FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Dermatologic and Ophthalmic Drugs Advisory Committee Meeting

HILTON WASHINGTON DC / SILVER SPRING
SILVER SPRING, MARYLAND

QUESTIONS TO ADVISORY COMMITTEE

June 17, 2008

Please discuss the efficacy of ustekinumab:

1. Has the applicant provided sufficient information to demonstrate efficacy of ustekinumab in the treatment of plaque psoriasis?

2. The applicant has proposed "dosing every 12 weeks". Has the applicant provided sufficient information to support this dosing schedule?

3. Please discuss the alternative weight-based dosing paradigms. Which dosing regimen do you recommend?

4. Has the applicant provided sufficient information to inform patients/physicians regarding when/how to stop treatment with ustekinumab?

Please discuss the safety of ustekinumab:

5. Discuss the critical safety concerns with ustekinumab and the sufficiency of the database to characterize them.
   Have a sufficient number of subjects been studied?
   Have subjects been followed for a sufficient length of time?

6. Discuss the potential for malignancy demonstrated by this class of compounds, including the findings from animal studies that indicated an increased carcinogenic risk with inhibition of IL-12/IL23.
   Is it important to communicate these findings to prescribers?
   Are additional animal studies needed?

Please discuss the relative benefits and risks for the use of ustekinumab in patients with moderate to severe plaque psoriasis:

7. Do the benefits of ustekinumab therapy in adult patients with moderate to severe psoriasis outweigh the risks?

8. Do you recommend approval of ustekinumab for the treatment of adult patients with moderate to severe plaque psoriasis?

a) If the answer is **no,** what additional premarketing studies do you suggest?

i) completion of the pivotal trials extensions prior to approval
ii) new randomized clinical trials
iii) other studies

b) If the answer is **yes,**

i) describe the recommended dosing regimen and the length of treatment
ii) should the product be labeled for patient self administration or only for prescriber administration?
iii) are the applicant's risk assessment proposals (PSOLAR, 5 year extension of pivotal trials) sufficient to characterize the long term safety of ustekinumab? Please discuss these options:

a) increasing sample size of PSOLAR
b) epidemiologic study (observational)
c) mandatory registry/restricted distribution
d) disease-based registry