February 2, 2022

The Honorable Xavier Becerra
Secretary
Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

Dear Secretary Becerra,

We are writing to urge the Department of Health and Human Services (HHS) to exercise the government's rights in patents on the prostate cancer drug enzalutamide (Xtandi). Doing so will permit generic competition in the US market, which, in turn, would remedy the abuse of patent rights contributing to unreasonable pricing in the country.

For decades, the US government has rejected requests to use the federal government's march-in or government use rights in federally-funded inventions to address price discrimination against US residents.[1] The enzalutamide case involves a drug to treat prostate cancer—one of the most common forms of cancer—and a taxpayer-funded invention that has earned more than $20 billion in global sales.

The average wholesale price for Xtandi is more than $500 per day, compared to $80 to $160 per day in other high-income countries. A key fact in the petition before HHS is that the drug was invented with grants from the US Army and the National Institutes of Health (NIH). The role of the government in funding the invention of the drug is important when considering if it is reasonable to charge US residents more than residents of other countries for a lifesaving drug.

As noted in a January 25, 2022 "Memorandum in support of the petition to HHS to exercise the march-in or paid up royalty right in patents on the prostate drug Xtandi," submitted by the petitioners:

> The standard sought in the Xtandi case is not to create a general standard for drug pricing, but to set one for products that were invented on a government grant. Specifically, the petitioners ask that U.S. residents not pay more than other high income countries for products invented on a U.S. government grant. The rationale for this standard is that it is not reasonable for the parties that paid for the R&D to invent a product to pay more than others with similar incomes. This is a modest standard, since one could easily argue that U.S. residents should pay less and even much less than others, having funded the most risky stage of the drug's development.

In evaluating the petition, the government should note that the discovery and pre-human use testing of a product are expensive, particularly when accounting for the risks and the time value of money. The most widely quoted estimate of drug development costs estimates that this stage accounts for 43% of the cost of developing a new drug.[2]

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[1] Treasure CL, Avorn J, Kesselheim AS. Do march-In rights ensure access to meedical products arising from federally funded research? A qualitative study. *Milbank Q.* 2015;93(4):761-87.

[2] DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: New estimates of R&D costs. *J Health Econ.* 2016;47:20-33.

When measuring the government's contribution to drug development, it is important to consider that, like the private sector, the federal government faces a risk of failure when it funds biomedical research. In the case of enzalutamide, the federal government's outlays were part of a large portfolio of grants relating to cancer generally and prostate cancer specifically. For every US Army or NIH grant that led to a successful product, countless other grants did not. Thus, on a risk adjusted basis, it is appropriate to view the government's role sharing in the cost of the development of the product as significant. DiMasi et al.'s estimate is a useful starting point for this assessment. Given the very high cost of enzalutamide, the large cumulative sales, and the government's role in funding the patented inventions, it is entirely appropriate that HHS consider the dramatic price discrimination against US residents as unreasonable.

Historically HHS, the NIH, and the Department of Defense (DoD) have avoided addressing pricing issues on federally funded inventions, with a concern that to do so would undermine collaborations with the federal government. These concerns deserve consideration but have been overstated.

The once widely quoted statistics on the number of CRADAs issued before and after the NIH policy change on the use of a reasonable pricing clause were misleading to the extent that lobbyists for rights holders inappropriately commingled standard and materials CRADA figures and ignored obvious relevant factors such as changes in NIH's budget and biomedical share prices.[3]

More recently, it is useful to note that the US government has entered multiple contracts with companies to develop or buy COVID-19 countermeasures, including drugs or vaccines, and these agreements include most favored nation or other reference pricing clauses. One such contract is the Pfizer contract for nirmatrelvir (Paxlovid), in which Pfizer agreed that the US government would be entitled to the lowest price in the G7 countries plus Switzerland. Pfizer, it should be noted, owns a share of the profits from the US market for enzalutamide.

Drug companies are clearly willing to enter contracts that have pricing clauses, and licensing and partnership agreements include all sorts of provisions on the division of geographic markets and sharing of costs, revenues, or profits. The critical issue for the motivation to enter into any agreement will be the expected efficacy and safety profile of a product.

To the extent that a policy of insisting on a most favored nation pricing standard, or a more modest standard of median pricing adjusted for differences in per capita incomes, results in disincentives to collaborate with the US government, the federal government is not without agency in managing the collaborations.

One overlooked partner in government funding agreements are US taxpayers, who are expected to enthusiastically pay for research and development projects. It is our opinion that the taxpaying public will be more positive about funding the grants budgets for the NIH or other federal agencies if the funding agency protects the public from price gouging.

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[3] Sarpatwari A, LaPidus AK, Kesselheim AS. Revisiting the National Institutes of Health fair pricing condition: promoting the affordability of drugs developed with government support. *Ann Intern Med.* 2020;172(5):348-50.

Right holders also are likely to overestimate the investor expectation that pricing discrimination against US residents is a sustainable forward-looking pricing strategy. The Presidential Executive Order 13948 of September 13, 2020, titled "Lowering Drug Prices by Putting America First," states "It is the policy of the United States that the Medicare program should not pay more for costly Part B or Part D prescription drugs or biological products than the most-favored-nation price." President Biden's frequent speeches about drug pricing often state that US residents should not have to pay more than those in other high-income countries for the same drugs, and many members of Congress make similar statements when communicating with voters.

One of the arguments put forward by petitioners is that price discrimination against US residents makes US employers less competitive internationally, an issue often raised in the broader concerns over the high cost of US health care.

In assessing the enzalutamide petition, HHS has been asked to hold a public hearing, in which supporters and opponents of the march-in petition can be heard. Such a hearing can be helpful in educating the public and industry about the issues and facts.

HHS has many options available in resolving this issue. It can ask Astellas to defend the price discrimination in a public hearing; it can give Astellas the opportunity to remedy the price discrimination to avoid a march-in; it can proceed to immediately permit generic entry under the government's royalty free right for Medicare and other federal programs (under the 35 U.S.C. § 202(c)(4) license) while granting the march-in to allow broader use of generics, and allowing the companies to pursue their right to appeals for the march-in case 35 U.S.C. § 203(b). Finally, the government can simply condone Astellas' position that radically high prices in the US are fine and reject the petition.

If the government acts to remedy the pricing discrimination, it can clarify the scope of the precedent, for example, by indicating that the action was taken because the record shows that the drug is frequently placed on restrictive formularies with higher co-payments or step-therapy, has a very high annual cost, and has already earned more than enough money to satisfy any reasonable return on investment standard.

We urge HHS to immediately permit generic entry under the government's royalty-free right for Medicare and other federal programs (under the section 202 license) while marching in to allow broader use of generics, or at a minimum, to tell Astellas it must eliminate the pricing discrimination or face those consequences. The worst outcome would be to endorse the current Astellas pricing policy. Inaction on the part of the government, or denial of the petition after a hasty and one-sided process, would do just that.

Thank you for your consideration of our request.

Sincerely,

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cc: Lawrence A. Tabak, DDS, PhD
Acting Director
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