropriate. *Elderly or children under 6 years:* Xaggitin XL should not be used due to lack of data. **Contra-indications:** Hypersensitivity to the active substance or to any of the excipients, glaucoma, phaeochromocytoma, during treatment with non-selective, irreversible monoamine oxidase (MAO) inhibitors, or within a minimum of 14 days of discontinuing those medicinal products, hyperthyroidism or thyrotoxicosis, diagnosis or history of severe depression, anorexia nervosa/anorexic disorders, suicidal tendencies, psychotic symptoms, severe mood disorders, mania, schizophrenia, psychopathic/borderline personality disorder, diagnosis or history of severe and episodic (Type I) Bipolar (affective) Disorder that is not well-controlled, pre-existing cardiovascular disorders including severe hypertension, heart failure, arterial occlusive disease, angina, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, potentially life- threatening arrhythmias and channelopathies (disorders caused by the dysfunction of ion channels), pre-existing cerebrovascular disorders, cerebral aneurysm, vascular abnormalities including vasculitis or stroke. **Precautions and Warnings: Refer to SPC for details and recommendations:** *Long-term use (more than 12 months) in children and adolescents:* Careful ongoing monitoring for cardiovascular status, growth, appetite, development of de novo or worsening of pre-existing psychiatric disorders. Psychiatric disorders to monitor for include (but are not limited to) motor or vocal tics, aggressive or hostile behaviour, agitation, anxiety, depression, psychosis, mania, delusions, irritability, lack of spontaneity, withdrawal and excessive perseveration. The use of methylphenidate for over 12 months in children and adolescents with ADHD should be periodically re-evaluated. Recommended that methylphenidate is de-challenged at least once yearly to assess the child's condition. *Use in adults, elderly or children under 6 years of age*: see above. *Cardiovascular status*: Careful history and physical exam should be carried out to assess for the presence of cardiac disease, and patients should receive further specialist cardiac evaluation if initial findings suggest such history or disease. Cardiovascular status should be carefully monitored. Blood pressure and pulse should be recorded at predefined intervals. *Sudden death and pre-existing structural cardiac abnormalities or other serious cardiac disorders:* Sudden death has been reported in association with the use of stimulants of the central nervous system at usual doses in children. *Misuse and cardiovascular events:* Misuse of stimulants of the central nervous system may be associated with sudden death and other serious cardiovascular adverse events. *Cerebrovascular disorders*: Contraindicated in those with certain cerebrovascular conditions (see above). Patients with additional risk factors should be assessed at every visit. Cerebral vasculitis is a very rare idiosyncratic reaction and this diagnosis should be considered in any patient who develops new neurological symptoms consistent with cerebral ischaemia. *Psychiatric disorders*: In the case of emergent psychiatric symptoms or exacerbation of pre-existing psychiatric disorders, methylphenidate should not be given unless the benefits outweigh the risks to the patient. *Consult SPC for additional information for specific psychiatric disorders. Growth:* Moderately reduced weight gain and growth retardation have been reported with the long-term use in children. Treatment interruption may be necessary. *Seizures*: Use with caution in patients with epilepsy. If seizure frequency increases or new-onset seizures occur, methylphenidate should be discontinued. *Abuse, misuse and diversion:* Use with caution in patients with known drug or alcohol dependency because of a potential for abuse. *Priapism*: Patients who develop abnormally sustained or frequent and painful erections should seek immediate medical attention. *Use with serotonergic medicinal products:* Serotonin syndrome has been reported following co-administration with serotonergic medicinal products. If concomitant use is warranted, prompt recognition of serotonin syndrome is important: these may include mental-status changes, autonomic instability, neuromuscular abnormalities, and/ or gastrointestinal symptoms. Discontinue methylphenidate as soon as possible if serotonin syndrome is suspected. *Withdrawal*: Careful supervision is required during withdrawal. Long-term follow up may be required. *Fatigue*: Should not be used for the prevention or treatment of normal fatigue states. *Choice of methylphenidate formulation:* This would be the decision of the treating specialist. *Drug screening:* Methylphenidate may induce a false positive laboratory test for amphetamines, particularly with immunoassay screen test. *Renal or hepatic insufficiency:* No data available. *Haematological effects:* Discontinuation of treatment should be considered in the event of leukopenia, thrombocytopenia, anaemia or other alterations, including those indicative of serious renal or hepatic disorders. *Excipients:* Contains lactose, therefore patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. **Interactions**: *Pharmacokinetic interaction:* Caution is recommended at combining methylphenidate with other medicinal products, especially those with a narrow therapeutic window. Methylphenidate is not metabolised by cytochrome P450 to a clinically relevant extent. Inducers or inhibitors of cytochrome P450 are not expected to have any relevant impact on methylphenidate pharmacokinetics. However, reports indicate that methylphenidate may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (e.g. phenobarbital, phenytoin, primidone), and some antidepressants (tricyclics and selective serotonin reuptake inhibitors). When starting or stopping treatment with methylphenidate, it may be necessary to adjust the dosage of these medicinal products already being taken and establish plasma concentrations (or for coumarin, coagulation times). *Pharmacodynamic interactions: Anti-hypertensive medicinal products:* may decrease the effectiveness of anti-hypertensives. *Use with medicinal products that elevate blood pressure:* Caution. *Use with alcohol:* Patients should abstain from alcohol during treatment. *Use with serotonergic medicinal products:* See above. *Use with halogenated anaesthetics:* Risk of sudden blood pressure increase during surgery. If surgery is planned, methylphenidate treatment should not be used on the day of surgery. *Use with centrally acting alpha-2 agonists (e.g. clonidine):* Long-term safety of concomitant administration has not been systematically evaluated. *Use with dopaminergic (agonists and antagonists including antipsychotics) medicinal products:* Caution. **Fertility, pregnancy and lactation:** *Fertility:* No relevant effects observed. *Pregnancy*: Data from a cohort study of in total approximately 3,400 pregnancies exposed in the first trimester do not suggest an increased risk of overall birth defects. There was a small increased occurrence of cardiac malformations corresponding to 3 additional infants born with congenital cardiac malformations for every 1000 women who receive methylphenidate during the first trimester of pregnancy, compared with non-exposed pregnancies. *Breast-feeding*: Methylphenidate is excreted in human milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from methylphenidate therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. **Effects on ability to drive and use machines:** Can cause dizziness, drowsiness and visual disturbances including difficulties with accommodation, diplopia and blurred vision. It may have a moderate influence on the ability to drive and use machines. If affected, patients should avoid potentially hazardous activities. **Undesirable effects**: *Very common (≥ 1/10):* insomnia, nervousness and headache. *Common (≥ 1/100 to < 1/10):* nasopharyngitis, upper respiratory tract infection, sinusitis, anorexia, decreased appetite, moderately reduced weight and height gain during prolonged use in children, affect lability, aggression, agitation, anxiety, depression, irritability, abnormal behaviour, mood swings, tics, initial insomnia, depressed mood, decreased libido, tension, bruxism, panic attack, dizziness, dyskinesia, psychomotor hyperactivity, somnolence, paraesthesia, tension headache, accommodation disorder, vertigo, arrhythmia, tachycardia, palpitations, hypertension, cough, oropharyngeal pain, upper abdominal pain, diarrhoea, nausea, abdominal discomfort, vomiting, dry mouth, dyspepsia, alopecia, hyperhidrosis, pruritus, rash, urticaria, arthralgia, muscle tightness, muscle spasms, erectile dysfunction, pyrexia, growth retardation during prolonged use in children, fatigue, irritability, feeling jittery, asthenia, thirst, changes in blood pressure and heart rate (usually an increase), weight decreased and alanine aminotransferase increased. **Consult SPC for other side effects. Overdose:** There is no specific antidote to methylphenidate overdosage. Treatment consists of appropriate supportive measures. See SPC for treatment guidance. **Marketing authorisation number and Basic NHS Price:** All strengths are sold in packs of 30 prolonged-release tablets. Xaggitin 18 mg PL 01883/0359 - £15.58; Xaggitin 27 mg PL 01883/0360 - £18.40; Xaggitin 36 mg PL 01883/0361 - £21.22 and Xaggitin 54 mg PL 01883/0362 - £36.80. **Marketing authorisation Holder:** Macarthys Laboratories Ltd, T/A Martindale Pharma, Bampton Road, Harold Hill, Romford, Essex, RM3 8UG, United Kingdom. **Legal category**: POM. **Further information:** Martindale Pharma, Bampton Road, Romford, RM3 8UG. Tel: 01277 266 600. **Date of Preparation:** February 2021

Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Martindale Pharma, an Ethypharm Group Company. Tel: 01277 266 600. e-mail: drugsafety.uk@ethypharm.com