



Two new long-acting psychostimulants for ADHD treatment launched in Canada: CADDRA Commentary

11 March, 2010: Two new treatments for ADHD are now available in Canada: a new medication, an amphetamine-based pro-drug, **lisdexamfetamine (Vyvanse™)** and **Novo-Methylphenidate ER-C**, a methylphenidate-based long acting product, just approved by Health Canada as a generic for **Concerta™**.

In Canada, pharmacological treatment options for ADHD include two different families of products: non stimulant medication (atomoxetine, **Strattera™**) and psychostimulants. Psychostimulants are divided into two groups: amphetamine-based and methylphenidate-based products. Some are immediately released and others are delivered progressively through different mechanisms. CADDRA suggests using long-acting medications first line and short-acting medication, second line. The Medication Chart (available on the CADDRA website under Physicians/Resources and Links) illustrating available dosages, starting doses and augmentation strategies has been updated with information concerning **Vyvanse™**.

Lisdexamfetamine (**Vyvanse™**) is a pro-drug and is a new addition to the amphetamine-based product portfolio in Canada. It contains a clinically inactive complex of dextro-amphetamine coupled to lysine. For dextro-amphetamine to be released, this product has to be biologically activated by an enzyme present mostly in blood and some in the gut. This delivery mechanism produces a clinical effect of 12 hours or more (12h: monograph information, 13h in a clinical trial in children and 14h in adults). This medication is highly soluble and can be diluted in water for titration if needed. This kind of delivery system is not influenced by gastric PH or transit time. Clinical effects have been described as more stable over time for each individual and more constant from one person to the other. Because of its pro-drug design, its delivery curve is not changed by mode of administration (oral, inhalation or injection), reducing its abuse potential.

Novo-Methylphenidate ER-C is a generic methylphenidate-based product, with a progressive delivery system, that has just been approved by Health Canada as a generic for **Concerta™**. The actual delivery mechanism of **Novo-Methylphenidate ER-C** has not been described. This medication is not delivered via the OROS pump system, which is utilized for **Concerta™**. The visual appearance of the medication is very similar to **Concerta™** capsules. However, unlike **Concerta™**, **Novo-Methylphenidate ER-C** can easily be divided, crushed and powdered, which could potentially increase its abuse potential. It is important to know that abuse potential is reduced if the medication is a non stimulant or a long-acting psychostimulant delivered in a non-crushable format. It has been shown that inhalation or injection of immediate-released methylphenidate-based or amphetamine-based medication can induce a pleasurable sensation, increasing the abuse potential.

As with all other generic products, **Novo-Methylphenidate ER-C** was made available in Canada after demonstrating bioequivalence to **Concerta™** according to Health Canada criteria. However, clinical equivalence to the original product has not yet been established. Bioequivalence does not mean clinical efficacy equivalence. Clinical equivalence data is needed to ensure that the generic

formulation will in fact have the same effect for patients. This is particularly a concern because of the different delivery system employed by the generic medication. We know that time necessary to obtain the maximal concentration (Tmax) is earlier with the generic medication, but we don't know if that will influence the side effects profile, onset and duration of action of **Novo-Methylphenidate ER-C** compared to **Concerta™**. For the time being, we don't have enough data to comment on its clinical efficacy. As things now stand, we will need to wait for clinical experience to offer clarity.

Pharmacists have the right to substitute an *innovative* or *original* product for a generic product. They have to make sure that the generic product is likely to produce the expected therapeutic effect, similar to the trade mark medication. If the pharmacist believes that the generic product will produce a therapeutic effect similar to the original product, he can decide to proceed to a substitution. Pharmacists that consider a substitution must analyze the clinical situation of the patient, taking into account the current medication profile, actual clinical considerations specific to the patient and his or her treatment history. It is logical that close follow-up would have to be put in place and that a discussion with the prescribing physician could be required. A patient has the option to reject the proposed substitution. If the patient is covered by a public medication insurance program, or in certain cases of private insurance programs, he or she may be required to pay more for the original product. Physicians may decide to write *do not substitute* on the prescription.

Only clinical experience will help answer the questions of clinical efficacy and abuse potential. In the mean time, **Novo-Methylphenidate ER-C should be considered an additional ADHD treatment option**, instead of a product that can automatically replace **Concerta™**. Each case is unique and it is crucial to personalize treatment taking into account the needs of each patient.