CADDAC
CENTRE FOR ADD/ADHD ADVOCACY, CANADA

22 February 2010

Dr. Supriya Sharma
Director General
Therapeutic Products Directorate
Health Canada
1600 Scott Street
Ottawa, Ontario, K1A 0K9

Dear Dr. Sharma:

Re: Novo-Methylphenidate -ER-C (Novo-Methylphenidate ER-C)
Concerns of CADDAC

The purpose of this letter is to express concern about the availability of Novo-Methylphenidate ER-C and the potential for interchangeability at the provincial formulary level. We ask you to request additional data to unequivocally demonstrate the interchangeability of Concerta® and Novo-Methylphenidate ER-C before investing taxpayer dollars in this product.

Our concern is that patients who are currently being successfully treated with Concerta® will be switched with or without their knowledge, or permission, to a generic medication that does not offer identical coverage. Inadequately treated ADHD offers a host of well documented risks, especially if the risk is not being adequately monitored due to an unrecognized change in medication.

CADDAC is a national, not-for-profit organization providing leadership and support in education and advocacy for ADHD organizations and individuals across Canada. CADDAC will be celebrating its 5th Anniversary in June 2010.

ADHD is the most treatable childhood mental health disorder. As communicated in the past by CADDAC, it is vital that provincial formulary authorities invest in child and adolescent education by providing access to high quality medications for the treatment of ADHD. Medication is an important component of a successful treatment plan along with other interventions such as tutoring, counseling and education about their disease. It is our belief that the safety, efficacy and effectiveness of ADHD medications must be unequivocally demonstrated scientifically prior to children and adolescents having access to them. The long-term consequences of inadequate treatment are too high from a societal point of view. Should you wish to have more information on this topic, CADDAC would be pleased to meet with you.

Our concerns with Novo-Methylphenidate ER-C are twofold.

1. Efficacy: Evidence to demonstrate true clinical interchangeability has not yet been generated.

2. Safety: The Novo-Methylphenidate ER-C formulation could represent a step backwards in patient care in that no abuse potential studies have been conducted. There is a potential for abuse which is not present with the innovator product.

Efficacy: Evidence of interchangeability

Although Novopharm has met the threshold for bioequivalence set out by Health Canada, the method to demonstrate bioequivalence was devised before the Oros™ technology used in Concerta® was available. Health Canada's various guidance on bioequivalence did not anticipate such a product and therefore, the requirements do not necessarily apply in this case from a scientific point of view. A scientific analysis should be conducted to determine whether the current requirements are sophisticated enough to discern potential differences in this type of product.

We are not aware that Health Canada consulted with its own Expert Advisory Committee prior to issuing the NOC for Novo-Methylphenidate ER-C. We are not aware that this product has been approved in any other country. It is not listed on either the EMEA or FDA websites. In fact, it appears that the FDA will require additional data before approving such a product.

Based on the information provided in the Product Monograph for Novo-Methylphenidate ER-C, the time to peak concentration occurs at 4.6 hrs with Novo-Methylphenidate ER-C, three hours earlier than the 7.6 hrs with Concerta® (in a non-fasting state). Although the relative mean of the Cmax is less than 125% of the innovator, the upper limit of the confidence interval does not (126.17%). Do these anomalies impact on blood levels throughout the day? The sponsor should be requested to demonstrate the clinical impact this has on children, adolescents and adults in school and work environments before the taxpayer invests in this product.

The Product Monograph for Novo-Methylphenidate ER-C does not adequately explain the release mechanism. The Clinical Trial section does not describe any clinical testing done in a laboratory classroom to determine the reliability or inter-individual variability. Previous experience with release mechanisms, such as Ritalin SR®, has demonstrated that the pharmacokinetic profile does not guarantee reliable release in all patients. The Cmax of the Novopharm product indicates that the course of release over the whole day is distinct from the Innovator drug and, in this case, that may mean children or adults taking it will have altered response at different time periods.

Bioequivalence data in children and adolescents was not generated. Therefore, the rate and extent of absorption in a large proportion of patients has not been investigated.

Provincial authorities should request additional clinical pharmacology (such as partial AUC) and if scientifically warranted based on partial AUC data, clinical trial evidence to establish the actual comparative effectiveness of the two products throughout the duration of action of the innovator product to ensure continuous coverage for the patient.

Abuse potential

One of the important improvements to the treatment of ADHD brought about by the introduction of Concerta® was the reduction and/or elimination of abuse potential. The target patient

population is at risk from several viewpoints. There is a strong genetic link in ADHD; therefore it is possible that a parent or parents are also affected. Many parents were never diagnosed and suffer the consequences of long-term complications of untreated ADHD. One of these complications is drug abuse. In addition, children and adolescents in possession of a format of MPH that has abuse potential could be targets of those who wish to abuse this drug. Finally, some patients may choose to abuse MPH themselves. The advantage of Concerta® is that it makes this virtually impossible. The Novopharm product uses a long-acting release system that is *not* the same Oros™ Technology found in Concerta®. The Novopharm product is a tablet. A crushable tablet is more likely to have abuse and diversion potential and may put patients at risk. Novo-Methylphenidate ER-C is comparable to other short acting psychostimulant medications in this regard.

Conclusion

In principle, CADDAC does not object to generic drugs and in fact for many families, a lower cost alternative would relieve a financial burden. However, substituting generic medication without first confirming the medication has the same clinical impact and can be used safely (vis-à-vis abuse potential) is irresponsible.

- The mechanism of action (release mechanism) of Novo-Methylphenidate ER-C and a granular understanding of the profile of action are unknown.

- The abuse potential of Novo-Methylphenidate ER-C is unknown.

- There is currently no evidence to show the comparability of the two products throughout the school (or work) day.

Therefore, it is the position of CADDAC that taxpayers should not invest in Novo-Methylphenidate ER-C until these very important questions are adequately addressed with scientific evidence.

I look forward to discussing this with you or one of your staff before a decision is made as to the interchangeability of Concerta® and Novo-Methylphenidate ER-C. As always, we appreciate your efforts and the consideration you have show to patients with ADHD and their families.

Sincerely,

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