The ITCA 650 (exenatide in DUROS Device; NDA #209053; Intarcia Therapeutics, Inc.) has not demonstrated safety as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes

Testimony before the Food and Drug Administration's Endocrinologic and Metabolic Drugs Advisory Committee Meeting

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I'm Michael Abrams from Public Citizen's Health Research Group. I have no financial conflicts of interest on this matter.

The analysis conducted by Food and Drug Administration (FDA) scientists shows that ITCA 650 (the implantable, exenatide osmotic drug pump, DUROS device) has yet to demonstrate reasonable safety that would warrant its approval as an adjunctive drug-device treatment to improve glycemic control in adults with type 2 diabetes.

The available clinical trial data has been analyzed in a variety of ways by the sponsor and the FDA. These analyses revealed two difficult-to-dispute, disqualifying characteristics about the ITCA 650. First, the device failed to deliver a consistent and predictable dose of the GLP-1 agonist medication, exenatide. Second, some subjects experienced serious adverse events, including kidney and cardiovascular toxicity. The serious adverse events were markedly more evident with ITCA 650 use, compared to placebo, another drug (sitagliptin), and even compared to general GLP-1 agonist use without the ICTA 650 DUROS implant device.[1]

The ICTA 650 is designed to be implanted subcutaneously in the patient's abdomen for 3 or 6 months, without any external dosing controls.[2] However, data from the sponsor showed that the ICTA 650 sometimes delivers low daily doses (60% of prescribed) and other times high doses (180% of prescribed) when measured using ideal laboratory assays for such performance studies.[3] Moreover, separate analysis by the FDA's Center for Devices and Radiological Health established that the ICTA 650 sometimes even fails to deliver a dose of exenatide within the very wide range of 3% to 200% of the intended dose.

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[1] Food and Drug Administration. FDA briefing document, NDA #209053, Drug name: ITCA 650 (exenatide in DUROS Device) Applicant: Intarcia Therapeutics, Inc.; Nonprescription Drug Advisory Committee Meeting. September 21, 2023. https://www.fda.gov/media/172242/download. Accessed September 20, 2023. PDF pp. 10, 53.
[2] *Ibid*. PDF p. 23.
[3] *Ibid*. PDF pp. 9, 18.

Importantly, adverse events, some serious, are plausibly tied to ICTA 650 use.[4] For example, acute kidney illness was evident in 1.8% of those implanted with the ITCA 650 and 1.0% of controls, and two patients with acute kidney injury who received an ITCA 650 died.[5] Separate analyses revealed that cardiovascular morbidity (including, deaths, heart attack, stroke and unstable angina) was more common with ITCA 650 use. For example, 49 ITCA 650 cardiovascular deaths were observed in 2,075 patients followed for 32 months versus 40 in a comparable, high-risk group of 2,081 patients receiving placebo.[6]

In the view of Public Citizen's Health Research Group, these safety concerns combined with the manufacturing sterility concerns that have kept the drug-device on a clinical hold since 2017,[7] require that the FDA and this committee reject ITCA 650 at this time as a safe and effective adjunctive treatment for type 2 diabetes.

Thank you.

[4] *Ibid*. PDF p. 52.
[5] *Ibid*. PDF pp. 10, 49.
[6] *Ibid*. PDF pp. 10, 35, 58.
[7] *Ibid*. PDF pp. 11, 16-17.