Methylphenidate Hydrochloride 2mg/ml oral solution

Product information pack

Pip code – 127-0784 EAN – 5391512458256

Methylphenidate hydrochloride oral solution is indicated as a part of a comprehensive treatment programme for attention-deficit hyperactivity disorder (ADHD) in children aged 6 years of age and over when remedial measures alone prove insufficient.

The aim of this product information pack is to provide healthcare professionals with the information they require for activities such as completion of a formulary request for Methylphenidate hydrochloride 2mg/ml oral solution for its licensed indication.

Prescribing information and adverse event reporting can be found at the end of the document.

UK-MPH-2(1)a | March 2024

Contents

Consilient Health

Introduction

The information pack has been developed to provide a central resource that may be used for activities such as completion of a formulary request. The systems and processes required for formulary development are detailed in the NICE Medicines Practice Guideline 'Developing and updating local formularies[1]. Healthcare professionals should submit applications to consider a new medicine for inclusion in the formulary; manufacturers may support evidence gathering.

The following should be included:

- Details of the healthcare professional making the application, including a declaration of interests
- Local patient population
- Details of the medicine, including strength, formulation, therapeutic drug class, indication, monitoring requirements and cost
- Evidence submission, with relevant supporting literature, covering efficacy, safety and cost effectiveness
- Comparison with existing treatments
- Likely place in therapy
- Recommendation for the decommissioning of a current formulary medicine, if applicable
- Resource impact

Consilient Health

Background

Attention deficit hyperactivity disorder

- Attention deficit hyperactivity disorder (ADHD) is defined as a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development[2]
- The definition of ADHD requires that symptoms: start before 12 years of age; occur in two or more settings, such as at home and school; have been present for at least 6 months; interfere with or reduce the quality of social, academic or occupational functioning; do not occur exclusively during the course of a psychotic disorder and are not better explained by another mental disorder[2]
- The cause of ADHD is unknown, but an interplay of multiple genetic and environmental factors that are thought to lead to altered brain neurochemistry and structure[3]
- The global prevalence of ADHD in children is estimated to be around 5%, increasing to between 8% and 10% in studies based on US populations (where rates of diagnosis and treatment tend to be highest)[4]
- ADHD is more commonly diagnosed in boys than girls (prevalence ratios are generally estimated at 2–5:1, while clinic populations show a ratio as high as 10:1)[4]
- The greater prevalence of ADHD in boys may be because they are more likely to present with disruptive behaviour that prompts a referral, whereas girls more commonly have the inattentive subtype[4]
- ADHD is associated with a range of psychiatric or neurodevelopmental comorbidity, including oppositional defiant disorder (ODD), conduct disorder, substance use disorder, and possibly mood disorders (e.g. depression and mania)[5]
- Autism spectrum disorder, dyslexia, dyscalculia and dyspraxia are over-represented in the ADHD patient population[5]

Background

Treatment of ADHD

- NICE guideline NG87 states that people with ADHD should have a comprehensive, holistic shared treatment plan that addresses psychological, behavioural and occupational or educational needs[6]
- When pharmacotherapy is considered appropriate, NICE guideline NG87 recommends offering methylphenidate (either short or long acting) as the first-line treatment for children aged 5 years and over and young people with ADHD[6]
- All medication for ADHD should only be initiated by a healthcare professional with training and expertise in diagnosing and managing the condition[6]
- While ADHD stimulants are proven to be effective, adherence is poor across all patient age groups[7]
- Difficulty swallowing or an aversion to tablets may be a barrier to ADHD treatment[7]
- Paediatric patients are more likely to encounter difficulties swallowing solid dosage forms than adults[7]
- Despite evidence of efficacy, many children who try stimulant medications for ADHD stop taking them, with reported rates of adherence varying from 25% to 50% twelve months after starting treatment[8]
- Solid oral formulations may negatively affect adherence to ADHD therapy because of dosing inconvenience, patient discomfort or difficulty swallowing; efforts to refine stimulant formulations can potentially enhance adherence[7]
- Clinicians should consider both medication class and formulation when seeking to optimise in outcomes in patients with ADHD[7]
- Clinicians initiating medication for ADHD should ensure that treatment is tailored to the individual needs of the child, young person or adult (NICE NG87)[6]
- Titrate the dose against symptoms and adverse effects in line with the British National Formulary (BNF) or BNF for Children until dose optimisation is achieved; that is, reduced symptoms, positive behaviour change, improvements in education, employment and relationships, with tolerable adverse effects (NICE NG87)[6]
- Ensure that dose titration is slower and monitoring more frequent if any of the following are present in people with ADHD (NICE NG87):[6]
  - Neurodevelopmental disorders (e.g., autism spectrum disorder, tic disorders, learning disability [intellectual disability])
  - Mental health conditions (e.g., anxiety disorders [including obsessive-compulsive disorder], schizophrenia or bipolar disorder, depression, personality disorder, eating disorder, post-traumatic stress disorder, substance misuse)
  - Physical health conditions (for example, cardiac disease, epilepsy or acquired brain injury)

Consilient Health

Therapeutic advantage

Mechanism of action	Methylphenidate is a mild central nervous system (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 denantiomer is considered as the pharmacologically active enantiome
Therapeutic advantage over some existing treatments	Methylphenidate (MPH) Hydrochloride 2mg/ml oral solution is the only licensed non-solid MPH formulation available for treatment of ADHD in children (aged 6 years and over when remedial measures alone prove insufficient). MPH Hydrochloride 2mg/ml oral solution has been developed to address the problem that, despite evidence of efficacy, children's adherence to stimulant medications is poor – and difficulty swallowing or an aversion to tablets can be a barrier to treatment.[7] Many children who try stimulant medications for ADHD stop taking them, with adherence rates varying from 25% to 50% twelve months after starting treatment.[8] The ability to offer MPH Hydrochloride 2mg/ml oral solution expands treatment options for children with ADHD, who may have swallowing difficulties, an aversion to tablets or a preference for non-solid formations. Prescribers will already be familiar with the efficacy and safety profile of MPH Hydrochloride 2mg/ml oral solution, as it bioequivalent to Ritalin (Methylphenidate Hydrochloride) 10mg tablets.[9]

Consilient Health

Medicine details[10]

Medicine details	Methylphenidate Hydrochloride 2mg/ml oral solution
Marketing Company	Consilient Health Ltd.
Pharmacology/ BNF class	Pharmacotherapeutic group: psychostimulants ATC code: NO6B AO4
Licensed indication	Methylphenidate is indicated as a part of a comprehensive treatment programme for attention-deficit hyperactivity disorder (ADHD) in children aged 6 years of age and over when remedial measures alone prove insufficient.
Dosage and administration	Treatment must be initiated under the supervision of a specialist in childhood and/or adolescent behavioural disorders. Careful dose titration is necessary at the start of treatment with methylphenidate. Dose titration should be started at the lowest possible dose. The maximum daily dose is 60mg. Children: (over 6 years). Begin with 5mg once or twice daily (e.g. at breakfast and lunch), increasing the dose and frequency of administration if necessary by weekly increments of 5-10mg in the daily dose. Doses above 60mg daily are not recommended. The total daily dose should be administered in divided doses. If the effect of the drug wears off too early in the evening, disturbed behaviour and/ or inability to go to sleep may recur. A small evening dose may help to solve this problem. The oral solution should be swallowed with a drink of water.

Consilient Health

Medicine details[10]

Monitoring	Growth, psychiatric and cardiovascular status should be continuously monitored. Blood pressure and pulse should be recorded on a centile chart at each adjustment of dose and then at least every 6 months; height, weight and appetite should be recorded at least 6 monthly with maintenance of a growth chart; development of *de novo* or worsening of pre-existing psychiatric disorders should be monitored at every adjustment of dose and then at least every 6 months and at every visit. Patients should be monitored for the risk of diversion, misuse and abuse of methylphenidate.
Interactions	**Anti-hypertensive drugs** Methylphenidate may decrease the effectiveness of drugs used to treat hypertension. **Use with drugs that elevate blood pressure** Caution is advised in patients being treated with methylphenidate with other drugs that can also elevate blood pressure. Because of possible hypertensive crisis, methylphenidate is contraindicated in patients being treated (currently or within the preceding 2 weeks) with MAO inhibitors. **Use with alcohol** Alcohol may exacerbate the adverse CNS effects of psychoactive drugs, including methylphenidate. 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, methylphenidate treatment should not be used on the day of surgery.

Medicine details[10]

Interactions	**Use with centrally-acting alpha-2 agonists (e.g. clonidine)** The long term safety of using methylphenidate in combination with clonidine or other centrally acting alpha-2 agonists has not been systematically evaluated. **Use with dopaminergic drugs** Caution is recommended when administering methylphenidate with dopaminergic drugs, including antipsychotics. Because a predominant action of methylphenidate is to increase extra cellular dopamine levels, methylphenidate 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.
Shelf life	Unopened: 18 months After opening: 30 days

Consilient Health

Place in therapy

It is anticipated that Methylphenidate (MPH) Hydrochloride 2mg/ml oral solution will be used as part of a comprehensive treatment programme for attention-deficit hyperactivity disorder (ADHD) in children aged 6 years of age and over when remedial measures alone prove insufficient, as stated in its licensed indication.[10] MPH Hydrochloride 2mg/ml oral solution has bioequivalence to Ritalin (Methylphenidate Hydrochloride) 10mg tablets,[9] so prescribers will already be familiar with its efficacy and safety profile.

MPH Hydrochloride 2mg/ml oral solution was developed to have a child-friendly neutral to sweet taste.[11] As the sorbitol component of the formulation provides adequate sweetness, the product has no artificial flavouring agents or sweeteners. A palatability study in found that acceptance of this oral solution was high, with 97.22% of subjects responding that daily dosing would be easy to accept and no subjects replying that they would be unable to take this medicine every day.[11] While this study was conducted in adults, it is assumed that these results would be similar in children.

As MPH Hydrochloride 2mg/ml oral solution is the only licensed non-solid MPH formulation, it has particular utility for children who have difficulty swallowing or an aversion to tablets, which can be a barrier to treatment.[7] However, it is also anticipated that MPH Hydrochloride 2mg/ml oral solution will have a place in therapy for children who simply prefer a non-solid formulation to tablets, even though they have no strong aversion to the latter, as it is easier for them to take. Providing choice in this regard is consistent with NICE guideline NG87 (Attention deficit hyperactivity disorder: diagnosis and management), which states that:[6]

"Before starting any treatment for ADHD, discuss the following with the person, and their family or carers as appropriate, encouraging children and young people to give their own account of how they feel: the importance of adherence to treatment and any factors that may affect this."

"Healthcare professionals initiating medication for ADHD should: ensure that treatment is tailored effectively to the individual needs of the child, young person or adult."

It is further anticipated that MPH Hydrochloride 2mg/ml oral solution will play a role in the care of some children who are receiving an extended release MPH formulation, but require an additional immediate release MPH top-up to achieve desired efficacy. While they will still be taking an extended release MPH formulation, the ability to top-up with MPH Hydrochloride 2mg/ml oral solution will reduce their solid 'pill burden' versus topping-up with tablets. This has the potential to support long-term compliance, particularly in children who find taking tablets difficult or simply prefer non-solid formulations.

Consilient Health

Place in therapy

Where would prescribing of Methylphenidate Hydrochloride 2mg/ml oral solution take place?

Methylphenidate Hydrochloride 2mg/ml oral solution is expected to be prescribed as first-line pharmacotherapy in child psychiatric settings and paediatric practice. Treatment will be initiated under the supervision of a specialist in childhood and/or adolescent behavioural disorders.

Will Methylphenidate Hydrochloride 2mg/ml oral solution replace any drugs already on the Formulary?

It is anticipated that Methylphenidate (MPH) Hydrochloride 2mg/ml oral solution will be an additional formulation option that will reduce the use of MPH tablets in children.

How does the cost of Methylphenidate Hydrochloride 2mg/ml oral solution compare with drugs already on the Formulary?

The NHS indicative price for a 150ml bottle of Methylphenidate Hydrochloride 2mg/ml oral solution is £85 (November 2023).

Methylphenidate IR tablets already on formulary (November 2023)

Product	NHS indicative price for pack of 30 (£)
Medikinet 5mg tablets (Medice UK Ltd)	3.03
Methylphenidate 5mg tablets (AAH Pharmaceuticals Ltd)	3.63
Methylphenidate 5mg tablets (Kent Pharma [UK] Ltd)	3.03
Methylphenidate 5mg tablets (Viatris UK Healthcare Ltd)	2.58
Tranquilyn 5mg tablets (Genesis Pharmaceuticals Ltd)	3.03
Medikinet 10mg tablets (Medice UK Ltd)	5.49
Methylphenidate 10mg tablets (AAH Pharmaceuticals Ltd)	3.22
Methylphenidate 10mg tablets (Kent Pharma [UK] Ltd)	5.29
Methylphenidate 10mg tablets (Viatris UK Healthcare Ltd)	4.67
Ritalin 10mg tablets (InfectoPharm Arzneimittel und Consilium GmbH)	6.68
Tranquilyn 10mg tablets (Genesis Pharmaceuticals Ltd)	5.49
Medikinet 20mg tablets (Medice UK Ltd)	10.92
Methylphenidate 20mg tablets (AAH Pharmaceuticals Ltd)	10.92
Methylphenidate 20mg tablets (Kent Pharma [UK] Ltd)	10.92
Methylphenidate 20mg tablets (Viatris UK Healthcare Ltd)	9.28
Tranquilyn 20mg tablets (Genesis Pharmaceuticals Ltd)	10.92

IR: immediate release
All information is taken from bnf.nice.org.uk (accessed 23/11/2023)

Consilient Health

Guidelines and recommendations

NICE guideline NG87 (Attention deficit hyperactivity disorder: diagnosis and management) states that:[6]

- People with ADHD should have a comprehensive, holistic shared treatment plan that addresses psychological, behavioural and occupational or educational needs
- All medication for ADHD should only be initiated by a healthcare professional with training and expertise in diagnosing and managing the condition
- When pharmacotherapy is considered appropriate, offer methylphenidate (either short or long acting) as the first-line treatment for children aged 5 years and over and young people with ADHD
- Before starting any treatment for ADHD, discuss the importance of adherence to treatment and any factors that may affect this with the person and their family/carers, encouraging children and young people to give their own account of how they feel
- Healthcare professionals initiating medication for ADHD should ensure that treatment is tailored effectively to the individual needs of the child, young person or adult
- Titrate the dose against symptoms and adverse effects in line with the British National Formulary (BNF) or BNF for Children until dose optimisation is achieved; that is, reduced symptoms, positive behaviour change, improvements in education, employment and relationships, with tolerable adverse effects
- Ensure that dose titration is slower and monitoring more frequent if any of the following are present in people with ADHD:
  - Neurodevelopmental disorders (e.g., autism spectrum disorder, tic disorders, learning disability [intellectual disability])
  - Mental health conditions (e.g., anxiety disorders [including obsessive–compulsive disorder], schizophrenia or bipolar disorder, depression, personality disorder, eating disorder, post-traumatic stress disorder, substance misuse)
  - Physical health conditions (for example, cardiac disease, epilepsy or acquired brain injury)

There may also be local guidelines and recommendations in addition to NICE guideline NG87, which should also be considered.

Efficacy and Safety

Methylphenidate Hydrochloride 2mg/ml oral solution has been shown to bioequivalent to Ritalin (Methylphenidate Hydrochloride) tablets 10 mg by Novartis Pharmaceuticals UK.[9]

BIOEQUIVALENCE STUDY[9]

Design

A randomised, open-label, balanced, two treatment, two period, two sequence, single dose, crossover bioequivalence study compared Methylphenidate 2 mg/ml oral solution to Ritalin (Methylphenidate Hydrochloride) tablets 10 mg (distributed by Novartis Pharmaceuticals UK Ltd) in normal, healthy, adult, human subjects under fasting conditions.

The study was open-label in nature because blood concentration levels cannot be influenced by knowledge of the identity of the treatment. Use of a crossover design is appropriate since it enables comparison of treatments within the same study participant using intra-subject variability thus improving the precision of treatment comparisons. The 2 periods were separated by a washout period of 7 days, which is sufficient to ensure that blood concentrations are below the limit of quantitation at the start of the second period since the elimination half-life of methylphenidate after oral administration is approximately 2 hours.

A total of 36 subjects were planned and enrolled in the study. Out of which, one subject dropped out from period 2. Therefore, a total of 35 subjects completed all periods of the study. Pharmacokinetic analyses were performed on plasma concentration data of 36 subjects and data from 35 subjects who completed both periods of the study were considered for statistical analyses as per approved protocol. Plasma samples were analysed for methylphenidate hydrochloride using validated methodology.

Efficacy and Safety

Results Mean Pharmacokinetic Parameters of Methylphenidate (N=35)

Pharmacokinetic Parameters (Units)	Mean ± SD (%CV) (N=35)	
	Oral solution 2mg/ml	Tablets 10mg
Cmax (ng/mL)	8.72 ± 2.56 (29.39)	8.49 ± 2.36 (27.84)
AUC0-t (hr*ng /mL)	42.24 ± 11.68 (27.66)	40.43 ± 10.93 (27.03)
AUC0-inf (hr*ng /mL)	43.71 ± 11.85 (27.11)	41.84 ± 10.90 (26.06)
Tmax (hr)	1.25 (0.75 – 2.67)	1.50 (0.75 – 2.67)
NKel	7.63 ± 4.02 (52.64)	7.54 ± 2.98 (39.56)
Kel (hr-1)	0.21 ± 0.03 (15.41)	0.20 ± 0.03 (13.69)
Kel lower (hr)	4.44 ± 2.69 (60.65)	4.09 ± 2.11 (51.65)
Kel upper (hr)	17.49 ± 2.76 (15.78)	17.49 ± 2.58 (14.77)
t½ (hr)	3.47 ± 0.60 (17.32)	3.46 ± 0.56 (16.24)
AUC Ratio (%)	96.49 ± 1.36 (1.41)	96.42 ± 1.35 (1.40)
Residual Area (%)	3.51 ± 1.36 (38.82)	3.58 ± 1.35 (37.83)

Consilient Health

Efficacy and Safety

Results Bioequivalence Assessment of Methylphenidate (N=35)

PK Parameters (Unit)	Geometric Least Square Means†			ISCV %§	90% confidence interval limits‖
	Oral solution 2mg/ml	Tablets 10mg	(T/R) %‡		
LnC_{max} (ng/mL)	8.38	8.17	102.56	12.76	97.41% - 107.97%
LnAUC0-t (hr*ng /mL)	40.82	39.07	104.48	8.47	100.97% - 108.12%

†For loge-transformed results (Ln), value is the least-squares geometric mean
‡Ratio% of geometric least-squares means for loge-transformed results
§ISCV%= %Intra-subject coefficient of variation calculated from the mean square term of the ANOVA
‖Confidence interval on ratio

Rate of absorption (C_{max})

The 90% Confidence Interval of 97.41–107.97% was within the standard 90% CI of 80.00–125.00%. Based on these results, Methylphenidate 2 mg/ml Oral Solution is bioequivalent to Ritalin (Methylphenidate Hydrochloride) Tablets 10 mg by Novartis Pharmaceuticals UK Ltd with respect to the rate of absorption under fasting conditions.

Extent of absorption (AUC_{0-t})

The 90% Confidence Interval of 100.97–108.12% was within the standard 90% CI of 80.00–125.00%. Based on these results, Methylphenidate 2 mg/ml Oral Solution is bioequivalent to Ritalin (Methylphenidate Hydrochloride) Tablets 10 mg by Novartis Pharmaceuticals UK Ltd with respect to the extent of absorption under fasting conditions.

Safety assessment

Methylphenidate 2 mg/ml Oral Solution and Ritalin (Methylphenidate Hydrochloride) tablets 10 mg were well tolerated by all subjects. No adverse events was reported during the study.

Overall conclusions

Participants is this bioequivalence study demonstrated good tolerance to Methylphenidate 2 mg/ml Oral Solution. Based on the pharmacokinetic data presented, it can be concluded that this formulation is bioequivalent to Ritalin (Methylphenidate Hydrochloride) Tablets 10 mg by Novartis Pharmaceuticals UK Ltd under fasting conditions.

Consilient Health

Efficacy and Safety

ADVERSE EVENTS

The following information is taken from the Methylphenidate Hydrochloride 2 mg/ml Oral Solution Summary of Product Characteristics and shows all adverse drug reactions (ADRs) observed during clinical trials and post market spontaneous reports with methylphenidate – and those which have been reported with other methylphenidate hydrochloride formulations.[10] If ADRs with methylphenidate and the methylphenidate formulation frequencies were different, the highest frequency of both databases was used.

Frequency estimate: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1000 to <1/100); rare (≥1/10,000 to <1/1000); very rare (< 1/10,000); not known (cannot be estimated from available data).

Infections and infestations
Common: Nasopharyngitis

Blood and lymphatic disorders
Very rare: Anaemia, leucopenia, thrombocytopenia, thrombocytopenic purpura
Not known: Pancytopenia

Immune system disorders
Uncommon: Hypersensitivity reactions such as angioneurotic oedema, anaphylactic reactions, auricular swelling, bullous conditions, exfoliative conditions, urticaria, pruritis, rashes and eruptions.

Metabolism and nutritional disorders*
Common: Anorexia, decreased appetite, moderately reduced weight and height gain during prolonged use in children.

Psychiatric disorders*
Very common: Insomnia, nervousness
Common: Anorexia, affect lability, aggression*, agitation*, anxiety*, depression*, irritability, abnormal behaviour, bruxism.
Uncommon: 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
Rare: Mania*, disorientation, libido disorder
Very rare: Suicidal attempt (including completed suicide)*, transient depressed mood*, abnormal thinking, apathy, repetitive behaviours, over-focusing
Not known: Delusions*, thought disturbances*, confusional state, dependence, logorrhea.

Consilient Health

Efficacy and Safety

ADVERSE EVENTS

Cases of abuse and dependence have been described, more often with immediate release formulations (frequency not known)

Nervous system disorders
Very common: Headache
Common: Dizziness, dyskinesia, psychomotor hyperactivity, somnolence
Uncommon: Sedation, tremor
Very rare: 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 drugs, so the role of methylphenidate is unclear).
Not known: Cerebrovascular disorders* (including vasculitis, cerebral haemorrhages, cerebrovascular accidents, cerebral arteritis, cerebral occlusion), grand mal convulsions*, migraine, dysphemia.

Eye disorders
Uncommon: Diplopia, blurred vision
Rare: Difficulties in visual accommodation, mydriasis, visual disturbance

Cardiac disorders*
Common: Arrhythmia, tachycardia palpitations
Uncommon: Chest pain
Rare: Angina pectoris
Very rare: Cardiac arrest, myocardial infarction
Not known: Supraventricular tachycardia, bradycardia, ventricular extrasystoles, extrasystoles

Vascular disorders*
Common: Hypertension
Very rare: Cerebral arteritis and/or occlusion, peripheral coldness, Raynaud's phenomenon

Respiratory, thoracic and mediastinal disorders
Common: Cough, pharyngolaryngeal pain
Uncommon: Dyspnoea
Not known: Epistaxis

Gastro-intestinal disorders:
Common: 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.
Uncommon: Constipation

Consilient Health

Efficacy and Safety

ADVERSE EVENTS

Hepatobiliary disorders
Uncommon: Hepatic enzyme elevations
Very rare: Abnormal liver functions, including hepatic coma

Skin and subcutaneous tissue disorders
Common: Alopecia, pruritis, rash, urticaria
Uncommon: Angioneurotic oedema, bullous conditions, exfoliate conditions
Rare: Hyperhidrosis, macular rash, erythema
Very rare: Erythema multiforme, exfoliate dermatitis, fixed drug eruption

Musculoskeletal, connective tissue and bone disorders
Common: Arthralgia
Uncommon: Myalgia, muscle twitching,
Very rare: Muscle cramps
Not known: Trismus**

Renal and urinary disorders
Uncommon: Haematuria
Not known: Incontinence

Reproductive system and breast disorders
Rare: Gynaecomastia
Not known: Erectile dysfunction, priapism, erection increased and prolonged erection

General disorders and administration site conditions
Common: Pyrexia, growth retardation during prolonged use in children*
Uncommon: Chest pain, fatigue
Very rare: Sudden cardiac death*
Not known: Chest discomfort, hyperpyrexia

Investigations
Common: Changes in blood pressure and heart rate (usually an increase)*, weight decreased*
Uncommon: Cardiac murmur*, hepatic enzyme increased
Very rare: Blood alkaline phosphatase increased, blood bilirubin increased, platelet count decreased, white blood count abnormal

* See section 4.4 "Special warnings and precautions for use" of the Summary of Product Characteristics
** Based on the frequency calculated in adult ADHD studies (no cases were reported in the paediatric studies)

Consilient Health

Financial implications

What is the cost per patient of the medicine each year?

Cost per patient per year will vary according to individual dosing needs. The NHS indicative price for a 150ml bottle of Methylphenidate Hydrochloride 2mg/ml oral solution is £85 (November 2023). Treatment is initiated with 5mg once or twice daily, carefully increased in weekly increments of 5-10mg in the daily dose as needed. Doses above 60mg daily are not recommended. See Section 4.2 of the Summary of Product Characteristics for full details of posology and administration.[10]

Is homecare available?

N/A

Estimated number of months of treatment per year

It is anticipated that Methylphenidate Hydrochloride 2mg/ml oral solution will be used for up to 12 months per year. Physicians electing to use methylphenidate for extended periods (over 12 months) in children and adolescents with ADHD should periodically re-evaluate the long term usefulness of the drug for the individual patient with trial periods off medication to assess the patient's functioning without pharmacotherapy.

Service impact

How will using this medicine affect how services are delivered to patients?

The use Methylphenidate Hydrochloride 2mg/ml oral solution will not require any additional clinic visits than those currently required for children receiving MPH tablets for ADHD.

Are there any other non-medicine costs or savings related to using this medicine?

No

Equity of access

All patients with equal needs will have equal opportunities to access this medicine.

References

1. National Institute of Health and Care Excellence – Developing and updating local formularies. Medicines Practice Guide: Available https://www.nice.org.uk/guidance/mpg1 - Accessed 20/12/2023.
2. National Institute of Health and Care Excellence – Attention deficit hyperactivity disorder: What is it? Available at: https://cks.nice.org.uk/topics/attention-deficit-hyperactivity-disorder/background-information/definition/ - Accessed 20/12/2023.
3. National Institute of Health and Care Excellence – Attention deficit hyperactivity disorder: What causes it? Available at: https://cks.nice.org.uk/topics/attention-deficit-hyperactivity-disorder/background-information/causes/ - Accessed 20/12/2023.
4. National Institute of Health and Care Excellence – Attention deficit hyperactivity disorder: How common is it? Available at: https://cks.nice.org.uk/topics/attention-deficit-hyperactivity-disorder/background-information/prevalence/ - Accessed 20/12/2023.
5. National Institute of Health and Care Excellence – Attention deficit hyperactivity disorder: What is the prognosis? Available at: https://cks.nice.org.uk/topics/attention-deficit-hyperactivity-disorder/background-information/prognosis/ - Accessed 20/12/2023.
6. National Institute of Health and Care Excellence – Attention deficit hyperactivity disorder: diagnosis and management (NG87). Last updated: 13 September 2019. Available at: https://www.nice.org.uk/guidance/ng87 - Accessed 20/12/2023.
7. Cutler AJ and Mattingly GW. Beyond the pill: new medication options for ADHD. CNS Spectrums 2017; 22: c. doi:10.1017/S1092852916000936.
8. Charach A, Skyba A, Cook L and Antle BJ. Using stimulant medication for children with ADHD: What to parents say? A brief report. J Can Acad Child Adolesc Psychiatry 2006; 15(2): 75–83.
9. Data on file, Module 2.5 – Clinical Overview, Consilient Health Ltd.
10. Methylphenidate Hydrochloride 2mg/ml oral solution Summary of Product Characteristics. Last revised 06/09/2023. Consilient Health Ltd.
11. Data on file, Methylphenidate Palatability Evaluation Assessment (10-2023), Consilient Health Ltd.

Consilient Health

Prescribing Information

Methylphenidate Hydrochloride 2mg/mL oral Solution

PRESCRIBING INFORMATION

Methylphenidate Hydrochloride 2mg/mL oral Solution **(Methylphenidate hydrochloride).**

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

Indication Methylphenidate Hydrochloride 2mg/mL Oral Solution is indicated as part of a comprehensive treatment programme for Attention Deficit / Hyperactivity Disorder (ADHD) in children aged 6 years of age and over and adolescents when remedial measures alone prove insufficient. Treatment must be initiated under the supervision of a specialist in childhood and/or adolescent behavioural disorders. **Presentation** Methylphenidate Hydrochloride Oral Solution contains the active ingredient methylphenidate at 2mg/mL in solution. **Dosage and administration** Solution for oral use. Careful dose titration is necessary at the start of treatment with methylphenidate - 5mg once or twice daily increasing the dose and frequency of administration if required by weekly increments of 5-10mg in the daily dose. Doses above 60mg daily are not recommended. **Contraindications** Hypersensitivity to the active substance or to any of the inactive ingredients. Contraindicated in Glaucoma; phaeochromocytoma; during or within 14 days of discontinuing treatment with MAO; 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. Please refer to SmPC. **Warning and precautions** Patients on long term therapy (more than 12 months) require ongoing monitoring for cardiovascular status); for neurological signs and symptoms; for psychiatric/ neurological conditions; for growth. Methylphenidate should be de-challenged at least once yearly to assess the child's condition. Caution is indicated in treating patients whose underlying medical conditions might be compromised by increases in blood pressure or heart rate. Potential for abuse, misuse or diversion in patients with known drug or alcohol dependency. Caution is advised in patients being treated with methylphenidate with any other active substances that can also elevate blood pressure. Alcohol may exacerbate the adverse CNS effect of psychoactive medicinal products, including methylphenidate. Caution is recommended when administering methylphenidate with dopaminergic substances. **Pregnancy and lactation** Not recommended. **Effects on ability to drive and use machines** Potentially hazardous activities such as driving or operating machinery should be avoided. **Undesirable effects** (*Very common*): insomnia, nervousness and headache. (*Common*): Naso-pharyngitis, 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, libido decreased, tension, bruxism, panic attack. Dizziness, dyskinesia, psycho-motor hyper-activity, somnolence, paraesthesia, tension headache, accommodation disorder, vertigo. Arrhythmia, tachy-cardia, palpitations, hyper-tension, cough, oro-pharyngeal pain, abdominal pain upper, diarrhoea, nausea, abdominal discomfort, vomiting, dry mouth, dyspepsia, alopecia, pruritis, 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. (*Frequency not known*): Pancytopenia disorders (including vasculitis, cerebral haemorrhages, cerebro-vascular accidents, cerebral occlusion), grand mal convulsion, migraine, dysphemia, mydriasis. Supra-ventricular tachycardia, bradycardia, ventricular extra-systoles, extra-systoles, trismus, incontinence, priapism, erection increased and prolonged erection, chest discomfort, hyperpyrexia. For uncommon, rare and very rare side effects please see SmPC for further information. **NHS Price** £85 per 150ml bottle **Legal Category** POM.MA **Number** PL 24837/0166 **Market Authorisation Holder** Consilient Health Ltd. Floor 3, Block 3, Miesian Plaza, Dublin 2, D02Y754, Ireland. September 2023 **Job Code** UK-MPH-4(1).

Date of preparation of PI January 2024.

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 Consilient Health (UK) Ltd, No. 1 Church Road, Richmond upon Thames, Surrey TW9 2QE UK or drugsafety@consilienthealth.com

Consilient Health

Consilient Health UK Ltd
No1 Church Road
Richmond upon Thames
Surrey, TW9 2QE
UK

Tel: **+44 (0)20 3751 1888**
For UK enquiries, please contact
infouk@consilienthealth.com

Consilient Health