Novo-Methylphenidate

February 2011 – Attention deficit hyperactivity disorder

Trademark : Novo-Methylphenidate ER-C
Generic name : Methylphenidate
Manufacturer : Teva
Form : Extended-release capsules (12 hours)
Dosage : 18 mg, 27 mg, 36 mg and 54 mg

Added to List of Medications – Exceptional Medication status

About this medication

Methylphenidate is a central nervous system stimulant. It is listed in the regular section of the drug coverage as per other immediate-release capsules (Ritalin™ et al) and long acting medications (Ritalin SR™). For its part, Concerta™ is an extended release methylphenidate formulation indicated "for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children (6 to 12 years), adolescents (13 to 18 years) and adults (18 and older)". Novo-Methylphenidate ER-C™ is indicated in the lists of drugs for the treatment of ADHD in children, adolescents and adults under certain conditions. Novo-Methylphenidate ER-C™ is a generic methylphenidate-based product. It has been deemed bioequivalent to Concerta™ by Health Canada.

Therapeutic value
Bioequivalence
Health Canada recognizes the bioequivalence between a generic and an innovative product when certain pharmacokinetics criteria are met. The comparison results of Novo-Methylphenidate ER-C™ and Concerta™ met the bioequivalence standards set by Health Canada. However, the *Conseil du médicament* notes differences between the formulations with respect to certain pharmacokinetic parameters, but these are not considered in the determination of bioequivalence between two products. Although concerned about the bioequivalence requirements for modified-release dosage forms, the *Conseil du médicament* considers that it is for Health Canada to determine the bioequivalence of the products. To this end, Health Canada convened a group of experts in June 2010 to discuss the requirements for bioequivalence for drugs with modified-release. The group recommended to not change the criteria for bioequivalence.

Formulation of the two products
Concerta™ uses a biphasic delivery system that provides immediate release of methylphenidate and gradually releases the remainder of the dose over a period of 12 hours. In addition, the formulation makes it difficult to extract the active substance. Although the bioequivalence of Novo-Methylphenidate ER-C™ with Concerta™ is recognized, the generic version does not use the same controlled-release system or the same formulation.

Clinical efficacy
No clinical trial has compared the efficacy of Novo-Methylphenidate ER-C™ to Concerta™ or that of an immediate-release methylphenidate. Therefore the clinical implications of pharmacokinetic or formulation differences are not supported by evidence. However, when transferring to Novo-Methylphenidate ER-C™, cases of efficiency loss, particularly evident by a return of hyperactivity, destabilization, or physical or verbal difficulties, have been reported by some health professionals.

Interchangeability and application of the lowest price
It is important to note that the List of Medications is not intended to establish, for a given drug, its interchangeability with other products listed on the list. The fact that two products are registered under the same title does not imply that they are interchangeable. Thus, it is up to the physician and the pharmacist to pay attention to the form of methylphenidate to offer, especially for patients already on treatment. However, the *Conseil du médicament* may, for therapeutic or other reasons, exclude a product from the application of the method of the lowest price by including it in Appendix IV of the List of Medications.

Conclusion
Although concerned about the bioequivalence requirements for modified-release dosage forms, the *Conseil du médicament* considers that it is for Health Canada to determine the bioequivalence of the products. However, the generic version of methylphenidate in the study met the bioequivalence standards set by Health Canada. Therefore, the *Conseil du médicament* recognizes the therapeutic value of Novo-Methylphenidate ER-C™ and deems appropriate its inclusion in the List of Medications. Nonetheless, the *Conseil du médicament* believes that certain differences between these two products could result in clinical differences and a greater potential for illicit use. As a precaution, considering that the consequences in destabilization of the disorder can be substantial, the *Conseil du médicament* do not want to apply the method of lowest price to the generic name "methylphenidate Co. LA (12 h)".

Economic and pharmacoeconomic aspects
Novo-Methylphenidate ER-C™ is available in 18 mg, 27 mg, 36 mg and 54 mg. Prices are consistent with the *Politique du médicament* and comply with the undertaking by the manufacturer which states that the guaranteed selling price must not be higher than any selling price granted by the manufacturer for the same drug under other Canadian provincial drug coverage. The monthly cost of treatment corresponding to a daily dose of 18 mg to 54 mg is $39 to $58.

Health consequences of the population and the health system

The *Conseil du médicament* is aware of some cases of destabilization of the disorder involving individuals with ADHD and treated with Concerta™ that would have been less well controlled during the transfer to a generic version. Destabilization of the disorder may have important consequences for the child, but also for those around her/him. In addition, the formulation of Concerta™ makes its use difficult for illicit purposes, contrary to its generic version. Therefore, despite the potential for substantial savings, the *Conseil du médicament* favours the addition of "methylphenidate Co. LA (12 h)" in Appendix IV of the List of Medications in order to exclude it from the application of the method of the lowest price.

Conclusion
Taking into account all the criteria under the law, the *Conseil du médicament* recommended the inclusion of Novo-Methylphenidate ER-C™ in the section of Exceptional Medications with the same reference recognized with Concerta™. It does not, however, recommend the application of the method of lowest price to the generic name "methylphenidate Co. LA (12 h)". The indication recognized for Novo-Methylphenidate ER-CTM is:

- To treat people with Attention Deficit Disorder, in whom the use of short-acting methylphenidate or of dexamphetamine has resulted in poor symptom control;

Before concluding to the ineffectiveness of these treatments, the stimulant must have been titrated optimally, unless proper justification.

Note: Published and unpublished references have been consulted.

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