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April 9, 2024

Chiquita Brooks-LaSure
Administrator
Centers for Medicare and Medicaid Services
7500 Security Boulevard,
Baltimore, MD 21244

April 9, 2024

Dear Administrator Brooks-LaSure,

This letter is a request from Knowledge Ecology International (KEI) the Union for Affordable Cancer Treatment(UACT) and Universities Allied for Essential Medicines (UAEM) to the Centers for Medicare and Medicaid Services (CMS) to use the federal government rights as set out in 35 U.S.C. § 202(c)(4) (referred to below as the Section 202 government use license), and the right of the government to use patents under 28 U.S.C. § 1498, to authorize qualified companies to make and sell generic versions of enzalutamide.

Xtandi (enzalutamide) is a treatment for prostate cancer that is sold by Astellas and Pfizer at a price three to six times higher in the United States than it is priced in other similar high-income countries.

Prostate cancer is among the three most common forms of cancer. It is not a rare disease, yet Astellas is charging very high prices for the drug. In 2022 the average Medicaid price of Xtandi was $130.66 per capsule. The 2022 Medicare Part D price was $131.30 per capsule, up from $112.28 the year before.

The 2023 Average Wholesale Price (AWP) for Xtandi is $136.50 per 40 mg capsule. The standard dose is 4 x 40mg per day. This means the AWP price for Xtandi in 2023 was $546 per day, or $199,290 for a year.

Astellas is headquartered in Japan, where the price of Xtandi is much lower. The capsule with a 2023 AWP price of $136.50 in the United States sells for $22 in Japan. The price is $20.75 in Australia. Prices are lower in every high-income country than in the US, despite the fact that Xtandi was invented at University of California-Los Angeles (UCLA) on grants from the U.S. Army and the National Institutes of Health (NIH).

Global sales of Xtandi are roughly $5 billion per year, of which the U.S. market accounts for roughly half. In 2022, Medicare Part D and Medicaid spending on Xtandi was $2.568 billion.

There are four patents on Xtandi listed in the FDA Orange Book. Three of the patents (7,709,517, 8,183,274 and 9,126,941) disclose federal rights based upon grants from the U.S. Army and the NIH. The fourth patent is an unimportant formulation patent, granted December 12, 2023, more than eleven years after Xtandi was approved by the FDA.

The U.S. government has a "world wide nonexclusive, nontransferrable, irrevocable, paid-up license to practice or have practiced for or on behalf of the United States any subject invention throughout the world" (35 USC § 202(c)(4)). This worldwide paid-up license can be used at any time by the U.S. government, including to acquire generic versions of enzalutamide for federal programs such as Medicare, Medicaid or health care provided to federal employees or veterans.

In 2016, Biolyse Pharma (a Canadian company), offered to sell generic versions of enzalutamide to the Medicare program for $3 per 40 mg pill, at a time when the Medicare Part D price was $69.41 per pill. Then-acting CMS Administrator Andy Slavitt declined the offer. Several generic versions of the drug are available in countries where patents are not a blocking factor, at prices lower than $3 per 40 mg capsule.

The government use authorization and consent clause

In addition to the rights the United States government has in inventions it funds under the Bayh-Dole Act is the right of the federal government to use or give third parties the right to use any U.S. granted patent on an invention. The 28 U.S.C. § 1498(a) statute reads in part:

> *(a)Whenever an invention described in and covered by a patent of the United States is used or manufactured by or for the United States without license of the owner thereof or lawful right to use or manufacture the same, the owner's remedy shall be by action against the United States in the United States Court of Federal Claims for the recovery of his reasonable and entire compensation for such use and manufacture. . . . For the purposes of this section, the use or manufacture of an invention described in and covered by a patent of the United States by a contractor, a subcontractor, or any person, firm, or corporation for the Government and with the authorization or consent of the Government, shall be construed as use or manufacture for the United States*.

In this case, since the government has the Bayh-Dole Section 202 license to the three patents required to make and sell enzalutamide, the required compensation for a use by or for the government will be zero.

The federal government often implements this statute by incorporating a reference in a contract to a standard contract clause in the Federal Acquisition Regulation (FAR) 52.227-1, Authorization and Consent. This clause, which reads "The Government authorizes and consents to all use and manufacture, in performing this contract or any subcontract at any tier, of any invention described in and covered by a United States patent," can be incorporated in a contract as is, or the contract can be written more narrowly to only refer to specific patents. In this case, the contract only needs to apply to patents 7,709,517, 8,183,274 and 9,126,941, the three patents in the FDA Orange Book that are required to make and sell generic versions of enzalutamide.

The inclusion of an Authorization and Consent clause in contracts has been used extensively by the federal government for a wide variety of purposes, including to provide all US citizens with free doses of the Moderna mRNA vaccine for COVID-19. (See: https://drugdatabase.info/far-52-227-1-contracts/).[1]

We are requesting CMS to provide any qualified drug company with contracts to supply generic enzalutamide to patients in any federal program, including but not limited to Medicare, Medicaid and other drug purchase or reimbursement programs for federal employees and veterans.

When using an authorization and consent clause in a contract, the federal government will eliminate the possibility of patent holders obtaining injunctions against the generic manufacturers to make, register and sell to persons covered by these federal programs.

As noted, while in other cases, the federal government would be liable for compensating patent holders for use of the patents, in this case, the federal government already has a paid-up license to use the inventions, and the compensation for those three patents will be zero.

The following companies are currently making generic versions of enzalutamide, including some that have already received tentative FDA approval to sell the drugs in the United States.

- **Actavis Laboratories FL, Inc.** Has received tentative FDA approval to sell generic enzalutamide.
- **Apotex Inc.** Has received tentative FDA approval to sell generic enzalutamide.
- **Biolyse Pharma.** Has previously expressed a willingness to supply a generic version of enzalutamide to patients in the US and the developing world.[2]
- **BDR Pharma.** Currently produces generic enzalutamide in India.
- **Allieva pharma.** Currently produces generic enzalutamide in India.

[1] See: https://drugdatabase.info/far-52-227-1-contracts/
[2] See: https://www.keionline.org/wp-content/uploads/BiolysePharma-letter-CMS-22April2016.pdf

- **Glenmark.** Currently produces generic enzalutamide in India.
- **Aprazer.** Currently produces generic enzalutamide in India.
- **Dr Reddy's Laboratories Ltd.** Currently produces generic enzalutamide in India.
- **Zydus Cadila.** Currently produces generic enzalutamide in India.

We request a meeting with your staff to discuss this issue. Thank you for your attention to this request.

Sincerely,

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