

**Addendum to New Drug Application
NDA 20-825 S-032**

Drug: Ziprasidone Hcl Capsules
Sponsor: Pfizer, Inc.
Indication: Acute treatment of bipolar I disorder, manic and mixed episodes, in patients aged 10-17 years of age
Date of Addendum: 22 June 2009

I. Background

New Drug Application 20-825 S-032 was filed with the Agency on 21 October 2008. At the time of the filing, two additional atypical antipsychotic medications were either filed or also being reviewed for a similar indication. Due to clinically significant safety signals seen with use of atypical antipsychotics in children during review of the applications, the Agency held a meeting of the Psychopharmacological Advisory Committee (PAC) on 9-10 June 2009 to review the efficacy and safety data of these antipsychotics (including ziprasidone) and provide regulatory recommendations.

Consequently this reviewer had finished review of the application on 24 April 2009 but did not offer a recommendation on the application pending results of the June 2009 PAC. This addendum is being completed by the review as a result of review and analysis of the NDA data presented at the June 2009. The following sections of the NDA are amended as follows.

II. Amendments to April 2009 New Drug Application

1 EXECUTIVE SUMMARY

1.1 Recommendation on Regulatory Action

As a result of this reviewer's analysis of this New Drug Application's data and recommendations received and analyzed from the June 9-10, 2009 Psychopharmacological Advisory Committee,

(b) (5)

1.2 Recommendation on Post marketing Actions

1.2.1 Risk Management Activity

(b) (5)

1.2.2 Required Phase 4 Commitments

(b) (5)

1.2.3 Other Phase 4 Requests

(b) (5)

8.5 Advisory Committee Meeting

An advisory committee meeting was held on June 9-10th, 2009 to review the results of the clinical development program for pediatric bipolar disorder.

Although the data clearly demonstrated efficacy for the diagnosis of pediatric bipolar disorder, discussions regarding the phenotypic presentations of bipolar disorder in the patients enrolled in the study was discussed. As debate continues to occur in the field of child psychiatry as to which phenotypic presentation [i.e Narrow Phenotype, Bipolar I disorder as described via use of the WASH-U K-SADS, Bipolar, NOS or Severe Mood Dysregulation (Geller 2008, Leibenluft 2003)], the committee recommends that approval of atypical antipsychotic for the diagnosis of pediatric bipolar disorder include discussion of this uncertainty of diagnostic phenotype.

(b) (5)

9 Overall Assessment

9.1 Conclusions

Based on the review of this New Drug Application and review of the discussions and recommendations made by the Psychopharmacological Advisory Committee for this New Drug Application being presented on June 9 and 10th, 2009, efficacy was clearly demonstrated for ziprasidone for the acute treatment of pediatric bipolar disorder. In addition, this reviewer has recommended that the Warnings for QTc prolongation with ziprasidone use be extended for the pediatric population and incorporation of a table delineating the common, drug related adverse events that occurred in the placebo controlled trial. This recommendation was also recommended by the advisory committee.

9.2 Recommendation on Regulatory Action

After review of the discussions and recommendations made by the Psychopharmacological Advisory Committee for this New Drug Application being presented on June 9 and 10th, 2009,

(b) (5)

9.3 Recommendation on Post marketing Actions

(b) (5)

9.3.1 Risk Management Activity

(b) (5)

(b) (5)

9.3.2 Required Phase 4 Commitments

(b) (5)

9.4 Other Phase 4 Requests

(b) (5)

III. CHANGES TO TABLES

(b) (5)

REFERENCES

Geller B, Tillman R, Bolhofner K, Zimmerman B (2008) Child bipolar I disorder: prospective continuity with adult bipolar 1 disorder; characteristics of second and third episodes; predictors of 8-year outcome. *Arch Gen Psychiatry* Oct; 65(10): 1125-33.

Leibenluft E, Charney DS, Pine DS (2003) Defining clinical phenotypes of juvenile mania. *Am J Psychiatry* June; 160(6): 1172-4.

Mark Ritter, MD

CC: HFD-130 Div File
HFD-130 Laughren/Mathis/Levin/Ritter

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/s/

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