

## Discussion Points for the Oncology Drugs Advisory Committee

(December 18 Meeting)

NDA 20-498/s012 (Casodex 150 mg tablets)

1. Across ongoing Trials 24 and 25, only 15.6% of patients (Sponsor-preferred endpoints) and 9.3% of patients (FDA-requested endpoints) had objective progression of prostate cancer or died from any cause in the absence of disease progression. At the time of data cutoff (June 2000), median follow up was 2.6 years (Trial 24) and 3.0 years (Trial 25). In the absence of meaningful survival data or quality of life benefits, are these studies sufficiently mature to conclude with a reasonable level of confidence that patients treated with Casodex in these trials will derive clinically significant long-term benefit? If not, what additional information is needed?
2. Do the lack of valid Gleason scores and the variation in PSA values in Trials 24 and 25 allow for the adequate definition of a patient population that can be extrapolated from the non-U.S. studies to a defined group(s) of U.S. patients who will derive significant benefit from Casodex therapy?
3. Based on the findings in Trial 23 as of the June 2000 data cutoff, it appears that Casodex does not offer a significant benefit for men with early prostate cancer who initially are treated by radical prostatectomy or radiation therapy with a curative intent. In light of this observation:
  - a) What population of patients, if any, who are initially treated by radical prostatectomy or radiation therapy of curative intent in the U.S., would benefit from adjuvant treatment with Casodex?
  - b) If you have identified a population that you believe would derive clinically significant benefit, what are the data in the Sponsor's submission that support your recommendation? Please identify
    1. The specific study(s) and patient population(s).
    2. The specific benefits and risks for this population.
    3. Any additional need for data (be specific)
  - c) If you were unable to identify a population, what additional data would you require to allow you to conclude that Casodex adjuvant would provide a clinically significant benefit for U.S. patients?
4. In the U.S. Trial (Trial 23), there was no watchful waiting (surveillance) treatment group.
  - a) Has the Sponsor demonstrated in Trials 24 and 25 (both non-U.S. trials) that U.S. patients with localized non-metastatic prostate cancer who are presently managed by surveillance (i.e., watchful waiting) would derive sufficient benefit from Casodex monotherapy or immediate treatment to justify the adverse events that would be associated with such treatment?

- b) If you answered “yes”
  - 1. What are the data that support your decision?
  - 2. What are the characteristics of the U.S. patients who would derive benefit?
  - 3. What are the specific benefits and risks for these patients?
- c) If you answered “no”
  - 1. What additional data would you require to allow you to conclude that Casodex monotherapy would provided clinically significant benefit for U.S. patients presently managed by watchful waiting?