PROTON PUMP INHIBITOR (PPI) WRITTEN REQUEST TEMPLATE FOR PEDIATRIC GERD

DRAFT QUESTIONS FOR DISCUSSION

A. Neonates and Premature infant patients

1. Does the Committee agree that the effectiveness of a PPI, for the treatment of pathologic GER in neonates and premature infant patients, cannot be extrapolated from older pediatric patients and adults?

    a. If the Committee agrees that it is possible to extrapolate to this sub-population, what safety or long term follow-up issues would be most critical in developing trials for the neonatal and premature infant patient population?

    b. If the Committee agrees that it is not possible to extrapolate to this sub-population, is it ethically acceptable to conduct the requested randomized, placebo controlled withdrawal trial design to establish the effectiveness and safety of proton pump inhibitors in neonates and premature infants? If not, please suggest an alternative, ethically acceptable trial design to establish effectiveness and safety.

2. Are the efficacy and safety endpoints chosen for this PPI template study acceptable? If not, please suggest alternative clinically meaningful efficacy endpoints for pathologic GER or additional safety endpoints.

3. Are the specified trial design inclusion criteria, monitoring, and assessments adequate? If not please suggest alternative or additional criteria, monitoring and/or assessments.

4. Is the duration of proposed follow-up at 6 and 12 months after enrollment for developmental, growth and safety assessments adequate? If not, what duration of follow-up safety assessment is recommended?

5. Are the study designs for single dose PK and safety, and repeated dose PK/PD studies in neonates and premature infants acceptable, i.e., are there additional and/or alternative assessments recommended for study of a PPI in neonates and infants?

B. 1- month through 11-month old infant patients

1. Does the Committee agree that the effectiveness of a PPI, for the treatment of pathologic GER in infant patients 1-month to 11 months of age, cannot be extrapolated from older pediatric patients and adults?

    a. If the Committee agrees that it is possible to extrapolate to this sub-population, what safety issues would be most critical in developing trials for the 1-month through 11-month old infant patient population?

b. If the Committee agrees that it is not possible to extrapolate the data to this sub-population, is it ethically acceptable to conduct the requested randomized, placebo controlled withdrawal trial design to establish the effectiveness and safety of proton pump inhibitors? If not, please suggest an alternative, ethically acceptable trial design to establish effectiveness and safety.

2. Are the specified trial design inclusion criteria, monitoring, and assessments adequate? If not please suggest alternative or additional criteria, monitoring and/or assessments.

3. Are the efficacy and safety endpoints chosen for this PPI template study acceptable? If not, please suggest alternative or additional endpoints.

4. A longer-term follow-up safety assessment was not requested in this WR template. Do you recommend such a study be included as part of the WR? If yes, please recommend the duration and safety assessment endpoints of such follow-up.

5. Are the study designs for single dose PK and safety, and repeated dose PK/PD, and safety studies in pediatric patients 1 month-11 months of age acceptable, i.e., are there additional and/or alternative assessments recommended for study of a PPI in neonates and infants?

C. 1-year old though 11 year old pediatric patients

1. Does the Committee agree that approval for pediatric use in patients 1 year to 11 years of age, inclusive, can be based on adequate and well controlled studies in adults with additional pharmacokinetic, exposure/response, and safety information?

2. Are the study designs for single dose PK and safety, and repeated dose PK and safety studies in pediatric patients 1 year to 11 years of age acceptable, i.e., are there additional and/or alternative assessments recommended for study of a PPI in this population?

3. Is the exposure/response study design for in pediatric patients 1 year to 11 years of age acceptable?

D. 12 year old through 16 year old pediatric patients

1. Does the Committee agree that approval for pediatric use in patients 12 years through 16 years of age, can be based on adequate and well controlled studies in adults with additional pharmacokinetic and safety information. In other words, does the Committee agree that extrapolation is justified because the course of GERD in this age group is similar to that in adults, and the effects of the PPI, both beneficial and adverse, are expected to be similar in this pediatric age group and adults?

2. Does the Committee have any concerns about the single and repeated dose PK studies and eight-week safety study component outlined in this WR, for patients 12 years through 16 years of age?