HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
24 JUNE 2020
The legally binding text is the original French opinion version

methylphenidate
CONCERTA LP 18 mg, 36 mg and 54 mg prolonged-release tablets

Reevaluation of medicinal products containing methylphenidate and Renewal of inclusion

Key points

Favourable opinion for maintenance of reimbursement in the MA indication, i.e., 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.

Role in the care pathway?

Indication of ADHD in children aged 6 years of age and over when remedial measures alone prove insufficient
In view of the available data, the Committee considers that the role of methylphenidate in the therapeutic strategy is unchanged.
Pharmacotherapy with methylphenidate is a second-line treatment that can be initiated in children aged 6 years and over with an established diagnosis of ADHD in accordance with the MA criteria, when psychological, educational, social and family remedial measures alone prove insufficient. In this case, pharmacotherapy is part of a comprehensive treatment programme in combination with remedial measures.

As regards the prescribing conditions for methylphenidate, it is reiterated, in particular, that:
- **treatment must only be initiated by a specialist in childhood and/or adolescent behavioural disorders in the context of an established ADHD diagnosis and in accordance with the MA criteria,**

- **comprehensive pre-treatment screening must be carried out** in view of the safety profile of methylphenidate,
- **treatment with methylphenidate must be started at the lowest possible dose, then gradually increased** in weekly increments,
- **the principle of time-limited prescription must be systematically adopted when initiating treatment,**
- **medicinal treatment with methylphenidate must be part of a comprehensive treatment programme,** with the continuation of psychological, educational and social measures along with the pharmacotherapy,
- **regular ongoing monitoring of patients on methylphenidate is required** in order to reassess the efficacy of treatment, identify any adverse effects and ensure compliance and the absence of any misuse,
- **efficacy and safety data are limited beyond 12 months of treatment;** consequently, it is necessary to review the continuation of treatment beyond this period.

Finally, the Committee reiterates that methylphenidate currently has no MA **in the initiation of treatment in adults with ADHD**; only the continuation of treatment in adolescents whose symptoms persist into adulthood and in whom a clear benefit of treatment has been demonstrated is currently authorised for CONCERTA LP (methylphenidate) and MEDIKINET (methylphenidate) medicinal products, with the need for regular reassessment.

Concerning the integration of patients in the care pathway, in view of 2014 HAS guidelines relative to the procedure to be followed by primary care physicians in the event of a suspected diagnosis of ADHD, in particular, the following are highlighted:
- **the essential role of the primary care physician**, who, when confronted with a child presenting symptoms suggestive of ADHD, has the role of launching a diagnostic process, with the performance of an initial assessment (elimination of differential diagnosis, investigating for associated comorbidities, etc.) and initiating management (family information/support, treatment of comorbidities, educational support measures, etc.),
- **following the initial assessment having led to a suggested diagnosis of ADHD, the importance of referral by the primary care physician to a specialist in the disorder** (with expertise in the diagnosis and treatment of ADHD [child psychiatrist, psychiatrist, paediatrician, paediatric neurologist, neurologist]),
- **the need for early diagnosis and appropriate treatment of ADHD** to prevent any exacerbation of the psychological, educational and social impacts on the child; this aspect is particularly emphasised in a context in which delayed access to hospital specialists in the disorder due to regional inequalities in terms of access to care have been reported by experts, patient associations and users,
- **the importance of coordination between the specialist physician and the primary care physician, once the diagnosis has been made, in order to guarantee regular monitoring of patients in the context of this chronic disorder.** In particular, in the event of initiation of medicinal treatment, the follow-up frequency depends on the frequency of treatment prescription renewals, which are every 28 days;
- **the importance of multidisciplinary management** with hospital-community coordination between the ADHD specialist, the primary care physician (serving as the link between the various players involved), the pharmacist and other professionals treating comorbidities (psychologist, speech therapist, psychomotor therapist, etc.) and information-sharing in order to optimise patient follow-up.

It is reiterated that information documents aimed at patients and/or their families and a website for use by healthcare professionals to support the initiation and prescription of methylphenidate and patient monitoring (http://www.methylphenidate-guide.eu) are available.

Proposed modification of prescribing conditions for methylphenidate in ADHD by the Committee

At present, medicinal products containing methylphenidate are included in the list of narcotics for which prescription is limited to 28 days. In addition, in accordance with their MA, they are subject to restricted initial annual hospital prescription reserved for specialists and/or specialised departments in neurology, psychiatry or paediatrics. Annual prescription renewals are also reserved for these same hospital specialists, while other renewals can be issued by any doctor.

Considering the available efficacy and safety data, use data, data relative to the non-conformity of certain prescriptions which could prevent a delay in treatment, the need for early diagnosis/treatment of ADHD and the need to maintain the supervision of prescriptions in the MA indication, the Committee raises the question of whether it might be appropriate the revise

the initial prescription conditions defined in the MA of methylphenidate in order to guarantee better access to these treatments for patients requiring them, while at the same time maintaining the safeguards that are necessary in view of the drug's safety profile (see Committee recommendations).

Special recommendations

In the ADHD indication, the Committee raises the question of whether it might be appropriate the revise the prescribing conditions as defined in the MA, and, in particular, to extend initial prescription, in addition to hospital specialists, to:
- non-hospital independent-practice neurology, psychiatry or paediatrics specialists concerned by ADHD, who would be incorporated into multidisciplinary care networks for this condition,
- these same specialists practising in medico-social facilities caring for patients with ADHD and who are able to prescribe drugs.
The Transparency Committee also reiterates the importance of maintaining safeguards and specific prescribing conditions given updated data on misuse in France, as well as the efficacy and safety data.
Hence, the Committee proposes that the other conditions be maintained, in particular prescription limited to 28 days.

The Committee also encourages more uniform restructuring of current health networks focusing on learning difficulties in France in order to promote the coordination of care, which plays a key role in the management of these patients.

COMMITTEE'S CONCLUSIONS

Considering the "Reevaluation of medicinal products containing methylphenidate" assessment report of 24 June 2020 and further to debate and voting, the Committee considers:

Clinical benefit

Attention Deficit Hyperactivity Disorder (ADHD) can result in a significant deterioration in social relationships and educational integration and hence the quality of life of patients and their families.
Methylphenidate in combination with remedial measures is a second-line, symptomatic treatment of ADHD in children aged 6 years and over.
Considering:
previous efficacy data from the 2012 reevaluation having reported a short-term efficacy of methylphenidate compared to placebo on the symptoms of ADHD (signs of hyperactivity, inattention and impulsiveness) in children of school age, without, however, being able to clearly quantify the effect size of methylphenidate due to the high level of diversity in the scales assessed,
new efficacy data confirming the efficacy of methylphenidate in terms of short-term improvement of symptoms (less than 6 months), without eliminating the uncertainties concerning the real effect size of methylphenidate in its current role combined with remedial measures,
the continuing lack of data on the long-term efficacy of methylphenidate,
the absence of conclusive data for methylphenidate concerning quality of life,
the known and unchanged safety profile of methylphenidate with continued uncertainties with respect to the long-term effects, particularly in terms of neuropsychiatric, cardiovascular and cerebrovascular adverse effects and effects on the child's growth,
the efficacy/adverse effects ratio of methylphenidate is unlikely to be modified and remains moderate in the short term and still inadequately established in the long term.

When remedial measures alone prove insufficient, there is no medicinal alternative in children aged 6 years of age and over and adolescents with ADHD.
Methylphenidate is indicated as part of a comprehensive treatment programme for ADHD in children aged 6 years of age and over when remedial measures, combining psychological, educational and social management, alone prove insufficient.
The prescription of methylphenidate must scrupulously comply with the indication authorised by the MA and concern ADHD only, excluding all other behavioural disorders.

Public health impact:

Considering:
- the seriousness of the disorder and its impact on the quality of life of patients and their families,
- its prevalence,
- the partially met medical need,
- the absence of any demonstrated additional impact on morbidity or on quality of life, in view of a moderate efficacy demonstrated on the symptoms of ADHD (signs of hyperactivity, inattention and impulsiveness) and the safety profile, identified in the short term and inadequately elucidated in the long term,
- the absence of any demonstrated impact on the organisation of care and the patient's care or life pathway; in fact, the prescription of methylphenidate is part of a multidisciplinary and comprehensive treatment programme combined with educational, psychological and social measures. The prescription of methylphenidate is supervised at present in terms of prescribing and dispensing, with:
- a narcotic status, with prescription limited to 28 days,
- restricted initial annual hospital prescription reserved for specialists and/or specialised departments in neurology, psychiatry or paediatrics,
- annual prescription renewals also reserved for these same hospital specialists, while other renewals can be issued by any doctor,
- funding by the French national health insurance system subject to requirement of the doctor to indicate the name of the pharmacist who will dispense the prescription.

With respect to these aspects, patients eligible for treatment with methylphenidate could benefit from:

- a more fluid prescribing/dispensing circuit for the drug in order to facilitate access for patients requiring it, at the same time maintaining the necessary safeguards adapted to the safety profile of these drugs and their risk of misuse,
- improved structuring of management, which must be comprehensive, in order to better integrate remedial measures since methylphenidate continues to contribute to cover of the medical need in this condition,
  methylphenidate is unlikely to have an additional impact on public health.

Given all of these elements, the Committee considers that the clinical benefit of CONCERTA LP (methylphenidate) remains substantial as part of a comprehensive treatment programme for ADHD in children aged 6 years of age and over, when psychological, educational and social measures alone prove insufficient.

The Committee issues a favourable opinion for maintenance of inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use as part of a comprehensive treatment programme for ADHD in children aged 6 years of age and over, when psychological, educational and social measures alone prove insufficient.

Recommended reimbursement rate: 65%