July 26, 2021

CMS # 608717

Andy Jassy, CEO
Amazon.com, Inc.
2021 7th Ave
Seattle, WA 98121-2601 US
Regulatory-inquiries@amazon.com

Dear Mr. Jassy:

This letter concerns your firm's distribution of products that violate the Federal Food, Drug, and Cosmetic Act (the "FD&C Act"). As explained below, the United States Food and Drug Administration (FDA) purchased on your website, www.amazon.com, dozens of products intended for sexual enhancement and weight loss and, after subsequent laboratory analysis, determined that all tested products contain undeclared and potentially harmful drug ingredients.[1] As discussed further below, your firm is responsible for introducing, delivering, or causing the introduction or delivery into interstate commerce of products that are unapproved new drugs under section 505(a) of the FD&C Act, 21 U.S.C. 355(a), and/or misbranded drugs under section 502 of the FD&C Act, 21 U.S.C. 352, and for introducing or delivering for introduction into interstate commerce a food which is prohibited under section 301(ll) of the FD&C Act.

December 2019 to February 2020 Purchases from Amazon

Between December 2019 and February 2020, FDA purchased samples of 26 sexual enhancement products through your website, www.amazon.com. See Appendix A for a list of these products. All of these products were introduced or delivered for introduction into interstate commerce by Amazon via your Fulfillment by Amazon service.[2] FDA confirmed through laboratory analyses that all 26 products sampled contain one or more of the drug ingredients sildenafil, tadalafil, and/or vardenafil. None of these drug ingredients is declared on the products' labeling. Sildenafil, tadalafil, and vardenafil are phosphodiesterase type 5 (PDE-5) inhibitors, and they are the active ingredients in the FDA-approved prescription drugs Viagra, Cialis, and Levitra, respectively, which are used to treat erectile dysfunction (ED). These undeclared drug ingredients may interact with nitrates found in some prescription drugs, such as nitroglycerin, and may lower blood pressure to dangerous levels.

Information on the labels and/or labeling of these products demonstrates that 25 of the 26 sampled sexual enhancement products are marketed as dietary supplements[3]; however, these products do not meet the definition of "dietary supplement" under section 201(ff) of the FD&C Act, 21 U.S.C. 201(ff). Under section

[1] This is also explained in FDA's December 2020 press regarding these products at https://www.fda.gov/news-events/press-announcements/fda-warns-consumers-avoid-certain-male-enhancement-and-weight-loss-products-sold-through-amazon-ebay

[2] See Appendix A below for a list of such products. Amazon distributed each of the products directly to individual U.S. consumers on behalf of third parties. Each of the products discussed below was "fulfilled" by Amazon;your website states, "*With Fulfillment by Amazon (FBA), [sellers] store [their] products in Amazon's fulfillment centers, and [Amazon] pick[s], pack[s], ship[s], and provide[s] customer service for these products*" (see https://sell.amazon.com/fulfillment-by-amazon.html). The "Red Spartan 3000" product was sold by Amazon as well as shipped by Amazon.

[3] All of the sexual enhancement products, except "Kopi Jantan Tradisional Natural Herbs Coffee," include a Supplement Facts panel.

201(ff)(3)(B)(i) of the FD&C Act, 21 U.S.C. 321(ff)(3)(B)(i), a product is not a dietary supplement if it includes an article that is approved as a new drug under section 505 of the FD&C Act, unless that article was marketed as a dietary supplement or food before its approval as a drug. Sildenafil, tadalafil, and vardenafil were not marketed as dietary supplements or as food before Viagra, Cialis, and Levitra were FDA approved.[4] Accordingly, these products, which contain one or more of the undeclared drug ingredients sildenafil, tadalafil, and/or vardenafil, are excluded from the definition of a dietary supplement under section 201(ff)(3)(B)(i) of the FD&C Act.

The remaining product, "Kopi Jantan Tradisional Natural Herbs Coffee," is a food. This product was confirmed through laboratory analysis to contain sildenafil.

As noted above, on December 17, 2020, FDA issued public notifications regarding the undeclared drug ingredients found in the 26 sexual enhancement products purchased on www.amazon.com. FDA communicated with Amazon several times in December 2020 and January 2021 regarding Amazon's distribution of these 26 sexual enhancement products, during which you indicated that Amazon had "restricted" the sale of the 26 sexual enhancement products and their corresponding sellers.

January 2021 Purchase from Amazon

Despite your representation that Amazon had "restricted" the 26 sexual enhancement products that FDA had previously purchased, as well as the corresponding sellers of these products, FDA purchased one of the same 26 violative products from the same seller on www.amazon.com on January 15, 2021.[5] In your communications with us you acknowledged that you previously failed to detect this product sold by the identified seller.

March 2021 Purchases from Amazon

In March 2021, FDA purchased samples of two additional and different sexual enhancement products and one weight loss product through your website, www.amazon.com, all of which were introduced or delivered for introduction into interstate commerce by Amazon via your Fulfillment by Amazon service.[6] FDA confirmed through laboratory analyses that the sampled sexual enhancement products (products 27 and 28 in the appendix) contain tadalafil. In addition, FDA confirmed through laboratory analyses that the sampled weight loss product "Miss Slim" (hereinafter referred to as the weight loss product and is noted as product 29 in the appendix) contains sibutramine. None of these drug ingredients is declared in the products' labeling.

Information on the labels and/or labeling of these products demonstrates that the sampled sexual enhancement products and the weight loss product are marketed as dietary supplements[7]; however, these products do not meet the definition of "dietary supplement" under section 201(ff) of the FD&C Act, 21 U.S.C. 201(ff). Under section 201(ff)(3)(B) of the FD&C Act, 21 U.S.C. 321(ff)(3)(B), a product is not a

[4] FDA approved Viagra (containing sildenafil as the active ingredient) as a new drug on March 27, 1998. FDA approved Cialis (containing tadalafil as the active ingredient) as a new drug on November 21, 2003. FDA approved Levitra (containing Vardenafil as the active ingredient on August 19, 2003).

[5] The product "Kopi Jantan Tradisional Natural Herbs Coffee" was offered for sale by the same seller as FDA's original sample, and the product was listed as fulfilled via your Fulfillment by Amazon service. We also note that a June 30, 2021 search did not find this product on www.amazon.com.

[6] See Appendix A below for a list of the products.

[7] The labels of these products contain a Supplement Facts panel.

dietary supplement if (i) it includes an article that is approved as a new drug under section 505 of the FD&C Act, unless that article was marketed as a dietary supplement or food before its approval as a drug; or (ii) it includes an article authorized for investigation as a new drug for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, unless that article was marketed as a dietary supplement or food before such authorization for investigation. Tadalafil was not marketed as a dietary supplement or as a food before Cialis was FDA approved.[8] Accordingly, the two sexual enhancement products that contain the undeclared drug ingredient tadalafil are excluded from the definition of a dietary supplement under section 201(ff)(3)(B)(i) of the FD&C Act. Sibutramine is a schedule IV controlled substance and the active ingredient in Meridia, a new drug approved by FDA in 1997 for prescription treatment of obesity. Approval of the Meridia new drug application was subsequently withdrawn on December 21, 2010, after clinical data indicated sibutramine poses an increased risk of heart attack and stroke and FDA determined that the benefits of Meridia no longer outweighed its risks. The investigational new drug (IND) application for Meridia (sibutramine) was received by FDA on December 24, 1985, and the product became authorized for investigation as a new drug under an IND on January 23, 1986. When Meridia was approved for marketing as a new drug in the United States, the existence of substantial clinical investigations of sibutramine became public. Based on the information available to FDA, sibutramine was not marketed as a dietary supplement or as a food before it was authorized for investigation as a new drug. Therefore, “Miss Slim” is excluded from the definition of dietary supplement under section 201(ff)(3)(B)(ii) of the FD&C Act.

Unapproved New Drugs

The sexual enhancement products and weight loss product identified in Appendix A that are marketed as dietary supplements are drugs as defined by section 201(g)(1) of the FD&C Act, 21 U.S.C. 321(g)(1), because they are intended to prevent, treat, mitigate, or cure disease and/or to affect the structure or function of the body. Based on statements observed on the label and/or the labeling of these products, they are intended for, among other things, sexual enhancement, preventing premature ejaculation, increase in orgasms, increasing the volume of ejaculate, prostate improvement, and/or weight loss.

These sexual enhancement products and weight loss product are also new drugs under section 201(p) of the FD&C Act, 21 U.S.C. 321(p), because they are not generally recognized as safe and effective under the conditions prescribed, recommended, or suggested in their labeling. Under sections 301(d) and 505(a) of the FD&C Act, it is a prohibited act to introduce or deliver or to cause the introduction or delivery for introduction into interstate commerce of a new drug unless an FDA-approved application or investigational new drug exemption is in effect for it. There are no approved applications on file with FDA for these sexual enhancement products and weight loss product. Your distribution of these sexual enhancement products and weight loss product in interstate commerce without an approved application has violated these provisions of the FD&C Act.

Misbranded Drugs

Under section 502(a) of the FD&C Act, 21 U.S.C. 352(a), a drug is misbranded if its labeling is false or misleading in any particular. Section 201(n) of the FD&C Act, 21 U.S.C. 321(n), provides that, in determining whether an article's labeling or advertising “is misleading there shall be taken into account . . . not only representations made or suggested . . . but also the extent to which the labeling or advertising fails to reveal facts material in light of such representations.” The respective labeling for these sexual enhancement products and weight loss product listed in Appendix A does not declare that the products

[8] See footnote 6.

contain the drug ingredients sildenafil, tadalafil, vardenafil and/or sibutramine. The presence of undeclared PDE-5 inhibitors and/or sibutramine contained in these products may pose serious health risks because consumers with underlying medical issues may take these products without knowing that they can cause serious harm or interact in dangerous ways with other drugs they may be taking. For example, PDE-5 inhibitors may interact with nitrates found in some prescription drugs (such as nitroglycerin) and can lower blood pressure to dangerous levels. People with diabetes, high blood pressure, high cholesterol, or heart disease often take nitrates. Those consumers who have been advised against taking PDE-5 inhibitors because of comorbidities or potential drug interactions may seek products, like these sexual enhancement products, because they are marketed as dietary supplements and/or conventional food. In addition, as described earlier, sibutramine poses an increased risk of heart attack and stroke. Thus, the failure to disclose the presence of sildenafil, tadalafil, vardenafil and/or sibutramine in the products' labeling renders these sexual enhancement products and weight loss product misbranded under section 502(a) of the FD&C Act.

Additionally, these sexual enhancement products and weight loss product are also misbranded under section 502(f)(1) of the FD&C Act, 21 U.S.C. 352(f)(1), in that their labeling fails to bear adequate directions for use. "Adequate directions for use" means directions under which a layman can use a drug safely and for the purposes for which it is intended (see 21 CFR 201.5). Prescription drugs, as defined in section 503(b)(1) of the FD&C Act, 21 U.S.C. 353(b)(1), include those that, because of their toxicity or other potentiality for harmful effect, and/or the method of their use, and/or the collateral measures necessary for their use, are not safe for use except under supervision of a practitioner licensed by law to administer them. PDE-5 inhibitors are prescription drugs that can be used safely only at the direction, and under the supervision, of a licensed practitioner. It is not possible to write "adequate directions for use" such that a layperson can use these drugs safely for their intended uses. As such, all PDE-5 inhibitors that have been approved for marketing by FDA are limited by an approved new drug application to use under the professional supervision of a practitioner licensed by law to administer such drugs. The sexual enhancement products and weight loss product listed in Appendix A are not exempt from the requirements that their labeling bear adequate directions for use by a layperson (see 21 CFR 201.100(c)(2) and 201.115) because there is no FDA-approved application or investigational new drug exemption in effect for these products. For these reasons, these sexual enhancement products and weight loss product are misbranded under section 502(f)(1) of the FD&C Act.

These sexual enhancement products and weight loss product sold on www.amazon.com and fulfilled by your Fulfillment by Amazon service are also misbranded under section 502(f)(2) of the FD&C Act, 21 U.S.C. 352(f)(2), because the labeling for these products lacks adequate warnings against unsafe dosage or methods or duration of administration or application, in such manner and form, as are necessary for the protection of users. As previously noted, there is potential for serious adverse events and drug interactions associated with the use of products containing PDE-5 inhibitors and/or sibutramine. For example, the FDA approved labeling for prescription nitrate-containing drugs bears a warning against concomitant use of PDE-5 inhibitors. However, someone who takes the previously noted sexual enhancement products listed in Appendix A would be unaware of the presence of the undeclared PDE-5 inhibitor ingredients and may unknowingly be at risk of life-threatening hypotension. In addition, sibutramine poses an increased risk of heart attack and stroke.[9]

The introduction, delivery for introduction, or causing the introduction or delivery for introduction into interstate commerce of these misbranded drugs is a prohibited act under section 301(a) of the FD&C Act,

[9] See https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-recommends-against-continued-use-meridia-sibutramine.

21 U.S.C. 331(a).

Prohibited Act under Section 301(ll)

It is a prohibited act under section 301(ll) of the FD&C Act, 21 U.S.C. 331(ll), to introduce or deliver for introduction into interstate commerce any food to which has been added a drug approved under section 505 of the FD&C Act or for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public. As noted above, FDA purchased your "Kopi Jantan Tradisional Natural Herbs Coffee" and confirmed through laboratory testing that the product contains sildenafil. Based on available evidence, FDA has determined that the prohibition in section 301(ll) applies to sildenafil.[10] The introduction or delivery for introduction into interstate commerce of "Kopi Jantan Tradisional Natural Herbs Coffee" is therefore prohibited under section 301(ll) of the FD&C Act.

Previous Corrective Actions by Amazon

The sexual enhancement products and weight loss product described above are not the first unapproved new drugs, misbranded drugs with undeclared ingredients, and/or foods to which have been added an approved drug that FDA has alerted Amazon were being sold on www.amazon.com. For example, in May 2018, FDA alerted Amazon about sexual enhancement products featuring the brand name "Rhino," which FDA laboratories had found to contain undeclared drug ingredients. Subsequently, in May 2019, FDA alerted Amazon about male enhancement products featuring the brand name "Man Fuel," which FDA laboratories had found to contain undeclared drug ingredients including sildenafil and tadalafil.

Amazon's response to prior FDA communications about such unapproved new drugs, misbranded drugs with undeclared drug ingredients, and/or foods to which have been added an approved drug has not been sufficient to protect the public from the serious and continuing risk of harm posed by such products sold on www.amazon.com. Generally, Amazon has responded by making efforts to restrict the sale of specific products covered by FDA alerts or notifications as well as similar products offered by the same third-party sellers. These efforts have had mixed success, as evidenced by Amazon continuing to distribute the "Kopi Jantan Tradisional Natural Herbs Coffee" product described above after having been specifically advised by the FDA that it contained the undeclared drug ingredient sildenafil. In addition, during a meeting in October 2018, FDA advised Amazon that dozens of "Rhino" sexual enhancement products were still being sold on www.amazon.com despite Amazon having placed these products on its "Restricted Products" list in response to the May 2018 alert from the FDA. Amazon also continues to distribute unapproved new drugs, misbranded drugs with undeclared drug ingredients, and/or foods to which an unapproved new drug has been added after the FDA has published public warnings to consumers that those products contained hidden drug ingredients.[11]

More significantly, while Amazon has taken some action when alerted by the FDA about sales of specific unapproved new drugs, misbranded drugs with undeclared ingredients, and/or foods to which have been

[10] There is an exception if the substance was marketed in food before the drug was approved or before the substantial clinical investigations involving the drug had been instituted. However, based on available evidence, FDA has concluded that this is not the case for sildenafil.

[11] Product 27, "Adam's Secret Extra Strength 1500," was offered for sale on www.amazon.com with Fulfillment by Amazon in March 2021 after FDA had issued a public notification on January 19, 2021 warning consumers that the product contained undeclared tadalafil and sildenafil. FDA issued a public notification on June 4, 2021 warning consumers that Product 29, "Miss Slim," contained undeclared sibutramine, but the product was still offered for sale on www.amazon.com as of July 7, 2021.

added an approved drug product, FDA has found that **other** such products continue to be offered for sale on www.amazon.com with Fulfillment by Amazon. Amazon has acknowledged that your systems sometimes fail to detect specific products Amazon attempts to restrict. Based on this information, FDA is concerned that your filters are inadequate. In addition, we are concerned that after Amazon has informed us that it removed products similar to those identified by FDA to contain undeclared drug ingredients, FDA has continued to find products nearly identical to those products offered for sale by the same third-party sellers on your platform, fulfilled by Amazon.[12] Consequently, despite actions Amazon has taken to date, the continued availability on www.amazon.com of these unapproved new drugs, misbranded drugs, and/or foods to which an approved drug product has been added poses a continuing risk of harm to the American public.

Conclusion

The violations cited in this letter are not intended to be an all-inclusive statement of past or present violations that exist in connection with the products you distribute. You are responsible for investigating and determining the causes of any violations and for preventing their recurrence or the occurrence of other violations. It is your responsibility to ensure that your firm complies with all requirements of federal law, including FDA regulations.

This letter notifies you of our concerns and provides you an opportunity to address them. Please submit a written response to this letter within fifteen working days from the date of receipt, explaining the specific steps you have taken to address any violations. Include an explanation of each step being taken to prevent the recurrence of violations, including steps you will take to ensure that Amazon will no longer introduce, deliver, or cause the introduction or delivery into interstate commerce of, unapproved new drugs and/or misbranded products with undeclared drug ingredients, as well as copies of related documentation. If you believe that your products are not in violation of the FD&C Act, include your reasoning and any supporting information for our consideration within fifteen working days from the date of receipt of this letter.

Your response should be sent to U.S. Food and Drug Administration, Center for Drug Evaluation and Research/Office of Compliance/Office of Unapproved Drugs and Labeling Compliance by e-mail to FDAADVISORY@fda.hhs.gov.

Sincerely,

/s/

_____
Donald D. Ashley
Director
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration

[12] For example, one of the sellers FDA previously shared with Amazon, UMMZY, continues to sell products through Amazon fulfillment that are similarly labeled to products that FDA has warned about. As of June 30, 2021, this seller is offering for sale the product "Magnum 24k Gold," which is similarly labeled to "Magnum 50K XXL," a product that FDA found to contain undeclared sildenafil. This seller previously recalled the Amazon fulfilled products, "Thumbs up 7 Red 70K," "Shogun-X 15000mg," and "Krazy Night." See https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/ummzy-llc-issues-voluntary-nationwide-recall-thumbs-7-red-70k-shogun-x-15000mg-and-krazy-night-due. Also see footnote 5.

Appendix A – Tainted Products

December 2019 to February 2020 Purchases from Amazon

	Product Name	Undeclared Drug Ingredient(s)	Amazon Seller
1	Imperial Gold 2000	Sildenafil, Tadalafil	seller: Q Mart Fulfilled by Amazon
2	Hot Rod	Tadalafil	seller: Brandzilla Fulfilled by Amazon
3	PremierZen Platinum 5000	Tadalafil	seller: e-Factory NY Fulfilled by Amazon
4	PremierZen Black 5000	Sildenafil, Tadalafil	seller: All-R0under Fulfilled by Amazon
5	Imperial Extreme 2000	Sildenafil, Tadalafil	seller: HEALTHY STORY Fulfilled by Amazon
6	Burro Primavera 60000	Tadalafil	seller: Q MART Fulfilled by Amazon
7	Thumbs Up 7 Blue 69K	Sildenafil, Tadalafil	seller: BIT & BET Fulfilled by Amazon
8	Kopi Jantan Tradisional Natural Herbs Coffee	Sildenafil	seller: smile_elephant Fulfilled by Amazon
9	Thumbs up 7 Red 70K	Sildenafil, Tadalafil	seller: Antoto-K Fulfilled by Amazon
	Thumbs up 7 Red 70K	Sildenafil, Tadalafil, Vardenafil	seller: UMMZY Fulfilled by Amazon
10	OrgaZen Premium 7000	Sildenafil, Tadalafil	seller: beauty.kor Fulfilled by Amazon
11	Shogun-X Platinum 7000	Sildenafil, Tadalafil	seller: NURI TRADING Fulfilled by Amazon
12	Ginseng Power 5000	Tadalafil	seller: beauty.kor Fulfilled by Amazon
13	PremierZen Extreme 3000	Tadalafil	seller: Q Mart Fulfilled by Amazon
14	Shogun-X Black	Tadalafil	seller: UMMZY Fulfilled by Amazon
15	Original White Dragon	Tadalafil, Sildenafil	seller: A&D Health LLC Fulfilled by Amazon
16	Triple SupremeZen Plus 3500	Tadalafil	seller: Yolo Studio Fulfilled by Amazon

17	Triple SupremeZen Extreme 3500	Tadalafil, Sildenafil	seller: Otwo Fulfilled by Amazon
18	Triple SupremeZen Gold 3500	Tadalafil, Sildenafil	seller: e-Factory NY Fulfilled by Amazon
19	Thumbs Up 7 (Black) 25K	Tadalafil	seller: NURI TRADING Fulfilled by Amazon
20	Krazy Night	Tadalafil	seller: UMMZY Fulfilled by Amazon
21	Thumbs Up 7 White 11K	Tadalafil, Sildenafil, Vardenafil	seller: NURI TRADING Fulfilled by Amazon
22	Imperial Platinum 2000	Tadalafil	seller: Q Mart Fulfilled by Amazon
23	3 KO Gold XT	Vardenafil	seller: Vitality Mate Fulfilled by Amazon
24	Rock Steady 72 Hours	Tadalafil, Sildenafil	seller: ROCKSTEADY72HOURS Fulfilled by Amazon
25	69MODE Blue 69	Tadalafil, Sildenafil	seller: NURI TRADING Fulfilled by Amazon
26	Red Spartan 3000	Tadalafil, Sildenafil	seller: Amazon.com Services, Inc. Fulfilled by Amazon

March 2021 Purchases from Amazon

	Product Name	**Undeclared Drug Ingredient(s)**	**Amazon Seller**
27	Adam's Secret Extra Strength 1500	Tadalafil	seller: SUPPLEMENTS 4 U Fulfilled by Amazon
28	Adam's Secret Extra Strength 2000	Tadalafil	seller: SUPPLEMENTS 4 U Fulfilled by Amazon
29	Miss Slim	Sibutramine	seller: SUPPLEMENTS 4 U Fulfilled by Amazon