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# Journal Pre-proof

“Etazene, safer than heroin and fentanyl”: Non-fentanyl novel synthetic opioid listings on one darknet market

Francois R. Lamy (Conceptualization) (Data curation) (Formal analysis) (Funding acquisition) (Investigation) (Methodology) (Software) (Supervision) (Validation) (Writing - original draft) (Writing - review and editing), Raminta Daniulaityte (Conceptualization) (Formal analysis) (Funding acquisition) (Investigation) (Methodology) (Project administration) (Resources) (Supervision) (Validation) (Writing - original draft) (Writing - review and editing), Monica J. Barratt (Conceptualization) (Funding acquisition) (Investigation) (Methodology) (Writing - original draft) (Writing - review and editing), Usha Lokala (Data curation) (Methodology) (Software) (Writing - review and editing), Amit Sheth (Conceptualization) (Funding acquisition) (Project administration) (Resources) (Supervision) (Writing - review and editing), Robert G. Carlson (Conceptualization) (Formal analysis) (Funding acquisition) (Investigation) (Supervision) (Validation) (Writing - original draft) (Writing - review and editing)

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## "Etazene, safer than heroin and fentanyl": Non-fentanyl novel synthetic opioid listings on one darknet market

Francois R. Lamy<sup>a</sup>, Raminta Daniulaityte<sup>b</sup>, Monica J. Barratt<sup>c,d</sup>, Usha Lokala<sup>e</sup>, Amit Sheth<sup>e</sup>, Robert G. Carlson<sup>f</sup>

<sup>a</sup> Department of Society and Health, Faculty of Social Sciences and Humanities, Mahidol University, Salaya, Thailand

<sup>b</sup> College of Health Solutions, Arizona State University, Phoenix, AZ, United States

<sup>c</sup> Social and Global Studies Centre, RMIT University, Melbourne, VIC, Australia

<sup>d</sup> National Drug and Alcohol Research Centre, UNSW Sydney, NSW, Australia

<sup>e</sup> Artificial Intelligence Center, University of South Carolina, Columbia, SC, United States

<sup>f</sup> Center for Interventions, Treatment, and Addictions Research, Department of Population and Public Health Sciences, Wright State University, Dayton, OH, United States

### Highlights

- 17 non-fentanyl novel synthetic opioids detected on EmpireMarket (06/2020-08/2020)
- Non-fentanyl novel synthetic opioids represented 2.9% of all opioids advertised
- 587 items sold during the study period for an average weight between 858g and 2.7kg
- 45.5% of non-fentanyl novel synthetic opioids were advertised as shipped from China

### Abstract

#### Background

Novel synthetic opioids are fueling the overdose deaths epidemic in North America. Recently, non-fentanyl novel synthetic opioids have emerged in forensic toxicological results. Cryptomarkets have become important platforms of distribution for illicit substances. This article presents the data concerning the availability trends of novel non-fentanyl synthetic opioids listed on one cryptomarket.

#### Methods

Listings from the EmpireMarket cryptomarket "Opiates" section were collected between June 2020 and August 2020. Collected data were processed using eDarkTrends Named Entity Recognition algorithm to identify novel synthetic opioids, and to analyze their availability trends in terms of frequency of listings, available average weights, average prices, quantity sold, and geographic indicators of shipment origin and destination information.

#### Results

35,196 opioid-related listings were collected through 12 crawling sessions. 17 nonfentanyl novel synthetic opioids were identified in 2.9 % of the collected listings for an average of 9.2kg of substance available at each data point. 587 items advertised as non-fentanyl novel synthetic opioids were sold on EmpireMarket for a total weight of between 858g and 2.7kg during the study period. 45.5% of these listings were advertised as shipped from China.

#### Conclusions

Fourteen of the 17 non-fentanyl novel synthetic opioids were identified for the first time on one large cryptomarket suggesting a shift in terms of novel non-fentanyl synthetic opioids availability. This increased heterogeneity of available novel synthetic opioids could reduce the efficiency of existing overdose prevention strategies. Identification of new opioids underpins the value of cryptomarket data for early warning systems of emerging substance use trends.

Keywords: Cryptomarkets; Synthetic Opioids; Darknet markets

## 1. Introduction

Since 2013, the emergence of illicit novel synthetic opioids, such as fentanyl, its analogs and other synthetic opioids has worsened the epidemic of opioid-related overdose deaths in North America. These substances constitute a major public health threat due to their potency, variety, and ease of production (Pardo et al., 2019). Moreover, the high potency of these substances facilitates concealment and distribution for traffickers as a small amount of a potent drug can be turned into thousands street-level doses (EMCDDA, 2019).

During the last five years, fentanyl and its analogs have been associated with over 130,000 deaths in North America (Scholl et al., 2019; Wilson, 2020). Although fentanyl and its analogs have overshadowed other types of novel synthetic opioids, recent reports have noted a growing number of overdoses caused by non-fentanyl novel synthetic opioids in early 2020 (Anson, 2020; DeMio, 2020; Krotulski et al., 2020). These substances belong to various groups of chemicals (e.g., benzimidazole, cinnamylpiperazines) and are selective  $\mu$ -opioid receptor agonists displaying various degrees of potency (Vandeputte et al., 2020). Despite their recent identification, there is a paucity of information regarding origin, type, and price of these emerging substances. The challenges posed by these opioids require epidemiological monitoring systems to rapidly identify emerging substances to timely alert policy makers and health professionals.

Darknet markets have become important platforms of distribution of illicit substances and goods in Western countries (Dolliver & Kuhns, 2016; Kruithof et al., 2016a; Kruithof et al., 2016b). Darknet markets are online marketplaces located within the dark web that rely on cryptocurrencies (e.g., Bitcoin, Monero) and advanced encryption techniques to ensure the anonymity of buyers and sellers (Barratt & Aldridge, 2016). Due to the nature of darknet markets, the exact share of the drugs supplied by these markets remain unknown. However, recent results from the Global Drug Survey (GDS) 2020 tend to indicate that the percentage of users purchasing drugs through darknet markets increased steadily since 2014 (4.7%) with a significant uptick in 2020 (15.0%) (Winstock et al., 2020) . With over 60% of listings offering psychoactive substances (Europol, 2017), darknet markets offer the possibility to collect timely non-routine type of data to complement more traditional data sources (Singleton et al., 2018). They also represent a unique source of information on evolving drug availability trends (Aldridge & Décary-Héту, 2016), especially for novel psychoactive substances that are difficult to identify using traditional epidemiological surveillance systems. However, collecting data from the darknet markets requires high level of technical skill because of the high instability of the market environments often due to law enforcement operations, or when market administrators close the market keeping the money held in escrow ("exit scam") (EMCDDA, 2017b).

This paper presents data collected from EmpireMarket between June and August 2020. The key aims are to describe the types of non-fentanyl novel synthetic opioids listed, the amounts advertised (both in terms of listings and total weight offered) and sold, and their shipment origin and destination.

## 2. Method

## 2.1 Data collection

Data were collected from the EmpireMarket "Opiates" section using a custom web crawler. The raw HyperText Markup Language files (HTML) of drug advertisements were then parsed using a dedicated parser to extract information regarding: advertised product, listing number, number of times the listed product was sold, number of times the listing was viewed, vendor unique name, vendor number of sales, product description, price (Bitcoin and US\$), country/region of shipment origin, and potential shipment destination country/region. Data were collected weekly from EmpireMarket. This darknet market gradually became one of the largest markets after the closure of DreamMarket on the 30th of April 2019. Data collection started on the 1<sup>st</sup> of June 2020, once the dedicated web crawler was successfully implemented, and it lasted until the 18<sup>th</sup> of August 2020, a few days before EmpireMarket closure on the 22<sup>nd</sup> of August 2020 (Muncaster, 2020).

## 2.2 Data processing

Duplicated listings collected during the same crawling session and sharing an identical item number were discarded from further analysis. The advertisement texts were processed using the eDarkTrends-dedicated Named Entity Recognition (NER) algorithm to detect relevant entities (more details in Lamy et al., 2020). In the case of listings displaying several weight values (e.g., "2F-VIMINOL.FREEBASE WITH CYCLODEXTRIN COATED 1-100 grams"), the maximum value was kept to calculate the total quantity available for sale. Advertised weight value distribution was not calculated for listings with several weight values, no weight value information or if only a single weight value was advertised for the same identified substance throughout the data collection period. Average prices (US\$ per gram) were calculated separately for retail and wholesale-level amounts. The weight limit between "retail" and

"wholesale" quantities was arbitrarily set to 5g to acknowledge the potency of novel synthetic opioids. The average prices of listings with multiple weight values were calculated based on the information provided in the "Product Description" if indicated, otherwise, the price per gram was calculated based on the available value. The total number of sales and total weight of substance sold during the data collection period were calculated based on the unique item number and weight advertised. For listings with several weight values, the total weight of substance sold during the data collection period account for both the minimum and maximum values to approximate the total weight sold. Listings with no specific information regarding the shipment origin (i.e., "World") were removed from the frequency calculations. Manual checks were performed to remove inconsistent data and outliers to prevent potential distortions in the calculations of averages.

### 3. Results

#### 3.1 Collected data

At each data point, an average of 34,961 drug-related listings were advertised on EmpireMarket with 2,933 listings advertised as opioids on average. In total, 35,196 listings were collected from EmpireMarket opioid section through 12 crawling sessions between the 1<sup>st</sup> of June 2020 until the 18<sup>th</sup> of August 2020. 87.1% (30,669/35,196) of collected listings were identified as opioid products. On average, 2,556 opioid-related listings were posted each week on EmpireMarket. The remaining 12.9% (4,527/35,196) of listings advertised a substance that was not identified as an opioid by the NER algorithm, "custom orders" from buyers who directly contacted the vendor, or "tip jar" for vendor to receive extra cryptocurrencies from their customers. These listings were discarded from further analysis.

Overall, heroin was the main opioid-type substance identified by the NER algorithm accounting for 47.9% of the total opioid listings (14,679/30,669) advertising on average 36.9kg of heroin per data point. The second most common type of opioid identified on EmpireMarket was oxycodone representing 21.4% of the total opioid listings (6,564/30,669) for an average of 67,056 pills advertised at each data point. Illicitly manufactured fentanyl accounted for 4.4% of the opioid listings (1,356/30,669) for an average weight of 1.47kg per data point. Pharmaceutical fentanyl was advertised in 0.9% of opioid-related listings (270/30,669) with 115 items listed on average. Non-fentanyl novel synthetic opioids were identified in 2.9% of the opioid listings (883/30,669).

### 3.2 Availability and type of non-fentanyl novel synthetic opioids

During the study period, the NER algorithm identified 20 different substances advertised as non-fentanyl novel synthetic opioids. However, two identified substances, 2F-Opidone and U-46,600, were subsequently discarded from analysis as they did not display any existing Chemical Abstracts Service Registry Number (CAS). Moreover, listings advertising "AP" (e.g., "AP HCl replaces Carf 1kg") were also discarded from the analysis because it was unclear they were referring to AP-237, 2-Methyl-AP-237, *para*-AP-237 or AP-238. Overall, seventeen non-fentanyl novel synthetic opioids were identified during the study period (Table 1). An average of 9.2 kg of non-fentanyl novel synthetic opioids were advertised as available for sale at every data collection point on EmpireMarket. SPM-003 (6.3 kg per crawl on average) and U-48,800 (1.9 kg per crawl on average) accounted for most of the volume available. In terms of total listings, etazene (195/883), 2-Methyl-AP-237 (136/883) and SPM-003 (117/883) were the most common non-fentanyl novel synthetic opioids advertised on EmpireMarket during the study period (Table 1).

### 3.3 Number of sales and total weight sold

During the study (1<sup>st</sup> June 2020-18<sup>th</sup> August 2020), 587 items advertised as non-fentanyl novel synthetic opioids were sold on EmpireMarket for a total estimated weight of between 858g and 2.7kg. 2-MAP-237 (66.6%, 391/587) and etazene (27.7%, 163/587) were the non-fentanyl novel synthetic opioids sold the most (Table 1). Only 4.9% (29/587) of listings advertising more than 5g were sold during the data collection period. 2-MAP-237 (14 listings of 7g and one listing of 14g sold) and etazene (3 listings of 10g and 2 listings of 25g sold) were the main non-fentanyl novel synthetic opioids sold in quantities above 5g.

### 3.4 Shipment characteristics

93.6% (827/883) of the listings contained information about the country or region of shipment origin. The listings of three substances (U-58,800, W15, and acetoxymethylketobemidone) were advertised by unique vendor names with no specific information concerning their shipment origin. Except SPM-003, 2-MAP-237, etazene and U-47,700, non-fentanyl novel synthetic opioids were predominantly advertised as shipped from China (Table 1), which was the shipment origin of 45.5% (375/827) of the substances advertised. Listings originating from China were always advertised as shipping "Worldwide," while listings originating from Australia, Europe or the United States were more likely to ship domestically only. Etazene was solely advertised as shipped from Europe (195/195) with 62.5% (122/195) advertised as shipping within Europe only. Australia appeared to be the main shipment origin of retail quantity (0.5-5g) of U-47,700 (44/50) with one fourth of these listings (11/44) shipping domestically only. Wholesale quantities (100g) of U-47,700 were advertised as shipped from Europe (3/50) or the United States (3/50) only.

### 3.5 Retail and Wholesale prices

Twenty-six listings did not contain any information about the weight of substances for sale. Among the listings with weight information, 43.4% (372/857) advertised quantity lower or equal to 5g (minimum 0.05g), while 56.6% (458/857) advertised quantity greater than 5g (maximum 1000g). The average retail price for a gram of non-fentanyl novel synthetic opioids was equal to US\$80.9 (min=61.1, max=481.1) and the average wholesale price was equal to US\$33.1 (min=13, max=45.9). In comparison, the retail price of a gram of heroin was equal to US\$89.5 and the wholesale price equal to US\$36.5. U-47,700 (US\$481.1) and etazene (US\$128.4) were the most expensive non-fentanyl novel synthetic opioids sold on EmpireMarket at the retail level (see Table 1).

### 4. Discussion

Our study provides a detailed description of the type, average amount, prices, quantity sold and shipment origin of non-fentanyl novel synthetic opioids advertised on one darknet market over a 12-week period (June 2020-August 2020). Non-fentanyl novel synthetic opioids represented 2.9% of the opioid-related listing advertised on EmpireMarket and 587 items were sold during the study period for an approximated total weight of 858g to 2.7kg. Our data also indicate that despite a large number of listings offering more than 5g of substance, they constituted only 5% of the non-fentanyl novel synthetic opioids that were sold on EmpireMarket during data collection, suggesting that most of the sales were most likely for personal consumption (Aldridge & Décary-Héту, 2016). Nevertheless, our findings suggest that a gram of these non-fentanyl novel synthetic opioids costs on average USD33.1 if purchased in quantities greater than 5g. The relative low purchase price and potency of these

substances make them a profitable alternative for drug dealers who can turn a gram of these products in dozens or hundreds of street-level doses.

Furthermore, the potency and lack of information about these non-fentanyl novel synthetic opioids is of concern. The spectrum of reported potency is very large, for example, etazene is 70 times more potent than morphine (Siczek et al., 2020), etonitazene 1000-2000 times more potent than morphine (Moolten et al., 1993), while 2-MAP-237 is considered equivalent to morphine (Vandeputte et al., 2020). Benzimidazole opioids (i.e., etazene-type) are full agonist of the mu opioid receptor that produces analgesia and respiratory depression: for example, etonitazene displays a 2,500-fold greater affinity than morphine on  $\mu_1$  site, but shows comparable affinity to the delta site and lower affinity to the kappa opioid receptor (Moolten et al., 1993). Piperazine opioids (e.g., AP-238, 2-MAP-237) also displayed affinity to the mu opioid receptor with low affinity to the delta and kappa opioid receptor (Barlocco et al., 1993). However, there is an overall lack of detailed knowledge regarding the effects and side-effects that this large variety of substances can produce on humans. This large variability in potency and other pharmacological features of these drugs could lead to serious adverse consequences for buyers not necessarily well-informed of the substances they consume.

This increased heterogeneity of available novel synthetic opioids has significant implications for overdose prevention strategies and their implementation. For example, use of rapid fentanyl test strips for overdose prevention may become less efficient with an increased diversification and availability of non-fentanyl novel synthetic opioids, some of which may not yet be identifiable by rapid fentanyl test strips or other available testing technologies (Krieger et al., 2018; Peiper et al., 2019; Silverstein et al., 2019). Further, increased availability of other novel synthetic opioids may also impact the efficacy of the established opioid use disorder treatment protocols, and emerging evidence suggest

potential need to modify buprenorphine-based treatment for some individuals exposed to street fentanyl and other novel synthetic drugs (Danilewitz & McLean, 2020; Silverstein et al., 2019).

Eight of the seventeen substances identified, namely, 2F-Viminol, AP-238, buprenorphine, isotonitazene, metonitazene, U-47,700, U-48,800, and piperidylthiambutene have already been identified by the National Forensic Laboratory Information System (NFLIS) and the Center for Forensic Science Research and Education (CFSRE). When compared to previous darknet market data from 2018 and early 2019, fourteen of the non-fentanyl novel synthetic opioids identified on EmpireMarket between June and August 2020, namely, 2F-Viminol, 2-MAP-237, acetoxymethylketobemidone (O-AMKD), AP-238, buprenorphine, etazene, fluonitazene, isotonitazene, metodesnitazene, metonitazene, piperidylthiambutene, spiradoline, SPM-003, and W-15 were not advertised in 2018 and early 2019 on DreamMarket, the largest darknet market at that time (Lamy et al., 2020). Furthermore, nine of these substances, 2-MAP-237, acetoxymethylketobemidone (O-AMKD), etazene, fluonitazene, metodesnitazene, spiradoline, SPM-003, U-58,800, and W-15 have not been detected by NFLIS and CFSRE at the time of writing this paper. Our findings suggest a shift from benzamide-type of opioids (e.g., U-47,700, U-48,800) to benzimidazole-type (e.g., etazene, fluonitazene) and piperazine-type compounds (e.g., AP-238, 2-MAP-237). This finding echoes the DEA "Emerging Threat Report" (DEA, 2019; 2020a; 2020b) and EMCDDA "Early Warning System" (EMCDDA, 2020) that reported less benzamide opioids from seizure data while identifying a growing number of benzimidazole- and piperazine-type opioids since mid-2019.

Although 54.5% of these substances were advertised as shipped from Europe and Australia, vendors located in China remain the main origin of non-fentanyl novel synthetic opioids

advertised on EmpireMarket. This suggests that several Chinese vendors circumvented the ban of fentanyl-type substances and precursors of May 2019 (Associated Press, 2019; Pardo & Kilmer, 2019), by (re)introducing new  $\mu$ -opioid receptor agonist substances, perpetuating, in turn, the regulatory "whack-a-mole" between traffickers and authorities.

Limitations are noted. Although EmpireMarket was the largest existing darknet market during the study period, additional listings may have been advertised on other darknet markets. Shipment origin data were only partial, covering large geographical zones and, in some cases, may not represent the real origin of shipment potentially introducing bias in the shipment origin calculation.

The results of this study underpin the importance of constant monitoring of the darknet market environment to timely inform the public health community about the emergence of new substance trends.

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**Contributors:**

Francois R. Lamy: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Supervision, Validation, Writing - original draft, Writing - review & editing.

Raminta Daniulaityte: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing -original draft, Writing - review & editing.

Monica J. Barratt: Conceptualization, Funding acquisition, Investigation, Methodology, Writing - original draft, Writing - review & editing.

Usha Lokala: Data curation, Methodology, Software, Writing - review & editing.

Amit Sheth: Conceptualization, Funding acquisition, Project administration, Resources, Supervision, Writing - review & editing.

Robert G. Carlson: Conceptualization, Formal analysis, Funding acquisition, Investigation, Supervision, Validation, Writing - original draft, Writing - review & editing.

Credit authorship contribution statement

Francois R. Lamy: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Software, Supervision, Validation, Writing - original draft, Writing - review & editing.

Raminta Daniulaityte: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing -original draft, Writing - review & editing.

Monica J. Barratt:

Conceptualization, Funding acquisition, Investigation, Methodology, Writing - original draft, Writing - review & editing.

Usha Lokala:

Data curation, Methodology, Software, Writing - review & editing.

Amit Sheth:

Conceptualization, Funding acquisition, Project administration, Resources, Supervision, Writing - review & editing.

Robert G. Carlson:

Conceptualization, Formal analysis, Funding acquisition, Investigation, Supervision, Validation, Writing - original draft, Writing - review & editing.

**Conflict of Interest:**

No conflict declared.

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Table 1. Total numbers of non-fentanyl novel synthetic opioid listings, average volume available, total number of views, total number of sales, number of items sold during data collection, approximated volume sold during data collection and associated unique vendor counts on EmpireMarket cryptomarket during the eDarkTrends data collection period (1st June 2020 - 18th August 2020).

Substance names	Total number of listings	Average volume available (g) (Min-Median-Max)	Total number of views	Total number of sale transactions	Sales during data collection	Amount (g) sold during data collection	Number of unique vendor names	Origin	Destination	Retail (<= 5g)		Wholesale (> 5g)	
										Average price (US\$/g)	Total number of listings	Average price (US\$/g)	Total number of listings
Etazene	195	158.3 [0.1-5-50]	126,167	3,933	163	240	1	Europe (100%)	Europe (62.6%), World (37.4%)	128.4	135	41.6	60
2-MAP-237	136	163.1 [0.5-10-100]	48,859	2,592	391	530.5	5	Australia (52.4%), China (40.1%), USA (7.5%)	Australia (52.4%), World (40.1%), USA (7.5%)	63.2	65	43.4	69
SPM-003*	117	6,252.8 [0.5-5-1000]	38,864	107	13	46-1,571	1	USA (30.4%), UK (13.0%), Canada (13.0%)	World (62.4%), Europe (10.3%), Australia (9.4%)	61.1	29	13	88
U-48,800	89	1,939.2 [10-50-1000]	23,225	85	1	10	2	China (100%)	World (100%)	ND	0	24.5	89
2F-Viminol	78	120.5 [0.5-10-100]	31,379	171	5	4	4	China (70.3%), USA (29.7%)	World (71.8%), USA (28.2%)	87.1	34	36.4	40
Isotonitazene	60	94.6 [5-28-50]	16,185	82	3	20	1	China (100%)	World (100%)	90	24	45.9	36
Spiradoline	60	95 [5-5-50]	2961	0	0	0	1	China (100%)	World (100%)	72	24	45.4	36

Brorphine	57	115 [0.05- 5- 100]	3,778	4	2	1	4	China (96.2%), USA (3.8%)	World (96.2%), USA (3.8%)	80	14	43.2	39
U-47,700	53	83.3 [0.5- 5- 100]	15,860	68	6	3.5	2	Australia (88%), Europe (6%), USA (6%)	World (100%)	481.1	44	36.5	9
AP-238	10	25.8 [1-5- 100]	189	2	0	0	3	China (50%), USA (50%)	USA (50%), World (50%)	65	3	25	3
Metodesni tazene	6	100* *	126	0	0	0	2	China (100%)	World (100%)	ND	0	28	3
Piperidylthi am-butene	6	100* *	78	0	0	0	2	China (100%)	World (100%)	ND	0	20	3
Metonitaze ne	4	100* *	229	4	2	2-200	2	China (100%)	World (100%)	ND	0	25	3
U-58,800	4	100* **	384	0	0	0	1	ND	World (100%)	ND	0	16	4
Fluonitaze ne	3	100* *	92	2	1	1-100	1	China (100%)	World (100%)	ND	0	30	3
W15	3	0 ****	70	0	0	0	1	ND	World (100%)	ND	0	ND	0
Acetoxyme thyl- ketobemid one	2	0 ****	20	0	0	0	1	ND	World (100%)	ND	0	ND	0
Total/Aver age	883	9,180 .9	308, 466	7,050	587	858- 2,680	13	-	-	80.9	372	33.1	485

\* Only one unique vendor name advertised SPM-003 from various locations.

\*\* All the listings related to these substances displayed several weight information.

\*\*\* Only one weight (100g) was advertised during the study period.

\*\*\*\* No weight information was displayed for these substances.