Ritalin® LA (methyl phenidate)

Minutes of the Scientific Advice Meeting between MPA and Novartis Pharma , 2 July, 2009 in Uppsala

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Attendees:

MPA:

Dr Hans Melander	Senior Statistician
Dr Bo Bergman	Drug Information

Novartis:

Dr Alison Bannon	Regulatory Affairs, Novartis Basel
Dr Vinod Kumar	Medical Director Neuroscience, Novartis US
Anita Soederqvist	Regulatory Affairs, Novartis Sweden

Subject of the discussion was Novartis' intent to file an application for an extension of the indication of Ritalin LA into treatment of ADHD in adult patients. Ritalin LA modified release hard capsules with the active ingredient methylphenidate hydrochloride are currently approved for the treatment of hyperkinetic disorder or attention deficit/hyperactivity disorder (ADHD) in children 6 years old or above.

Novartis applied for this scientific advice to discuss the clinical development program for this indication extension.

The discussion took place in a friendly, constructive atmosphere.

The clinical study proposed by Novartis was discussed on the basis of documents and the list of questions submitted by Novartis in preparation of the meeting.

Questions and Answers:

Question 1

Does the MPA agree that the pharmacokinetic and clinical data from the Focalin XR studies in adults can be used as the basis for dose selection in the proposed study and as supplemental efficacy and safety data to support Novartis' application for the extension of Ritalin® LA into the treatment of ADHD in adults?

MPA agreed with the Novartis proposal to use existing data from Focalin XR in adults to guide dosage for Ritalin LA, and to confirm the choice in the dose titration first phase of the proposed efficacy study

Question 2

Does the MPA agree that the proposed clinical study below is sufficient to evaluate the safety and efficacy of Ritalin LA in adults with ADHD?

The design is acceptable to show short and long term efficacy

Points to consider are:

- add responder analysis to phase 1 of the study
- keep investigator and patient blinded to the start of the withdrawal phase
- adjust the length of the phases- 6 week optimal dose could become 4 weeks, and 4 month withdrawal phase could become 5 months

Question 3

Does the MPA agree that there is no need to perform an active controlled trial in the event that another methyphenidate product is approved for the treatment of adult ADHD in the EU before the Novartis submission?

Unless clear that there is huge difference in efficacy, no active comparator study is needed. This is true for methylphenidate and non-methylphenidate products. MPA warned that this only applied to Sweden, and that other countries may have different view.

MPA say that approx 50% of methylphenidate treatments in Sweden are adults. MPA supported Novartis' position during referral, that patients treated during childhood could continue treatment into adulthood if benefit continued.

Question 4

Does the MPA agree with the proposed submission package for approval of the indication for Ritalin® LA in the treatment of ADHD in adult patients?

MPA agreed with Novartis proposal. The package cross refers to previous Ritalin LA data, provides Focalin XR adult data as support, and contains one new clinical efficacy and safety study.

Other comments

MPA was interested in data on substance abusing patients. This is not compulsory, but would be interesting. Novartis intends to exclude this group from study. This could require some wording to this effect in the final label. Novartis suggested that information on drug abuse might be available from the Drug Utilisation Study planned as one of the referral FUMs. The MPA agreed that this could be appropriate.