METHYLPHENIDATE 10 BIOTECH

SCHEDULING STATUS:

S6

1. NAME OF THE MEDICINE

METHYLPHENIDATE 10 BIOTECH tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 mg methylphenidate hydrochloride.
Sugar free.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets.
White, round, flat scored tablet marked with "RU 10" on one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Attention deficit hyperactivity disorder (ADHD) in children aged 6 years or older.
Narcolepsy in adults.

4.2 Posology and method of administration

Posology

The dosage of METHYLPHENIDATE 10 BIOTECH should be individualised according to the patient's clinical needs and responses.
METHYLPHENIDATE 10 BIOTECH should be started at a low dose, with increments at weekly intervals. Daily doses above 60 mg are not recommended for the treatment of narcolepsy in adults, or for the treatment of ADHD in children. Effective doses in adults may vary, and range from 40 mg – 80 mg per day.
If improvement is not observed after appropriate dosage adjustment over a one-month period, METHYLPHENIDATE 10 BIOTECH should be discontinued.
If paradoxical aggravation of symptoms or other adverse effects occur, METHYLPHENIDATE 10 BIOTECH should be discontinued.

Pre-treatment screening

Before initiating METHYLPHENIDATE 10 BIOTECH treatment, patients should be assessed for pre-existing cardiovascular and psychiatric disorders and a family history of sudden death, ventricular dysrhythmia and psychiatric disorders (see sections 4.3 and 4.4).

Narcolepsy

The average dosage is 20 to 30 mg daily, given in 2 to 3 divided doses. Some patients may require 40 to 60 mg daily. In others, 10 to 15 mg daily will be adequate. Patients who are unable to sleep if METHYLPHENIDATE 10 BIOTECH is taken late in the day should take the last dose before 6 p.m. (18:00). A total daily dose of 60 mg should not be exceeded.

Periodic assessment of the treatment in ADHD

Medicine treatment should not and need not be indefinite.
METHYLPHENIDATE 10 BIOTECH should be periodically discontinued to assess the patient's condition. Improvement may be sustained when the medicine is either temporarily or permanently discontinued. When used in children with ADHD, METHYLPHENIDATE 10 BIOTECH can usually be discontinued after puberty.

ADHD

Children and adolescents (6 years and older):

Start with 5 mg once or twice daily (before breakfast and lunch) with gradual increments of 5 to 10 mg weekly. The total daily dose should be administered in divided doses.
Daily dosage above 60 mg is not recommended.

Special populations

Elderly:

Safety and efficacy have not been established in patients over 60 years of age.

Hepatic impairment

METHYLPHENIDATE 10 BIOTECH has not been studied in patients with hepatic impairment. Caution should be exercised in these patients.

Renal impairment

METHYLPHENIDATE 10 BIOTECH has not been studied in patients with renal impairment. Caution should be exercised in these patients.

Paediatric population

Children under 6 years of age:

METHYLPHENIDATE 10 BIOTECH is not indicated in children less than six years of age.

Method of administration

METHYLPHENIDATE 10 BIOTECH is for oral administration and can be taken with or without food

4.3 Contraindications

- Known hypersensitivity to methylphenidate or to any of the excipients of METHYLPHENIDATE 10 BIOTECH (see section 6.1).
- Anxiety, tension, agitation, a family history or diagnosis of Tourette's syndrome, hyperthyroidism, glaucoma, phaeochromocytoma.
- Pre-existing cardiovascular disorders, including hypertension, angina, arterial occlusive disease; heart failure, haemodynamically significant congenital heart disease, cardiomyopathies, myocardial infarction, potentially life-threatening dysrhythmias, channelopathies (disorders caused by the dysfunction of ion channels) and QT prolongation either congenital, familial or caused by medication (see section 4.4).
- During treatment with monoamine oxidase (MAO) inhibitors, or within a minimum of 2 weeks of discontinuing those medicines, due to risk of hypertensive crisis (see section 4.5).
- Pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

General

Methylphenidate treatment is not indicated in all children with ADHD and the decision to use METHYLPHENIDATE 10 BIOTECH 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, and not simply on the presence of one or more abnormal behavioural characteristics.
METHYLPHENIDATE 10 BIOTECH should not be used for the treatment of attention deficit or hyperactivity secondary to amenable causes, including acute stress reactions.

Long-term use (more than 12 months) in children and adolescents

The safety and efficacy of long-term use of methylphenidate, as contained in METHYLPHENIDATE 10 BIOTECH, have not been systematically evaluated in controlled trials. METHYLPHENIDATE 10 BIOTECH treatment should not and need not be indefinite. Methylphenidate treatment is usually discontinued after puberty (see section 4.2).

Use in adults with ADHD

METHYLPHENIDATE 10 BIOTECH is not indicated for use in adults with ADHD. Safety and efficacy have not yet been established in this age group.

Use in the elderly

Safety and efficacy have not been established in patients over 60 years of age.

Use in children under 6 years of age

METHYLPHENIDATE 10 BIOTECH is not indicated in children less than six years of age.

Cardiovascular conditions

METHYLPHENIDATE 10 BIOTECH is contraindicated in patients with hypertension. METHYLPHENIDATE 10 BIOTECH increases heart rate and systolic and diastolic blood pressure. Therefore, caution is indicated 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 and severe cardiovascular disorders (see section 4.3).
Blood pressure should be monitored at appropriate intervals in all patients taking METHYLPHENIDATE 10 BIOTECH. Patients who develop symptoms suggestive of cardiac disease during METHYLPHENIDATE 10 BIOTECH treatment should undergo a prompt cardiac evaluation.

Sudden death and pre-existing cardiac structural 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, some of whom had structural cardiac abnormalities or other serious heart problems.
Although some serious heart problems alone may carry an increased risk of sudden death METHYLPHENIDATE 10 BIOTECH is not recommended in patients with known cardiac structural 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 medicine. Before initiating METHYLPHENIDATE 10 BIOTECH treatment, patients should be assessed for pre-existing cardiovascular disorders such as a congenital long QT syndrome, or a family history of sudden death and ventricular dysrhythmia.

Misuse and cardiovascular events

Misuse of stimulants of the central nervous system, such as METHYLPHENIDATE 10 BIOTECH, may be associated with sudden death and other serious cardiovascular adverse events.

Cerebrovascular disorders

Patients with pre-existing central nervous system (CNS) abnormalities, e.g. cerebral aneurysm and/or other vascular abnormalities such as vasculitis or pre-existing stroke should not be treated with METHYLPHENIDATE 10 BIOTECH.
Patients with additional risk factors (such as a history of cardiovascular disease, concomitant medicines that elevate blood pressure) should be assessed at every visit for neurological signs and symptoms after initiating treatment with METHYLPHENIDATE 10 BIOTECH.
Cerebral vasculitis appears to be a very rare idiosyncratic reaction to methylphenidate exposure. There is little evidence to suggest that patients at higher risk can be identified and the initial onset of symptoms may be the first indication of an underlying clinical problem.
Early diagnosis, based on a high index of suspicion, may allow the prompt withdrawal of METHYLPHENIDATE 10 BIOTECH and early treatment. The diagnosis should therefore be considered in any patient who develops new neurological symptoms that are consistent with cerebral ischaemia during METHYLPHENIDATE 10 BIOTECH therapy. These symptoms could include severe headache, numbness, weakness, paralysis, and impairment of coordination, vision, speech, language or memory.
Treatment with METHYLPHENIDATE 10 BIOTECH is not contraindicated in patients with hemiplegic cerebral palsy.

Psychiatric disorders

Co-morbidity of psychiatric disorders in ADHD is common and should be taken into account when prescribing METHYLPHENIDATE 10 BIOTECH. Prior to initiating treatment with METHYLPHENIDATE 10 BIOTECH, patients should be assessed for pre-existing psychiatric disorders and a family history of psychiatric disorders (see section 4.2). Treatment of ADHD with METHYLPHENIDATE 10 BIOTECH should not be initiated in patients with acute psychosis, acute mania or acute suicidality. These acute conditions should be treated and controlled before ADHD treatment is considered.
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.
Development or worsening of psychiatric disorders should be monitored at every adjustment of dose, then at least every 6 months, and at every visit; discontinuation of treatment may be appropriate.

Exacerbation of pre-existing psychotic or manic symptoms

In psychotic patients, administration of METHYLPHENIDATE 10 BIOTECH may exacerbate symptoms of behavioural disturbance and thought disorder.

Emergence of new psychotic or manic symptoms

Treatment-emergent psychotic symptoms (visual/tactile/auditory hallucinations and delusions) or mania in patients without prior history of psychotic illness or mania can be caused by METHYLPHENIDATE 10 BIOTECH at usual doses. If manic or psychotic symptoms occur, consideration should be given to a possible causal role for methylphenidate and discontinuation of treatment may be appropriate.

Aggressive or hostile behaviour

The emergence or worsening of aggression or hostility can be caused by treatment with stimulants. Patients treated with METHYLPHENIDATE 10 BIOTECH should be closely monitored for the emergence or worsening of aggressive behaviour or hostility at treatment initiation, at every dose adjustment and then at least every 6 months or every visit. Medical practitioners should evaluate the need for adjustment of the treatment regimen in patients experiencing behavioural changes, bearing in mind that upwards or downwards titration may be appropriate. Treatment interruption can be considered.

Suicidal tendency

Patients with emergent suicidal ideation or behaviour during treatment for ADHD should be evaluated immediately by their medical practitioner. Consideration should be given to the exacerbation of an underlying psychiatric condition and to a possible causal role of METHYLPHENIDATE 10 BIOTECH treatment. Treatment of an underlying psychiatric condition may be necessary, and consideration should be given to a possible discontinuation of METHYLPHENIDATE 10 BIOTECH.

Tics

Methylphenidate is associated with the onset or exacerbation of motor and verbal tics. Worsening of Tourette's syndrome has also been reported. Family history should be assessed and clinical evaluation for tics or Tourette's syndrome in children should precede use of METHYLPHENIDATE 10 BIOTECH. Patients should be regularly monitored for the emergence or worsening of tics during treatment with METHYLPHENIDATE 10 BIOTECH.

Anxiety, agitation or tension

METHYLPHENIDATE 10 BIOTECH is associated with the worsening of pre-existing anxiety, agitation or tension. METHYLPHENIDATE 10 BIOTECH is contraindicated in patients suffering from these conditions (see section 4.3).

Forms of bipolar disorder

Particular care should be taken in using METHYLPHENIDATE 10 BIOTECH to treat ADHD in patients with comorbid bipolar disorder (including untreated type 1 bipolar disorder or other forms of bipolar disorder) because of concern for possible precipitation of a mixed/manic episode in such patients. Prior to initiating treatment with METHYLPHENIDATE 10 BIOTECH, 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. Close ongoing monitoring is essential in these patients (see above "Psychiatric disorders" and section 4.2). Patients should be monitored for symptoms at every adjustment of dose, then at least every 6 months and at every visit.

Serotonin syndrome

Serotonin syndrome has been reported following co-administration of methylphenidate with serotonergic medicines such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs). The concomitant use of METHYLPHENIDATE 10 BIOTECH and serotonergic medicines is not recommended as this may lead to the development of serotonin syndrome. The symptoms of serotonin syndrome may include mental status changes (e.g. agitation, hallucinations, delirium, and coma), autonomic instability (e.g. tachycardia, labile blood pressure, dizziness, diaphoresis, flushing, hyperthermia), neuromuscular symptoms (e.g. tremor, rigidity, myoclonus, hyperreflexia, incoordination), seizures, and/or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea). Prompt recognition of these symptoms is important so that treatment with METHYLPHENIDATE 10 BIOTECH and serotonergic medicines can be immediately discontinued, and appropriate treatment instituted (see section 4.5).

Priapism

Prolonged and painful erections have been reported in association with methylphenidate products, mainly in association with a change in the methylphenidate treatment regimen. Patients who develop abnormally sustained or frequent and painful erections should seek immediate medical attention.

Growth retardation

Moderately reduced body mass gain and growth retardation have been reported with long-term use of methylphenidate in children.
Patients who are not growing or gaining height or body mass as expected may need to have their METHYLPHENIDATE 10 BIOTECH treatment interrupted and adjusted.

Seizures

METHYLPHENIDATE 10 BIOTECH should be used with caution in patients with epilepsy. Methylphenidate may lower the convulsive threshold in patients with prior history of seizures, in patients with prior EEG abnormalities in absence of seizures, and in patients without a history of convulsions and no EEG abnormalities. If seizure frequency increases or new-onset seizures occur, METHYLPHENIDATE 10 BIOTECH should be discontinued.

Abuse, misuse and dependence

Patients should be carefully monitored for the risk of diversion, misuse and abuse of METHYLPHENIDATE 10 BIOTECH.
METHYLPHENIDATE 10 BIOTECH should be used with caution in patients with known drug or alcohol dependency, because of a potential for abuse, misuse or diversion.
Chronic abuse of METHYLPHENIDATE 10 BIOTECH can lead to marked tolerance and psychological dependence with varying degrees of abnormal behaviour. Frank psychotic episodes can occur, especially in response to parenteral abuse.
Patient age, the presence of risk factors for substance use disorder (such as comorbid oppositional-defiant or conduct disorder and bipolar disorder), and previous or current substance abuse should be taken into account when deciding on a course of treatment for ADHD. Caution is called for in emotionally unstable patients, such as those with a history of drug or alcohol dependence, because such patients may increase the dosage on their own initiative.
For some high-risk substance abuse patients, METHYLPHENIDATE 10 BIOTECH may not be suitable.

Withdrawal

Careful supervision is required during withdrawal, since this may unmask depression as well as chronic overactivity. Some patients may require long-term follow-up. Careful supervision is required during withdrawal from abusive use since severe depression may occur.

Fatigue

METHYLPHENIDATE 10 BIOTECH should not be used for the prevention or treatment of normal fatigued states.

Drug screening

METHYLPHENIDATE 10 BIOTECH contains methylphenidate which may induce a false positive laboratory test for amphetamines, particularly with immunoassay screen test.

Renal or hepatic insufficiency

There is no experience with the use of METHYLPHENIDATE 10 BIOTECH in patients with renal or hepatic insufficiency.

Haematological effects

The long-term safety of treatment with methylphenidate, as in METHYLPHENIDATE 10 BIOTECH, is not fully known. Patients requiring long-term therapy should therefore be carefully monitored and complete and differential blood counts and a platelet count performed periodically. In the event of leucopenia, thrombocytopenia, anaemia or other alterations, including those indicative of serious renal or hepatic disorders, discontinuation of treatment should be considered.

4.5 Interaction with other medicines and other forms of interaction

It is not known how methylphenidate, as contained in METHYLPHENIDATE 10 BIOTECH, may affect plasma concentrations of concomitantly administered medicines. Therefore, caution is recommended at combining METHYLPHENIDATE 10 BIOTECH with other medicines, especially those with a narrow therapeutic window.

Pharmacokinetic interactions

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. Conversely, the d- and l-enantiomers of methylphenidate do not relevantly inhibit cytochrome P450 1A2, 2C8, 2C9, 2C19, 2D6, 2E1 or 3A.

However, there are reports indicating that methylphenidate, as contained in METHYLPHENIDATE 10 BIOTECH, may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (e.g. phenobarbital, phenytoin, primidone), and some antidepressants (tricyclic and selective serotonin reuptake inhibitors). When starting and stopping treatment with METHYLPHENIDATE 10 BIOTECH, it may be necessary to adjust the dosage of these medicines that are already being taken and establish plasma concentrations (or for coumarin, coagulation times).
METHYLPHENIDATE 10 BIOTECH coadministration did not increase plasma concentrations of the CYP2D6 substrate desipramine.

Pharmacodynamic interactions
Anti-hypertensive medicines
Methylphenidate may decrease the effectiveness of medicines used to treat hypertension.
Use with medicines that elevate blood pressure
Caution is advised in patients being treated with METHYLPHENIDATE 10 BIOTECH with other medicines that can also elevate blood pressure (see also sections on cardiovascular and cerebrovascular conditions in section 4.4).
Because of possible hypertensive crisis, METHYLPHENIDATE 10 BIOTECH or is contraindicated in patients being treated (currently or within the preceding 2 weeks) with MAO inhibitors (see section 4.3).
Use with alcohol
Alcohol may exacerbate the adverse CNS effects of psychoactive medicines, including METHYLPHENIDATE 10 BIOTECH. It is therefore advisable for patients to abstain from alcohol during treatment.
Use with anaesthetics
There is a risk of sudden blood pressure and heart rate increase during surgery. If surgery is planned, treatment with METHYLPHENIDATE 10 BIOTECH should not be used on the day of surgery.
Use with centrally acting alpha$_2$ agonists (e.g. clonidine or dexmedetomidine)
Serious adverse events including sudden death may occur in concomitant use with clonidine or dexmedetomidine.
Use with dopaminergic medicines
Caution is recommended when administering METHYLPHENIDATE 10 BIOTECH with dopaminergic medicines, including antipsychotics. Because a predominant action of methylphenidate is to increase extracellular dopamine levels, METHYLPHENIDATE 10 BIOTECH may be associated with pharmacodynamic interactions when co-administered with direct and indirect dopamine agonists (including DOPA and tricyclic antidepressants) or with dopamine antagonists including antipsychotics.
Use with serotonergic medicines
The concomitant use of METHYLPHENIDATE 10 BIOTECH and serotonergic medicines is not recommended as this may lead to the development of serotonin syndrome (see section 4.4). Methylphenidate has been shown to increase extracellular serotonin and norepinephrine and appears to have weak potency in binding serotonin transporter.
Medicine/Laboratory test
METHYLPHENIDATE 10 BIOTECH may induce false positive laboratory tests for amphetamines, particularly with immunoassays screen test.

4.6 Fertility, pregnancy and lactation
Pregnancy
METHYLPHENIDATE 10 BIOTECH is contraindicated during pregnancy (see section 4.3).
There is a limited amount of data from the use of methylphenidate, as contained in METHYLPHENIDATE 10 BIOTECH, in pregnant women.
Breastfeeding
METHYLPHENIDATE 10 BIOTECH is contraindicated during lactation as safety has not been demonstrated (see section 4.3).
Mothers taking METHYLPHENIDATE 10 BIOTECH should not breastfeed their infants.
Methylphenidate, as contained in METHYLPHENIDATE 10 BIOTECH, has been found in breast milk of women treated with methylphenidate.

4.7 Effects on ability to drive and use machines
METHYLPHENIDATE 10 BIOTECH may cause dizziness, drowsiness and visual disturbances including difficulties with accommodation, diplopia and blurred vision (see section 4.8). It may have a moderate influence on the ability to drive and use machines. Patients should be warned of these possible effects and advised that if affected, they should avoid potentially hazardous activities such as driving a vehicle or operating machinery.

4.8 Undesirable effects
Infections and infestations
Frequent: nasopharyngitis
Blood and lymphatic disorders
Less frequent: anaemia, leucopenia, thrombocytopenia, thrombocytopenic purpura
Frequency unknown: pancytopenia
Immune system disorders
Less frequent: hypersensitivity reactions such as angioneurotic oedema, anaphylactic reactions, auricular swelling, bullous conditions, exfoliative conditions, urticaria, pruritis, rashes and eruptions
Metabolism and nutritional disorders*
Frequent: anorexia, decreased appetite, moderately reduced body mass and height gain during prolonged use in children
Psychiatric disorders*
*Frequent: i*nsomnia, nervousness, affect lability, aggression*, agitation*, anxiety*, depression*, irritability, abnormal behaviour
Less frequent: psychotic disorders*, auditory, visual, and tactile hallucinations*, anger, suicidal ideation*, mood altered, mood swings, restlessness, tearfulness, tics*, worsening of pre-existing tics or Tourette's syndrome*, hypervigilance, sleep disorder, mania*, disorientation, libido disorder, suicidal attempt (including completed suicide)*, transient depressed mood*, abnormal thinking, apathy, repetitive behaviours, over-focussing
Frequency unknown: delusions*, thought disturbances*, confusional state, dependence, logorrhoea. Cases of abuse and dependence have been described, more often with immediate release formulations (frequency not known).
Nervous system disorders
Frequent: headache, dizziness, dyskinesia, psychomotor hyperactivity, somnolence
Less frequent: sedation, tremor, convulsions, choreo-athetoid movements, reversible ischaemic neurological deficit, neuroleptic malignant syndrome (NMS) (reports were poorly documented and in most cases, patients were also receiving other medicines, so the role of methylphenidate is unclear)
Frequency unknown: cerebrovascular disorders* (including vasculitis, cerebral haemorrhages, cerebrovascular incidents, grand mal convulsions*, migraine
Eye disorders
Less frequent: diplopia, blurred vision, difficulties in visual accommodation, mydriasis, visual disturbance
Cardiac disorders*
Frequent: dysrhythmia, tachycardia, palpitations
Less frequent: chest pain, angina pectoris, cardiac arrest, myocardial infarction, sudden cardiac death*
Frequency unknown: supraventricular tachycardia, bradycardia, ventricular extrasystoles, extrasystoles
Vascular disorders*
Frequent: hypertension
Less frequent: cerebral arteritis and/or occlusion, peripheral coldness, Raynaud's phenomenon
Respiratory, thoracic and mediastinal disorders
Frequent: cough, pharyngolaryngeal pain
Less frequent: dyspnoea
Gastro-intestinal disorders
Frequent: abdominal pain, diarrhoea, nausea, stomach discomfort and vomiting (these usually occur at the beginning of treatment and may be alleviated by concomitant food intake), dry mouth
Less frequent: constipation
Hepatobiliary disorders
Less frequent: hepatic enzyme elevations, abnormal liver functions, including hepatic coma
Skin and subcutaneous tissue disorders
Frequent: alopecia, pruritis, rash, urticaria
Less frequent: angioneurotic oedema, bullous conditions, exfoliate conditions, hyperhidrosis, macular rash, erythema, erythema multiforme, exfoliate dermatitis, fixed drug eruption
Musculoskeletal, connective tissue and bone disorders
Frequent: arthralgia
Less frequent: myalgia, muscle twitching, muscle cramps
Renal and urinary disorders
Less frequent: haematuria
Reproductive system and breast disorders
Less frequent: gynaecomastia
Frequency unknown: erectile dysfunction, priapism, increased erection and prolonged erection
General disorders and administration site conditions
Frequent: pyrexia, growth retardation during prolonged use in children*
Less frequent: fatigue
Frequency unknown: chest discomfort, hyperpyrexia
Investigations
Frequent: changes in blood pressure and heart rate (usually an increase)*, decreased body mass *
Less frequent: cardiac murmur*, increased hepatic enzyme, increased blood alkaline phosphatase, increased blood bilirubin, decreased platelet count, abnormal white blood count.
* See section 4.4 'SPECIAL WARNINGS AND PRECAUTIONS FOR USE'.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of METHYLPHENIDATE 10 BIOTECH is important. It allows continued monitoring of the benefit/risk balance of METHYLPHENIDATE 10 BIOTECH. Health care providers are asked to report any suspected adverse reactions via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose
Signs and symptoms
Acute overdose, mainly due to overstimulation of the central and sympathetic nervous systems, may result in vomiting, agitation, tremors, hyperreflexia, muscle twitching, convulsions (may be followed by coma), euphoria, confusion, hallucinations, delirium, sweating, flushing, headache, hyperpyrexia, tachycardia, palpitations, cardiac dysrhythmias, hypertension, mydriasis, dryness of mucous membranes and rhabdomyolysis.
Treatment
There is no specific antidote to methylphenidate overdosage. Treatment consists of appropriate supportive measures and symptomatic treatment of life-threatening events e.g. hypertensive crisis, cardiac dysrhythmias, convulsions. For the most current guidance for treatment of symptoms of overdose, the medical practitioner should consult a certified poison centre or current toxicological publication.
The patient must be protected against self-injury and against external stimuli that would aggravate over-stimulation already present. If the patient is conscious, administration of activated charcoal and a laxative is recommended. In the presence of severe intoxication, a carefully titrated dose of a benzodiazepine should be given.
Intensive care must be provided to maintain adequate circulation and respiratory exchange; external cooling procedures may be required to reduce hyperpyrexia.
Efficacy of peritoneal dialysis or extracorporeal haemodialysis for overdose of methylphenidate has not been established.

5. PHARMACOLOGICAL PROPERTIES
Category and class: A 1.2 Psychoanaleptics (antidepressants)

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Psychostimulants – ATC code: N06B A04.
Mode of action: Methylphenidate is a mild CNS stimulant with more prominent effects on mental than on motor activities. Its mode of action in man is not completely understood but its effects are thought to be due to an inhibition of dopamine reuptake in the striatum, without triggering the release of dopamine. The mechanism by which methylphenidate exerts its mental and behavioural effects in children is not clearly established, nor is there conclusive evidence showing how these effects relate to the condition of the central nervous system.
Methylphenidate is a racemic mixture containing d- and l-enantiomers, where the d-enantiomer is considered as the pharmacologically active enantiomer.

5.2 Pharmacokinetic properties
Absorption
The active substance methylphenidate hydrochloride is rapidly and almost completely absorbed from the tablets. Owing to extensive first-pass metabolism the absolute bioavailability was 22 ± 8 % for the d-enantiomer and 5 ± 3 % for the l-enantiomer. Ingestion together with food increased both the peak plasma concentration (C_{max}) by 23 % and the area under the concentration-time curve (AUC) by 15 %, but had no relevant effect on the rate of absorption of methylphenidate. Peak plasma concentrations of approximately 40 nmol/L (11 ng/mL) are attained, on average, 1 – 2 hours after administration of 0,30 mg/kg. The peak plasma concentrations, however, show considerable intersubject variability. The AUC and the C_{max} are proportional to the dose.
Distribution
In the blood, methylphenidate and its metabolites become distributed in the plasma (57 %) and the erythrocytes (43 %).
Methylphenidate and its metabolites have a low plasma protein-binding rate (10 – 33 %). The volume of distribution was 2,65 ± 1,11 L/kg for d-MPH and 1,80 ± 0,91 L/kg for l-MPH.
Biotransformation
Biotransformation of methylphenidate by the carboxylesterase CES1A1 is rapid and extensive. Peak plasma concentrations of α-phenyl-2-piperidyl acetic acid (ritalinic acid) (PPAA) are attained approximately 2 hours after administration of methylphenidate and are 30 – 50 times higher than those of the unchanged substance. The half-life of PPAA is roughly twice as long as that of methylphenidate, and the mean systemic clearance is 0,17 L/h/kg. Only small amounts of hydroxylated metabolites (e.g. hydroxymethylphenidate and hydroxyritalinic acid) are detectable. Therapeutic activity seems to be principally due to the parent compound.
Elimination
Methylphenidate is eliminated from the plasma with a mean half-life of 2 hours. The systemic clearance is 0,40 ± 0,12 L/h/kg for d-MPH and 0,73 ± 0,28 L/h/kg for l-MPH. Within 48 – 96 hours 78 – 97 % of the dose administered is excreted in the urine and 1 – 3 % in the faeces in the form of metabolites. Unchanged methylphenidate appears in the urine only in small quantities (< 1 %). The bulk of the dose is excreted in the urine as PPAA (60 – 86 %).
Characteristics in patients
There are no apparent differences in the pharmacokinetic behaviour of methylphenidate in hyperactive children and healthy adult volunteers.
Elimination data from patients with normal renal function suggest that renal excretion of the unchanged methylphenidate would hardly be diminished at all in the presence of impaired renal function. However, renal excretion of PPAA may be reduced.

5.3 Preclinical safety data
No further information of relevance available.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Calcium hydrogen phosphate dihydrate
Magnesium stearate
Maize starch
Microcrystalline cellulose.

6.2 Incompatibilities
None known.

6.3 Shelf life
4 years.

6.4 Special precautions for storage
- Store at or below 25 °C. Protect from moisture.
- Keep blister strips in outer carton until required for use.

6.5 Nature and contents of container
PVC/aluminium blister strip, containing ten tablets. Three blister strips are packed in an outer carton.
Pack size: 30 tablets.

6.6 Special precautions for disposal and other handling
None.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Biotech Laboratories (Pty) Ltd
Ground Floor, Block K West, Central Park
400 16th Road, Randjespark, Midrand, 1685
South Africa

8. REGISTRATION NUMBER
49/1.2/1000

9. DATE OF FIRST AUTHORISATION
20 July 2020

10. DATE OF REVISION OF THE TEXT
20 July 2020

Botswana: Reg. No.: BOT2304004	1A

METHYLPHENIDATE 10 BIOTECH

SKEDULERINGSTATUS

S6

1. NAAM VAN DIE MEDISYNE

METHYLPHENIDATE 10 BIOTECH-tablette

2. KWALITATIEWE EN KWANTITATIEWE SAMESTELLING

Elke tablet bevat 10 mg metielfenidaathidrochloried.
Suikervry.
Sien afdeling 6.1 vir die volledige lys van hulpstowwe.

3. FARMASEUTIESE VORM

Tablette
Wit, ronde, plat, tablet met "RU 10" op een kant en die ander kant skoon.

4. KLINIESE BESONDERHEDE

4.1 Terapeutiese indikasies

Aandagtekort hiperaktiwiteitversteuring ("Attention deficit hyperactivity disorder - ADHD") in kinders van 6 jaar of ouer.
Narkolepsie in volwassenes.

4.2 Posologie en metode van toediening

Posologie

Die dosis van METHYLPHENIDATE 10 BIOTECH moet volgens die pasiënt se kliniese behoeftes en reaksie geïndividualiseer word.
METHYLPHENIDATE 10 BIOTECH moet teen 'n lae dosis begin word, met inkremente met weeklikse intervalle.
Daaglikse dosisse van meer as 60 mg word nie aanbeveel vir die behandeling van narkolepsie in volwassenes of vir die behandeling van ADHD in kinders nie. Effektiewe dosisse vir volwassenes kan wissel van 40 mg tot 80 mg per dag.
As verbetering nie na toepaslike aanpassing in die dosis oor 'n periode van een maand waargeneem word nie, moet METHYLPHENIDATE 10 BIOTECH gestaak word.
As paradoksale verergering van simptome of ander nadelige effekte voorkom, moet METHYLPHENIDATE 10 BIOTECH gestaak word.

Sifting voor behandeling

Voordat behandeling met METHYLPHENIDATE 10 BIOTECH begin, moet pasiënte beoordeel word vir bestaande kardiovaskulêre en psigiatriese afwykings en 'n familiegeskiedenis van skielike dood, ventrikulêre ritmestoornisse en psigiatriese versteurings (sien afdelings 4.3 en 4.4).

Narkolepsie

Die gemiddelde dosis is 20 tot 30 mg daagliks, in 2 tot 3 verdeelde dosisse gegee. Party pasiënte kan 40 tot 60 mg daagliks nodig hê. In ander sal 10 tot 15 mg per dag voldoende wees. Pasiënte wat nie kan slaap as METHYLPHENIDATE 10 BIOTECH laat in die dag gedrink word nie, moet die laaste dosis voor 6 nm (18:00) drink.
'n Totale daaglikse dosis van 60 mg moet nie oorskry word nie.

Periodieke assessering van die behandeling vir ADHD

Behandeling met die medisyne moet en hoef nie onbepaald te wees nie.
METHYLPHENIDATE 10 BIOTECH moet periodiek gestaak word om die pasiënt se toestand te bepaal. Verbetering kan voortduur wanneer die medisyne tydelik of permanent gestaak word.
Wanneer dit vir kinders met ADHD gebruik word, kan METHYLPHENIDATE 10 BIOTECH gewoonlik na puberteit gestaak word.

ADHD

Kinders en adolessente (6 jaar en ouer)

Begin met 5 mg een of twee keer per dag (voor ontbyt en voor middagete) met geleidelike inkremente van 5 tot 10 mg per week. Die totale daaglikse dosis moet in verdeelde doserings toegedien word. Daaglikse dosisse bo 60 mg word nie aanbeveel nie.

Spesiale populasies

Bejaardes

Die veiligheid en effektiwiteit in pasiënte ouer as 60 jaar is nie bepaal nie.

Lewerinkorting

METHYLPHENIDATE 10 BIOTECH is nie in pasiënte met lewerinkorting bestudeer nie. Wees versigtig met hierdie pasiënte.

Nierinkorting

METHYLPHENIDATE 10 BIOTECH is nie in pasiënte met nierinkorting bestudeer nie. Wees versigtig met hierdie pasiënte.

Pediatriese populasie

Kinders jonger as 6 jaar

METHYLPHENIDATE 10 BIOTECH is nie aangedui vir kinders jonger as ses jaar nie.

Metode van toediening

METHYLPHENIDATE 10 BIOTECH is vir orale toediening en kan met of sonder kos gedrink word.

4.3 Kontra-indikasies

- Bekende hipersensitiwiteit vir metielfenidaat of vir enige van die hulpstowwe van METHYLPHENIDATE 10 BIOTECH (sien afdeling 6.1).
- Angs, spanning, agitasie, 'n familiegeskiedenis of diagnose van Tourette-sindroom, hipertireose, gloukoom, feochromositoom.
- Bestaande kardiovaskulêre versteurings, waaronder hipertensie, angina, arteriële okklusiewe siekte, hartversaking, hemodinamies beduidende aangebore hartsiektes, kardiomiopatie, miokardiale infarksie, potensieel lewensbedreigende ritmestoornisse, kanalopatie (versteurings veroorsaak deur die disfunksie van ioonkanale) en QT-verlenging, hetsy aangebore, familieel of deur medikasie veroorsaak (sien afdeling 4.4).
- Tydens behandeling met monoamienoksidase (MAO) -remmers, of binne 'n minimum van 2 weke nadat die medisyne gestaak is, vanweë die risiko vir hipertensiewe krisis (sien afdeling 4.5).
- Swangerskap en borsvoeding (sien afdeling 4.6).

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik

Algemeen

Behandeling metielfenidaat is nie vir alle kinders met ADHD aangedui nie en die besluit om METHYLPHENIDATE 10 BIOTECH te gebruik, moet gebaseer wees op 'n baie deeglike beoordeling van die erns en hoe chronies die kind se simptome in verhouding tot die ouderdom van die kind is, en nie bloot op die teenwoordigheid van een of meer abnormale gedragseienskappe nie.
METHYLPHENIDATE 10 BIOTECH moet nie gebruik word vir die behandeling van aandagafleibaarheid of hiperaktiwiteit sekondêr tot aanwesige oorsake nie, waaronder akute stresreaksies.

Langdurige gebruik (meer as 12 maande) deur kinders en adolessente

Die veiligheid en doeltreffendheid van langdurige gebruik van metielfenidaat, soos in METHYLPHENIDATE 10 BIOTECH, is nie stelselmatig in gekontroleerde proewe beoordeel nie. Behandeling met METHYLPHENIDATE 10 BIOTECH moet en hoef nie onbepaald te wees nie. Behandeling met metielfenidaat word gewoonlik na puberteit gestaak (sien afdeling 4.2).

Gebruik deur volwassenes met ADHD

METHYLPHENIDATE 10 BIOTECH is nie aangedui vir gebruik deur volwassenes met ADHD nie. Die veiligheid en doeltreffendheid vir hierdie ouderdomsgroep is nog nie bepaal nie.

Gebruik deur bejaardes

Die veiligheid en effektiwiteit vir pasiënte ouer as 60 jaar is nie bepaal nie.

Gebruik deur kinders van jonger as 6 jaar

METHYLPHENIDATE 10 BIOTECH is nie aangedui vir kinders jonger as ses jaar nie.

Kardiovaskulêre toestande

METHYLPHENIDATE 10 BIOTECH is teenaangedui vir pasiënte met hoë bloeddruk. METHYLPHENIDATE 10 BIOTECH verhoog die harttempo en sistoliese en diastoliese bloeddruk. Daarom moet pasiënte wie se onderliggende mediese toestande deur bloeddruk of hartklop in die gedrang kan kom, byvoorbeeld pasiënte met bestaande hipertensie en ernstige kardiovaskulêre afwykings versigtig behandel word (sien afdeling 4.3).
Die bloeddruk van alle pasiënte wat METHYLPHENIDATE 10 BIOTECH drink, moet met toepaslike tussenposes gemonitor word. Pasiënte wat tydens behandeling met METHYLPHENIDATE 10 BIOTECH simptome aanduidend van hartsiektes opdoen, moet dadelik vir hartfunksie geëvalueer word.

Skielike dood en bestaande abnormaliteite in hartstruktuur of ander ernstige hartversteurings

Skielike dood is met die gebruik van stimulante van die sentrale senustelsel teen gewone dosisse in kinders aangemeld, waarvan sommige strukturele hartafwykings of ander ernstige hartprobleme gehad het.
Alhoewel sommige ernstige hartprobleme alleen 'n hoë risiko vir skielike dood kan inhou, word METHYLPHENIDATE 10 BIOTECH nie aanbeveel vir pasiënte met bekende strukturele afwykings van die hart, kardiomiopatie, ernstige hartritmeafwykings of ander ernstige hartprobleme wat hulle meer kwesbaar vir simpatomimetiese effekte van stimulerende medisyne kan maak nie. Voordat behandeling met METHYLPHENIDATE 10 BIOTECH begin, moet pasiënte vir bestaande kardiovaskulêre afwykings, soos 'n aangebore lang QT-sindroom, of 'n familiegeskiedenis van skielike dood en ventrikulêre disritmie beoordeel word.

Misbruik en kardiovaskulêre voorvalle

Misbruik van stimulante van die sentrale senuweestelsel, soos METHYLPHENIDATE 10 BIOTECH, kan met skielike dood en ander ernstige kardiovaskulêre newe-effekte gepaardgaan.

Serebrovaskulêre afwykings

Pasiënte met voorafbestaande abnormaliteite van die sentrale senustelsel (SSS), bv. serebrale aneurisme en/of ander vaskulêre afwykings soos vaskulitis of voorafbestaande beroerte, moet nie met METHYLPHENIDATE 10 BIOTECH behandel word nie.
Pasiënte met addisionele risikofaktore (soos 'n geskiedenis van kardiovaskulêre siektes, gepaardgaande medisyne wat die bloeddruk verhoog) moet tydens elke besoek nadat die behandeling met METHYLPHENIDATE 10 BIOTECH begin is vir neurologiese tekens en simptome beoordeel word.
Dit lyk asof serebrale vaskulitis 'n baie seldsame idiosinkratiese reaksie op blootstelling aan metielfenidaat is. Daar is min bewyse wat daarop dui dat pasiënte met 'n hoër risiko geïdentifiseer kan word, en die aanvanklike aanvang van simptome kan die eerste aanduiding wees van 'n onderliggende kliniese probleem. Vroeë diagnose, gebaseer op 'n hoë indeks van vermoede, kan die onmiddellike onttrekking van METHYLPHENIDATE 10 BIOTECH en vroeë behandeling moontlik maak. Die diagnose moet dus oorweeg word vir enige pasiënt wat tydens behandeling met METHYLPHENIDATE 10 BIOTECH nuwe neurologiese simptome ontwikkel wat met serebrale iskemie ooreenstem. Hierdie simptome kan erge hoofpyn, gevoelloosheid, swakheid, verlamming en aftakeling van koördinasie, sig, spraak, taal of geheue wees.
Behandeling met METHYLPHENIDATE 10 BIOTECH is nie teenaangedui vir pasiënte met hemiplegiese serebrale gestremdheid nie.

Psigiatriese versteurings

Komorbiditeit van psigiatriese versteurings in ADHD is algemeen en moet in ag geneem word wanneer METHYLPHENIDATE 10 BIOTECH voorgeskryf word. Voordat die behandeling met METHYLPHENIDATE 10 BIOTECH begin, moet pasiënte beoordeel word vir bestaande psigiatriese versteurings en 'n familiegeskiedenis van psigiatriese versteurings (sien afdeling 4.2). Behandeling van ADHD met METHYLPHENIDATE 10 BIOTECH moet nie begin word vir pasiënte met akute psigose, akute manie of akute selfdoodneigings nie. Hierdie akute toestande moet behandel en beheer word voordat behandeling van ADHD oorweeg word.
metielfenidaat moet nie in geval van nuwe psigiatriese simptome of verergering van bestaande psigiatriese versteurings gegee word nie, tensy die voordele die risiko's vir die pasiënt oorskry. Die ontwikkeling of verergering van psigiatriese versteurings moet tydens elke dosisaanpassing gemonitor word, dan minstens elke 6 maande en tydens elke besoek; staking van behandeling kan gepas wees.

Verergering van bestaande psigotiese of maniese simptome

In psigotiese pasiënte kan toediening van METHYLPHENIDATE 10 BIOTECH die simptome van gedragsversteuring en gedagteversteurings vererger.

Die voorkoms van nuwe psigotiese of maniese simptome

Nuwe psigotiese simptome (visuele/tasbare/ouditiewe hallusinasies en delusies) of manie kan deur behandeling met METHYLPHENIDATE 10 BIOTECH teen gewone dosisse veroorsaak word in pasiënte sonder voorafgaande geskiedenis van psigotiese siektes of manie. As maniese of psigotiese simptome voorkom, moet die moontlike oorsaaklike rol van metielfenidaat in gedagte gehou word en staking van behandeling kan gepas wees.

Aggressiewe of vyandige gedrag

Die voorkoms of verergering van aggressie of vyandigheid kan deur behandeling met stimulante veroorsaak word. Pasiënte wat met METHYLPHENIDATE 10 BIOTECH behandel word, moet noukeurig gemonitor word vir die voorkoms of verergering van aggressiewe gedrag of vyandigheid tydens die aanvang van die behandeling, tydens elke dosisaanpassing en dan minstens elke 6 maande of met elke besoek. Mediese praktisyns moet die behoefte aan aanpassing van die behandelingsregimen vir pasiënte wat gedragsveranderings ondervind, evalueer, met inagneming dat op- of afwaartse titrasie gepas kan wees. Onderbreking van die behandeling kan oorweeg word.

Selfmoordneigings

Pasiënte met opkomende selfmoordgedagtes of -gedrag tydens behandeling vir ADHD moet onmiddellik deur hul geneesheer geëvalueer word. Die verergering van 'n onderliggende psigiatriese toestand en die moontlike oorsaaklike rol van die behandeling met METHYLPHENIDATE 10 BIOTECH moet in gedagte gehou word. Behandeling van 'n onderliggende psigiatriese toestand kan nodig wees, en die moontlike staking van METHYLPHENIDATE 10 BIOTECH moet oorweeg word.

Spiertrekkings

Metielfenidaat gaan gepaard met die aanvang of verergering van motoriese en verbale spiertrekkings. Verergering van die Tourette-sindroom is ook aangemeld. Familiegeskiedenis moet beoordeel word en kliniese evaluering van spiertrekkings of Tourette-sindroom in kinders moet voor gebruik van METHYLPHENIDATE 10 BIOTECHgedoen word. Pasiënte moet tydens behandeling met METHYLPHENIDATE 10 BIOTECH gereeld dopgehou word vir die ontstaan of verergering van spiertrekkings.

Angs, agitasie of spanning

METHYLPHENIDATE 10 BIOTECH gaan met die verergering van bestaande angs, agitasie of spanning gepaard. METHYLPHENIDATE 10 BIOTECH is teenaangedui in pasiënte wat aan hierdie toestande ly (sien afdeling 4.3).

Vorme van bipolêre versteuring

Wees besonder versigtig met die gebruik van METHYLPHENIDATE 10 BIOTECH vir die behandeling van ADHD in pasiënte met komorbiede bipolêre versteuring (waaronder onbehandelde tipe 1 bipolêre versteuring of ander vorme van bipolêre versteuring) vanweë kommer oor die moontlike aanbring van 'n gemengde/maniese episode in sulke pasiënte. Voordat die behandeling met METHYLPHENIDATE 10 BIOTECH begin, moet pasiënte met komorbiede depressiewe simptome voldoende ondersoek word om vas te stel of hulle 'n risiko vir bipolêre versteuring het; so 'n ondersoek moet 'n gedetailleerde psigiatriese geskiedenis insluit, waaronder 'n familiegeskiedenis van selfmoord, bipolêre versteuring en depressie. Noukeurige deurlopende monitering is noodsaaklik vir hierdie pasiënte (sien "Psigiatriese afwykings" hier bo en afdeling 4.2). Pasiënte moet tydens elke dosisaanpassing en dan minstens elke 6 maande en tydens elke besoek vir simptome gemonitor word.

Serotoniensindroom

Die serotoniensindroom is na die toediening van metielfenidaat saam met serotonerge medisyne soos selektiewe serotonienheropname-remmers (SSHR's) en serotonien-noradrenalienheropnameremmers (SNHR's) aangemeld. Die gelyktydige gebruik van METHYLPHENIDATE 10 BIOTECH en serotonergiese medisyne word nie aanbeveel nie, want dit kan tot die ontwikkeling van die serotoniensindroom lei. Die simptome van die serotoniensindroom kan veranderinge in die geestesstatus wees (bv. agitasie, hallusinasies, delirium en koma), asook outonome onstabiliteit (bv. tagikardie, labiele bloeddruk, duiseligheid, diaforese, blosing, hipertermie), neuromuskulêre simptome (bv. bewing, rigiditeit, mioklonus, hiperrefleksie, inkoördinasie), toevalle en/of gastro-intestinale simptome (bv. naarheid, braking, diarree). Die vinnige herkenning van hierdie simptome is belangrik, sodat behandeling met METHYLPHENIDATE 10 BIOTECH en serotonerge medisyne onmiddellik gestaak kan word en toepaslike behandeling ingestel kan word (sien afdeling 4.5).

Priapisme

Langdurige en pynlike ereksies is met metielfenidaatprodukte aangemeld, hoofsaaklik saam met 'n verandering in die behandelingsprogram van metielfenidaat. Pasiënte wat abnormale aanhoudende of gereelde en pynlike ereksies ontwikkel, moet onmiddellik mediese hulp verkry.

Groeivertraging

Matige laer toename in liggaamsmassa en groeivertraging is met langdurige gebruik van metielfenidaat in kinders aangemeld.
Pasiënte wat nie soos verwag of groei of liggaamsmassa opbou nie, moet moontlik hulbehandeling met METHYLPHENIDATE 10 BIOTECH onderbreek en aanpas.

Stuiptrekkings (toevalle)

METHYLPHENIDATE 10 BIOTECH moet versigtig gebruik word deur pasiënte met epilepsie. Metielfenidaat kan die konvulsiedrempel van pasiënte met 'n geskiedenis van vroeëre aanvalle verlaag, asook van pasiënte sonder aanvalle met vorige abnormaliteite in die EEG, en in pasiënte sonder 'n geskiedenis van stuiptrekkings en geen abnormaliteite in die EEG nie. As die frekwensie van toevalle toeneem of nuwe toevalle voorkom, moet METHYLPHENIDATE 10 BIOTECH gestaak word.

Misbruik, wangebruik en afhanklikheid

Pasiënte moet noukeurig dopgehou word vir die risiko vir verkeerde gebruik, wangebruik en misbruik van METHYLPHENIDATE 10 BIOTECH.
METHYLPHENIDATE 10 BIOTECH moet versigtig gebruik word deur pasiënte met 'n bekende afhanklikheid van dwelms of alkohol, as gevolg van die moontlikheid van misbruik, wangebruik of verkeerde gebruik. Chroniese misbruik van METHYLPHENIDATE 10 BIOTECH kan tot uitgesproke verdraagbaarheid en sielkundige afhanklikheid met verskillende grade van abnormale gedrag lei. Openlike psigotiese episodes kan voorkom, veral in reaksie op parenterale misbruik.
Die ouderdom van die pasiënt, risikofaktore vir dwelmgebruikversteuring (soos komorbiede teëstandige, uitdagende of gedragsversteuring en bipolêre versteuring), en vorige of huidige middelmisbruik moet in ag geneem word wanneer daar besluit word op 'n kursus vir behandeling van ADHD. Wees versigtig met emosioneel onstabiele pasiënte, soos pasiënte met 'n geskiedenis van dwelm- of alkoholafhanklikheid, omdat sulke pasiënte die dosis op eie inisiatief kan verhoog.
METHYLPHENIDATE 10 BIOTECH is moontlik nie geskik vir sommige pasiënte met 'n hoë risiko vir dwelmmisbruik nie.

Onttrekking

Noukeurige toesig is tydens onttrekking nodig, aangesien dit depressie sowel as chroniese ooraktiwiteit kan ontmasker. Sommige pasiënte het langtermynopvolg nodig.
Noukeurige toesig is tydens onttrekking van misbruik nodig, aangesien erge depressie kan voorkom.

Moegheid

METHYLPHENIDATE 10 BIOTECH moet nie vir die voorkoming of behandeling van normale toestande van moegheid gebruik word nie.

Toetse vir dwelmmiddels

METHYLPHENIDATE 10 BIOTECH bevat metielfenidaat wat 'n vals positiewe uitslag in laboratoriumtoetse vir amfetamiene kan veroorsaak, veral met 'n immuubepalende siftingstoets.

Nier- of lewer-ontoereikendheid

Daar is geen ervaring met die gebruik van METHYLPHENIDATE 10 BIOTECH deur pasiënte met nier- of lewer-ontoereikendheid nie.

Effekte op die bloed

Die veiligheid van behandeling met metielfenidaat, soos in METHYLPHENIDATE 10 BIOTECH, oor 'n lang termyn is nie volledig bekend nie. Pasiënte wat behandeling oor 'n lang termyn nodig het, moet dus noukeurig gemonitor word, en die volle en differensiële bloedtellings en 'n bloedplaatjietelling moet periodiek gedoen word. In geval van leukopenie, trombositopenie, bloedarmoede of ander veranderings, waaronder dié wat op ernstige nier- of lewerafwykings dui, moet die staking van die behandeling oorweeg word.

4.5 Interaksies met ander medisyne en ander vorms van interaksie

Dit is nie bekend hoe metielfenidaat, soos in METHYLPHENIDATE 10 BIOTECH, die plasmakonsentrasie van gelyktydig toegediende medisyne kan beïnvloed nie. Daarom word aanbeveel om METHYLPHENIDATE 10 BIOTECH versigtig met ander medisyne te kombineer, veral dié met 'n klein terapeutiese indeks.

Farmakokinetiese interaksies

Metielfenidaat word nie tot 'n klinies relevante mate deur sitochroom P450 gemetaboliseer nie. Dit word nie verwag dat induseerders of remmers van sitochroom P450 enige relevante impak op die farmakokinetika van metielfenidaat sal hê nie. Omgekeerd rem die d- en l-enantiomere van metielfenidaat nie sitochroom P450 1A2, 2C8, 2C9, 2C19, 2D6, 2E1 of 3A nie.

Daar is egter verslae wat toon dat metielfenidaat, soos in METHYLPHENIDATE 10 BIOTECH, die metabolisme van kumarienantistolmiddels, antikonvulsante (bv. fenobarbitoon, fenitoïen, primidoon) en sommige antidepressante (trisikliese en selektiewe serotonienheropnameremmers) kan inhibeer. Wanneer METHYLPHENIDATE 10 BIOTECH begin of gestop word, kan dit nodig wees om die dosis van hierdie medisyne wat reeds gebruik word, aan te pas en plasmakonsentrasies te bepaal(of vir kumariene, die stollingstye). Gelyktydige toediening van METHYLPHENIDATE 10 BIOTECH saam met die CYP2D6-substraat desipramien het nie plasmakonsentrasies daarvan verhoog nie.

Farmakodinamiese interaksies
Antihipertensiewe middels
Metielfenidaat kan die effektiwiteit van medisyne vir die behandeling van hipertensie verlaag.

Gebruik saam met medisyne wat bloeddruk verhoog
Wees versigtig met pasiënte wat behandel word met METHYLPHENIDATE 10 BIOTECH met ander medisyne wat ook die bloeddruk kan verhoog (sien ook gedeeltes oor kardiovaskulêre en serebrovaskulêre toestande in afdeling 4.4).
As gevolg van 'n moontlike hipertensiewe krisis, is METHYLPHENIDATE 10 BIOTECH teenaangedui in pasiënte wat (tans of in die voorafgaande twee weke) met MAO-remmers behandel word (sien afdeling 4.3).

Gebruik saam met alkohol
Alkohol kan die nadelige effek op SSS van psigo-aktiewe medisyne, waaronder METHYLPHENIDATE 10 BIOTECH, vererger. Dit is dus raadsaam dat pasiënte tydens die behandeling geen alkohol gebruik nie.

Gebruik saam met narkosemiddels
Daar is 'n risiko vir 'n skielike toename in bloeddruk en harttempo tydens die operasie. Indien 'n operasie beplan word, moet behandeling met METHYLPHENIDATE 10 BIOTECH nie op die dag van die operasie gebruik word nie.

Gebruik saam met alfa2-agoniste wat sentraal werk (bv. klonidien of deksmedetomidien)
Ernstige newe-effekte, waaronder skielike dood, kan tydens gebruik saam met klonidien of deksmedetomidien voorkom.

Gebruik saam met dopaminerge medisyne
Wees versigtig wanneer METHYLPHENIDATE 10 BIOTECH saam met dopaminerge medisyne, waaronder antipsigotika, toegedien word. Aangesien 'n belangrike werking van metielfenidaat is om die ekstrasellulêre dopamienvlakke te verhoog, kan METHYLPHENIDATE 10 BIOTECH met farmakodinamiese interaksies gepaardgaan wanneer dit met direkte of indirekte dopamienagoniste (insluitend DOPA en trisikliese antidepressante) of met dopamienantagoniste, insluitend antipsigotika, toegedien word.

Gebruik saam met serotonergiese medisyne
Die gebruik van METHYLPHENIDATE 10 BIOTECH saam met serotonergiese medisyne word nie aanbeveel nie, want dit kan tot die ontwikkeling van die serotoniensindroom lei (sien afdeling 4.4). Dit is getoon dat metielfenidaat ekstrasellulêre serotonien- en noradrenalienvlakke verhoog, en dit lyk asof dit swak bindingskrag vir die van serotonientransporter het.

Laboratorium/medisyne-toetse
METHYLPHENIDATE 10 BIOTECH kan 'n vals positiewe uitslag in laboratoriumtoetse vir amfetamiene kan veroorsaak, veral met 'n immuubepalende siftingstoets.

4.6 Vrugbaarheid, swangerskap en borsvoeding
Swangerskap
METHYLPHENIDATE 10 BIOTECH is teenaangedui tydens swangerskap (sien afdeling 4.3).
Daar is 'n beperkte hoeveelheid data oor die gebruik van metielfenidaat, soos in METHYLPHENIDATE 10 BIOTECH, deur swanger vroue.

Borsvoeding
METHYLPHENIDATE 10 BIOTECH is teenaangedui tydens borsvoeding, aangesien veiligheid nie aangetoon is nie (sien afdeling 4.3).
Moeders wat METHYLPHENIDATE 10 BIOTECH drink, moet nie hul babas borsvoed nie.
Metielfenidaat, soos in METHYLPHENIDATE 10 BIOTECH, is gevind in borsmelk van vroue wat met metielfenidaat behandel is.

4.7 Effek op vermoë om 'n voertuig te bestuur en masjiene te gebruik
METHYLPHENIDATE 10 BIOTECH kan duiseligheid, slaperigheid en visieversteurings veroorsaak, waaronder probleme met akkommodasie, diplopie en wasige visie (sien afdeling 4.8). Dit kan 'n matige effek hê op die vermoë om 'n voertuig te bestuur en masjiene te gebruik. Pasiënte moet gewaarsku word oor hierdie moontlike effekte en moet in kennis gestel word dat indien hulle aangetas word, hulle gevaarlike aktiwiteite moet vermy, soos die bestuur van 'n voertuig of die hantering van masjinerie.

4.8 Ongewensde effekte
Infeksies en infestasies
Gereeld: nasofaringitis
Versteurings van bloed en limfatiese stelsel
Minder gereeld: bloedarmoede, leukopenie, trombositopenie, trombositopeniese purpura
Frekwensie onbekend: pansitopenie
Versteurings van die immuunstelsel
Minder gereeld: hipersensitiwiteitsreaksies soos angioneurotiese edeem, anafilaktiese reaksies, aurikulêre swelling, blaasagtige toestande, afskilferende toestande, urtikarie, pruritus, uitslag en uitbarstings
Versteurings in metabolisme en voeding*
Gereeld: anoreksie, swak eetlus, matige laer liggaamsmassa en verlaagde groei in lengte tydens langdurige gebruik deur kinders
Psigiatriese versteurings*
Gereeld: slapeloosheid, senuagtigheid, labiele gemoed, aggressie*, agitasie*, angs*, depressie*, prikkelbaarheid, abnormale gedrag
Minder gereeld: psigotiese afwykings*, gehoor-, visuele en tasbare hallusinasies*, woede, selfmoordgedagtes*, gemoedsveranderings, gemoedswisselings, rusteloosheid, traneriheid, spiertrekkings*, verergering van bestaande spiertrekkings of Tourette-sindroom*, hiperwaaksaamheid, slaapstoornis, manie*, disoriëntasie, libido-afwyking, selfmoordpoging (waaronder suksesvolle selfmoord)*, kortstondige depressiewe gemoedstoestand*, abnormale denke, apatie, herhalende gedrag, oormatige fokus
Frekwensie onbekend: delusies*, gedagteversteurings*, verwarde toestand, afhanklikheid, logorree. Gevalle van misbruik en afhanklikheid is beskryf, meer dikwels met formulerings vir onmiddellike vrystelling (frekwensie nie bekend nie).
Versteurings van die senustelsel
Gereeld: hoofpyn, duiseligheid, diskinesie, psigomotoriese hiperaktiwiteit, slaperigheid
Minder gereeld: sedasie, bewing, stuiptrekkings, choreo-atetoïede bewegings, omkeerbare iskemiese neurologiese tekort, kwaadaardige neuroleptiese sindroom (KNS) (verslae was swak gedokumenteer en in die meeste gevalle het pasiënte ook ander medisyne ontvang, en die rol van metielfenidaat is dus onduidelik)
Frekwensie onbekend: serebrovaskulêre afwykings* (waaronder vaskulitis, serebrale bloedings, serebrovaskulêre insidente, stuiptrekkings*, migraine)
Oogversteurings
Minder gereeld: diplopie, wasige visie, probleme met visuele akkommodasie, midriase, versteuring in visie
Hartversteurings*
Gereeld: disritmie, tagikardie, hartkloppings
Minder gereeld: borskaspyn, angina pectoris, hartstilstand, miokardiale infarksie, skielike hartdood*
Frekwensie onbekend: supraventrikulêre tagikardie, bradikardie, ventrikulêre ekstrasistole, ekstrasistole
Vaskulêre versteurings*
Gereeld: hipertensie
Minder gereeld: serebrale arteritis en/of okklusie, perifere koudheid, Raynaud se verskynsel
Respiratoriese, toragiese en mediastinale versteurings
Gereeld: hoes, nasofaringeale pyn
Minder gereeld: dispnee
Gastro-intestinale versteurings
Gereeld: buikpyn, diarree, naarheid, ongemak in die maag en braking (dit kom gewoonlik aan die begin van die behandeling voor en kan deur gelyktydige voedselinname verlig word), droë mond
Minder gereeld: hardlywigheid
Hepatobiliêre versteurings
Minder gereeld: hoër vlakke lewerensieme, abnormale lewerfunksies, waaronder lewerkoma
Versteurings van die vel en subkutane weefsel
Gereeld: alopesie, pruritus, veluitslag, urtikarie
Minder gereeld: angioneurotiese edeem, blaasagtige toestande, afskilferingstoestande, hiperhidrose, makulêre uitslag, eriteem, multivorme eriteem, afskilferende dermatitis, vaste geneesmiddeluitbarsting
Versteurings van die muskuloskeletale stelsel, bindweefsel en skeletbene
Gereeld: artralgie
Minder gereeld: mialgie, spiertrekkings, spierkrampe
Versteurings van die niere en urienweg
Minder gereeld: hematurie
Versteurings in die voortplantingstelsel en borste
Minder gereeld: ginekomastie
Frekwensie onbekend: ereksiedisfunksie, priapisme, sterker ereksie en langdurige ereksie

Algemene versteurings en effekte by die plek van toediening
Gereeld: koors, groeivertraging tydens langdurige gebruik deur kinders*
Minder gereeld: moegheid
Frekwensie onbekend: ongemak in die bors, hiperpireksie
Ondersoeke
Gereeld: veranderinge in bloeddruk en hartklop (gewoonlik 'n toename)*, laer liggaamsmassa*
Minder gereeld: hartgeruis*, hoër vlakke lewerensieme, hoër vlakke alkaliese fosfatase in die bloed, hoër vlakke bilirubien in die bloed, laer plaatjietelling, abnormale witbloedseltelling.
* Sien afdeling 4.4 "Spesiale waarskuwings en voorsorgmaatreëls vir gebruik"

Aanmelding van vermeende nadelige reaksies
Dit is belangrik om vermeende nadelige reaksies wat na magtiging van METHYLPHENIDATE 10 BIOTECH voorkom, aan te meld. Dit maak voortgesette monitering van die balans tussen voordeel en risiko van METHYLPHENIDATE 10 BIOTECH moontlik. Gesondheidsorgverskaffers van word versoek om vermeende nadelige reaksies aan te meld die vorm "6.04 Adverse Drug Reaction Reporting Form" wat aanlyn by SAHPRA se publikasies gekry kan word: https://www.sahpra.org.za/Publications/Index/8.

4.9 Oordosis
Tekens en simptome
Akute oordosering, hoofsaaklik as gevolg van oorstimulasie van die sentrale en simpatiese senustelsels, kan lei tot braking, agitasie, bewing, hiperrefleksie, spiertrekkings, stuiptrekkings (kan deur koma gevolg word), euforie, verwardheid, hallusinasies, delirium, sweet, blosing, hoofpyn, hiperpireksie, tagikardie, hartkloppings, hartritmestoornisse, hipertensie, midriase, droogheid van die slymvliese en rabdomiolise.
Behandeling
Daar is geen spesifieke teenmiddel vir oordosering met metielfenidaat nie. Behandeling bestaan uit toepaslike ondersteunende maatreëls en simptomatiese behandeling van lewensbedreigende voorvalle, bv. hipertensiewe krisis, hartritmestoornisse, stuiptrekkings. Vir die nuutste riglyne vir die behandeling van simptome van oordosering, moet die geneesheer 'n gesertifiseerde gifsentrum of huidige toksikologiese publikasie raadpleeg.
Die pasiënt moet beskerm word teen selfbesering en teen uitwendige stimuli wat die reeds aanwesige oorstimulasie sal vererger. As die pasiënt by sy bewussyn is, word toediening van geaktiveerde houtskool en 'n lakseermiddel aanbeveel. In die teenwoordigheid van ernstige vergiftiging moet 'n versigtig getitreerde dosis bensodiasepien gegee word.
Intensiewe sorg moet verskaf word om voldoende sirkulasie en respiratoriese uitruiling te handhaaf; eksterne verkoeling kan nodig wees om hiperpireksie te verminder.
Die doeltreffendheid van peritoneale dialise of buite-liggaamlike hemodialise vir oordosering met metielfenidaat is nie vasgestel nie.

5. FARMAKOLOGIESE EIENSKAPPE
Kategorie en klas: A.1.2 Psigoanaleptika (antidepressante)

5.1 Farmakodinamiese eienskappe
Farmakoterapeutiese groep: Psigostimulante - *ATC-kode:* NO6B A04.
Werkingsmeganisme: Metielfenidaat is 'n ligte SSS-stimulant met meer prominente effekte op geestelike as op motoriese aktiwiteite. Die werking daarvan in die mens word nie heeltemal verstaan nie, maar die effekte daarvan is vermoedelik vanweë remming van die heropname van dopamien in die striatum, sonder om die vrystelling van dopamien te veroorsaak.
Die meganisme waardeur metielfenidaat sy effekte op die geestestoestand en gedrag van kinders uitoefen, is nie duidelik bepaal nie, en daar is ook nie afdoende bewys dat hierdie effekte verband hou met die toestand van die sentrale senustelsel nie.
Metielfenidaat is 'n rasemiese mengsel van die d- en l-enantiomere (d-MFD en l-MFD), waar die d-enantiomeer beskou word as die farmakologies aktiewe enantiomeer.

5.2 Farmakokinetiese eienskappe
Absorpsie
Die aktiewe bestanddeel metielfenidaathidrochloried word vinnig en byna volledig uit die tablette geabsorbeer. Vanweë uitgebreide eerstedeurgangmetabolisme is die absolute biobeskikbaarheid 22 ± 8 % vir die d-enantiomeer en 5 ± 3 % vir die l-enantiomeer. Inname saam met voedsel verhoog die piek plasmakonsentrasie (C_{maks}) met 23 % sowel as die oppervlakte onder die konsentrasietydkurwe (AOK) met 15 %, maar het geen relevante effek gehad op die absorpsiesnelheid van metielfenidaat nie. Piek plasmakonsentrasies van ongeveer 40 nmol/L (11 ng/ml) word gemiddeld 1-2 uur na toediening van 0,30 mg/kg bereik. Die piek plasmakonsentrasies toon egter 'n groot interpersoonvariasie. Die AOK en die C_{maks} is eweredig aan die dosis.
Verspreiding
In die bloed versprei metielfenidaat en sy metaboliete in die plasma (57 %) en die eritrosiete (43 %). Metielfenidaat en sy metaboliete het 'n lae binding aan plasmaproteïene (10 - 33 %). Die volume van verspreiding is 2,65 ± 1,11 L/kg vir d-MFD en 1,80 ± 0,91 L/kg vir l-MFD.
Biotransformasie
Biotransformasie van metielfenidaat deur die karboksi-esterase CES1A1 is vinnig en uitgebreid. Die piek plasmakonsentrasies van α-feniel-2-piperidielasynsuur (ritaliensuur) (FPA) word ongeveer 2 uur na toediening van metielfenidaat bereik en is 30-50 keer hoër as die van die onveranderde stof. Die halfleeftyd van FPA is ongeveer twee keer so lank as dié van metielfenidaat, en die gemiddelde sistemiese opruiming is 0,17 L/h/kg. Slegs klein hoeveelhede gehidroksileerde metaboliete (bv. hidroksimetielfenidaat en hidroksiritaliensuur) is waarneembaar. Terapeutiese aktiwiteit blyk hoofsaaklik van die moederverbinding te wees.
Uitskeiding
Metielfenidaat word met 'n gemiddelde terminale halfleeftyd van 2 uur uit die plasma uitgeskei. Die sistemiese opruiming is 0,40 ± 0,12 L/h/kg vir d-MFD en 0,73 ± 0,28 L/h/kg vir l-MFD. Binne 48 - 96 uur word 78 – 97 % van die toegediende dosis as metaboliete in die uriene uitgeskei en 1-3 % in die feses. Onveranderde metielfenidaat kom slegs in klein hoeveelhede in die urien voor (<1 %). Die grootste deel (60 – 86 %) van die dosis word as FPA in die uriene uitgeskei.
Eienskappe in pasiënte
Daar is geen duidelike verskille in die farmakokinetiese gedrag van metielfenidaat in hiperaktiewe kinders en gesonde volwasse vrywilligers nie.
Data van eliminasie uit pasiënte met normale nierfunksie dui daarop dat die nieruitskeiding van die onveranderde metielfenidaat amper nie minder sal wees in geval van swak nierfunksie nie. Nieruitskeiding van FPA kan egter minder wees.

5.3 Prekliniese veiligheidsdata
Geen verdere inligting van belang beskikbaar nie.

6. FARMASEUTIESE BESONDERHEDE
6.1 Lys van hulpstowwe
Kalsiumwaterstoffosfaatdihidraat
Magnesiumstearaat
Mieliestysel
Mikrokristallyne sellulose

6.2 Onverenigbaarhede
Geen bekend nie.

6.3 Raklewe
4 jaar.

6.4 Spesiale voorsorgmaatreëls vir bewaring
- Bewaar teen of benede 25 °C. Beskerm teen vog.
- Hou die stulpstroke in die karton totdat hulle benodig word.

6.5 Aard en inhoud van die houer
Stulppakke van PVC/aluminium met tien tablette elk. Drie stulpstroke is in 'n karton verpak.
Pakgrootte: 30 tablette

6.6 Spesiale voorsorgmaatreëls vir wegdoening en ander hantering
Geen

7. HOUER VAN DIE REGISTRASIESERTIFIKAAT
Biotech Laboratories (Edms) Bpk.
Grondvloer, Blok K Wes, Central Park
16de Weg 400, Randjespark, Midrand
Halfweghuis
Midrand, 1685

8. REGISTRASIENOMMER
49/1.2/1000

9. DATUM VAN EERSTE MAGTIGING
20 Julie 2020

10. DATUM VAN HERSIENING VAN DIE TEKS
20 Julie 2020

Botswana: Reg. Nr.: BOT2304004	1A