March 31, 2015

Thomas Abrams, M.D.
Director
Office of Prescription Drug Promotion
Center for Drug Evaluation and Research
Food and Drug Administration
Building 51, Room 3203
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Dear Dr. Abrams,

Public Citizen, a consumer advocacy group with more than 350,000 members and supporters nationwide, is writing today urging you to stop the apparently violative off-label promotional statements in the direct-to-consumer (DTC) advertisements of five prescription drugs approved for the treatment of Type 2 diabetes. The drugs are Farxiga (dapagliflozin), Jardiance (empagliflozin), Invokana (canagliflozin),¹ Victoza (liraglutide)² and Bydureon (extended-release exenatide), and the promotional materials in question are included in Appendix 1 to this letter.

This request comes in the context of a drastic reduction in recent years in the number of violative DTC and physician-targeted prescription drug ads cited by the FDA in Warning and Untitled letters sent to pharmaceutical companies. Between 1997 and 2001, the earliest five-year period for which data are publicly available, the agency sent an average of 111 such letters per year, while an average of only 29 letters per year were sent during the most recent five-year period, 2010 through 2014 (see Appendix 2).

The ads, which appear in print magazines as well as on the drugs’ official promotional websites, all contain statements describing the alleged weight-reducing properties of the medications. However, none of the drugs is approved for weight loss and, despite the presence of disclaimers that the medications are not weight-loss drugs, the implication is clearly that weight loss is an additional potential benefit of the drugs. The deliberate placement of the claims in such close proximity to the drugs’ approved indications serves to reinforce this impression.

¹ Unlike the other, consumer-directed advertisements, the advertisement in question for Invokana appeared in a physician-targeted publication, *Internal Medicine News*. However, because this advertisement could potentially be accessed by patients as well as physicians, we included it in this letter.
² The formulation of liraglutide branded as Victoza is approved only for the treatment of type 2 diabetes and has never been approved for the treatment of obesity. A higher-dose formulation of liraglutide was recently approved under the brand name Saxenda for the treatment of obesity.
In the case of Farxiga and Invokana, blood pressure reduction also is touted as a potential benefit. This is an especially egregious “benefit” claim, as hypotension is listed as an adverse effect in the medications’ labels, owing to the diuretic effect and possible volume depletion inherent in the drugs’ mechanism of action.3,4 Both the weight-loss and blood-pressure-reduction claims also were made in a recently aired TV commercial for Farxiga.5

These five drugs have been approved solely to lower hemoglobin A1C levels in patients with Type 2 diabetes, but the advertisements presented in this letter clearly convey the false perception to patients and doctors that the drugs have been deemed safe and effective for weight loss and/or reducing blood pressure. In addition, all five drugs have serious toxicities, including hypotension, urinary tract infections, yeast infections (Farxiga, Jardiance, and Invokana), bladder cancer (Farxiga), pancreatitis, thyroid C-cell tumors (Victoza and Bydureon), and renal impairment (all five drugs).6 By inflating the drugs’ perceived benefits, the advertisements dangerously skew the risk-benefit calculations made by physicians and patients in deciding whether to initiate or continue these therapies. This is especially likely to occur with a weight-loss claim targeted at overweight and obese Type 2 diabetics struggling with both their disease and their weight.

These advertisements prompt the following questions:

1. Has the Food and Drug Administration (FDA) reviewed and approved the advertisements presented in Appendix 1 prior to, or since, their release? If not, what is the agency’s position on the weight-loss claims, as well as the blood-pressure-reduction claims for Farxiga and Invokana, made in the advertisements? If the agency did review and approve the advertisements, what was its rationale for allowing the inclusion of the weight-loss and blood-pressure-reduction claims?

2. Has the FDA approved similar off-label efficacy claims in other DTC advertisements? If so, did these approvals result from a formal policy allowing such off-label efficacy claims in pharmaceutical DTC advertisements?

We urge you to immediately issue Warning Letters requiring the manufacturers to withdraw these and any other advertisements containing similar off-label promotional statements. Unfortunately, as mentioned above, we must note here that the FDA’s enforcement of misleading drug marketing (both DTC and physician-targeted materials) has fallen far short in recent years. In 2014, only 10 Warning and Untitled letters were issued to pharmaceutical companies for violative DTC and physician-targeted prescription drug ads, the fewest number since at least 1997. This was the culmination of a steady decline in such letters during Margaret

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Hamburg’s tenure, from a high of just 51 in 2010 to 31 in 2011, 28 in 2012, and 24 in 2013 (see Appendix 2).

The FDA’s dismal record on issuing Warning and Untitled letters heightens the importance of other enforcement avenues. In order to deter the release of similarly violative DTC ads in the future, we urge you to, for the first time ever, use the authority granted to you by the 2007 Food and Drug Administration Amendments Act to issue civil monetary penalties to the manufacturers responsible for the ads in this document. As of January 27, 2015, not a single such penalty has been assessed.

We look forward to a prompt response to our questions and to the implementation of our recommended actions.

Thank you for your attention to this important public health matter.

Sincerely,

Sammy Almashat, M.D., M.P.H.
Researcher

Sidney Wolfe, M.D.
Founder and Senior Advisor

Michael Carome, M.D.
Director
Public Citizen’s Health Research Group

Cc: Janet Woodcock, M.D.,
Director, Center for Drug Evaluation and Research, FDA

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8 Personal communication, on January 27, 2015, with Jean-Ah Kang of the Food and Drug Administration’s Office of Prescription Drug Promotion.
Appendix 1. Promotional Materials (red arrows indicate unapproved benefits statements)

Farxiga (dapagliflozin) official promotional website (Accessed March 13, 2015):

www.farxiga.com

Jardiance (empagliflozin) advertisement in the March 16, 2015 issue of TIME magazine.
Invokana (canagliflozin) advertisement in the February 15, 2015 (Vol. 48, No. 3) issue of Internal Medicine News.
Victoza (liraglutide) official promotional website (Accessed March 13, 2015):

http://www.victoza.com

http://www.victoza.com/considering/benefits
Bydureon (extended-release exenatide) official promotional website (Accessed March 13, 2015):

https://www.bydureon.com/considering-bydureon.html
Appendix 2. FDA Warning and Untitled Letters to Pharmaceutical Companies Over Violative Promotional Materials and Activities

* Includes both direct-to-consumer and physician-targeted advertisements. The Division of Drug Marketing and Communications (DDMAC) was redesignated the Office of Prescription Drug Promotion (OPDP) in 2011.