Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee
Pediatric Labeling for Oncology Products

March 4, 2003

Questions to the Committee

Federal government initiatives are aimed at developing therapeutics for pediatric patients and including product information in the approved package insert or product label. Although the majority of children with cancer in the United States are treated on protocols from National Cancer Institute supported study groups, the majority of products used in children with cancer are used without dosing and safety information in the package insert. Given that the U.S. Congress has indicated in the Best Pharmaceuticals for Children Act of 2002 that pediatric use information should be included in product labels as one of the mechanisms to publicly disseminate that information, consider each of the following situations.

If adequate and well controlled trials in children that independently establish safety and efficacy are submitted to the FDA as a New Drug Application (NDA) or Biological Licensing Application (BLA) or as a supplement to an NDA or BLA, then product labeling would follow standard procedures. The situations that follow describe circumstances when information other than adequate and adequate and well controlled trials sufficient to independently establish safety and efficacy are submitted.

The first questions pertain to the situation where a product is approved (safety and efficacy established) for an adult indication and the same disease or condition exists in a pediatric population.

Previously the Pediatric Subcommittee of the Oncologic Drugs Advisory Committee, at a meeting in November 2001, recommended that to extend efficacy from an adult indication to a pediatric population (use extrapolation), pediatric dosing studies and a demonstration of clinical proof of concept should be performed.

1. If a product is approved for an adult disease or condition that also exists in children and extrapolation is used, consider what information you would consider necessary and appropriate to be in the product label.

   Factors may include:
   - Dosing
   - Safety information
   - Proof of concept data regarding clinical effect in children
   - Separation of pediatric and adult safety data if differences exist

2. If pediatric dosing and safety information are available but clinical proof of concept has not been established, consider whether dosing and safety information be included in the product label. This circumstance could arise if studies were done in children with diseases other than the one that is being considered for an indication yet extrapolation is being considered on the basis of other evidence.

The next question pertains to the situation where there is not a linkage between an adult indication and data from pediatric studies.

3. If pediatric dosing information and proof of concept data exist for a pediatric disease or condition that does not exist in adults, what information, if any, should be included in the product label.

   An example may be that a product is approved for second line colorectal cancer in adults and pediatric data are available for dosing and pharmacokinetics plus a single arm phase II study showing a modest response rate in 20 pediatric patients with refractory or relapsed neuroblastoma (There is no existing product with this profile).

   Factors may include:
   - dosing
   - safety information
   - clinical response data

The following question pertains to the situation where there is no evidence of clinical benefit in a pediatric oncology population and there are data of a lack of activity

4. If dosing, safety, and lack of activity information are available from studies that enrolled children with cancer, consider what information, if any, be included in the product label. Factors may include:

   - a statement restricted to stating that no meaningful clinical activity has been observed
   - the number and diagnoses of the patients in the studies
   - dosing information

The following question pertains to the situation where no efficacy or safety data are available in pediatric patients.

5. When no efficacy or safety data are available in pediatric patients consider if a statement that safety and efficacy have not been tested in children be included in the product label