

DEPARTMENT OF UROLOGY

Chair

Edward M. Messing, M.D., FACS

Vice Chair

Ronald Rabinowitz, M.D., FAAP, FACS

Director of Education

William C. Hulbert, M.D., FAAP

November 27, 2002

ADULT/GENERAL UROLOGY

Robert S. Davis, M.D.

Professor of Urology  
Infertility/Erectile Dysfunction  
(585) 275-3343

Erdal Erturk, M.D.

Associate Professor of Urology  
Stone Disease  
Endourology/Laparoscopic Surgery  
Renal Transplant  
(585) 275-3690

Jean V. Joseph, M.D.

Assistant Professor of Urology  
Reconstructive Urology  
Laparoscopic Surgery  
(585) 756-5469

Robert D. Mayer, M.D.

Associate Professor of Urology  
Incontinence/Voiding Dysfunction  
(585) 275-2486

Edward M. Messing, M.D., FACS

W. W. Scott Professor of Urology  
Professor of Oncology/Pathology  
Urologic Oncology  
(585) 275-0998 (Clinical)  
(585) 275-3345 (Administrative)

PEDIATRIC UROLOGY

(585) 275-7509

William C. Hulbert, M.D., FAAP

Associate Professor of Urology  
Associate Professor of Pediatrics

Robert A. Mevorach, M.D., FAAP

Assistant Professor of Urology  
Assistant Professor of Pediatrics

Ronald Rabinowitz, M.D., FAAP, FACS

Professor of Urology  
Professor of Pediatrics

RESEARCH FACULTY

Chawnsang Chang, Ph.D.

George Hoyt Whipple Professor  
of Pathology  
Professor of Urology

Yi-Fen Lee, Ph.D.

Assistant Professor of Urology

Shu-Yuan Yeh, Ph.D.

Assistant Professor of Urology

Karen M. Templeton-Somers, PhD  
Executive Secretary  
Oncologic Drugs Advisory Committee  
Food and Drug Administration  
5600 Fishers Lane, HFD-21  
Rockville, MD 20857

Dear Dr. Templeton-Somers:

On December 18, 2002 an open hearing will be held concerning possible approval of bicalutamide 150 mg. for use in early prostate cancer. I am writing to you concerning this meeting, because, I unfortunately will not be able to attend it. However, I urge your committee to seriously consider approving this use of Casodex. By way of background, I have over a 20 year history of being involved in NIH and industry sponsored, basic, translational, and clinical research on urologic malignancies, was an institutional investigator in a recently closed trial using Casodex 150 mg. in adjuvant treatment of patients with localized prostate cancer following radical prostatectomy, have some familiarity with some of the other trials of Casodex at this dosage, and have considerable familiarity with hormonal therapy in both metastatic and earlier stage prostate cancer (among some of the trials I have designed and participated in include one of the few that has demonstrated a true survival benefit from early hormonal therapy [Messing, et al. NEJM 1999;341:1781]). A brief biographical sketch is enclosed with this letter simply to demonstrate that I have both familiarity and interest in this topic.

I urge you to consider approval of Casodex for use in non-widely metastatic prostate cancer, not only because its efficacy is not inferior to that of standard treatment (castrative therapies) in this scenario, but also because, as far as can be discerned, with the exception of breast tenderness and gynecomastia, its morbidity profile is clearly superior to that of castrative therapies. These include less bone demineralization, libido reduction, and erectile dysfunction. Indeed, it

is often these side effects that prevent young men at very high risk for disease recurrence, or with recurrent disease already, to receive hormonal therapy -- even in circumstances in which it has clearly been proven to be beneficial (e.g. N+ disease in patients who have undergone radical prostatectomy and lymphadenectomy). There are other clinical scenarios which may also be appropriate (e.g. Pound et al. J Urol 1999;162:762). Unfortunately, I have several patients in my own practice who have declined hormonal treatment because of adverse effects of castrative therapies, particularly on sexual desire and function. Moreover, with more and more evidence coming out indicating the benefits of earlier hormonal therapy, men stay on these treatments longer than the 2-3 years usually experienced by patients with widely metastatic disease. Thus, the consequences of prolonged castrative therapy will even be greater (particularly on osteoporosis).

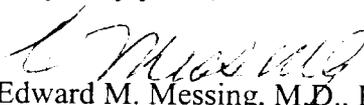
Currently, aside from Casodex, there are no effective hormonal therapies that approach the benefits of castration that have bicalutamide's relatively low morbidity profile. Without approval for this indication, however, the price of this medication is out of reach for most men.

Based on the data I am aware of, I strongly urge your approval of Casodex 150 mg. for early prostate cancer. I know that there are many times that I have wanted to prescribe it, but have not because of financial and other implications that occur with prescribing drugs not at an approved dosage or for an approved indication.

I greatly appreciate your willingness to read my comments, and regret my inability to attend the hearing on December 18<sup>th</sup>. I would be happy to speak with you about this matter at any time, and would be very interested in hearing the follow-up of your committee meeting.

Thank you very much for your attention to this matter.

Very truly yours,

  
Edward M. Messing, M.D., FACS  
W.W. Scott Professor  
Chairman, Dept. of Urology  
Professor of Oncology and Pathology  
Deputy Director, James P. Wilmot Cancer Center

EMM/kmf

**Somers, Karen M**

**From:** Richard Profit, Jr. [REDACTED]  
**Sent:** Monday, December 16, 2002 4:31 PM  
**To:** somersk@cder.fda.gov  
**Subject:** FDA approval of 150 mg. Casodex

Dear Ms. Templeton:

As the Director of PAACT and its 36,500 members world wide, we urge the FDA's approval of 150 mg. strength Casodex for the treatment of **Prostate Cancer**. This is a proven and successful treatment for all stages of PC, with minimal side effects as opposed to other available treatment options.

Yours truly,

Richard H. Profit, Jr.  
PAACT Director

December 16, 2002

Karen M. Templeton-Somers, Ph.D  
Executive Secretary  
Oncologic Drugs Advisory committee  
Food and Drug Administration  
5600 Fishers Lane, HFD-21  
Rockville, MD 20857

Dear Ms. Templeton-Somers:

My history of prostate cancer has followed a long and difficult trail. I was diagnosed with cancer September, 1998 in Sacramento, California. I then went to Seattle and received temporary high-dose radiation seeds followed by 30 days of external beam radiation. Both of these failed and my PSA continued to rise to 38. An MRI was ordered at that time and revealed that the cancer had metastasized to my spine. I was then referred to Dr. Peter Carroll at the University of California San Francisco Medical Center. Dr. Carroll placed me on the traditional hormonal therapy of 50 mg Casodex daily, plus a monthly injection of Lupron. I remained on this regimen for eight months. The multiple side effects were such as to not allow me to proceed with my normal life's activities. To say they were serious would be an understatement. I discontinued the hormone treatment and stayed off for several months. The side effects of the Lupron Casodex disappeared quickly but my PSA began to rise.

At that time I became aware of the 150 mg Casocex treatment being widely used in Europe and elsewhere in the world. I began this therapy, 3 – 50 mg of Casodex daily in September 2000. I have been on this for 28 months. My PSA remains undetectable. The side effects are virtually non-existent and my U.S. physicians and I believe the high dose Casodex is keeping me alive. Because of my experience, I believe that other men in the United States should be given the chance to experience this life saving treatment that does not include debilitating side effects. Please consider high-dose Casodex for approval on December 18.

Feel free to contact me if you have any questions.

Sincerely,

Robert C. Powell  
President

RCP/PJM:co