Use of Glucagon-Like Peptide-1 Receptor Agonists in the U.S. Food and Drug Administration's Sentinel System

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Background

There is a growing population of new users of glucagon-like peptide-1 receptor agonists (GLP-1RA) and glucose-dependent insulinotropic polypeptide (GIP)/GLP-1RA products approved for treatment of type 2 diabetes (T2D) or for weight management the United States (U.S.)

Objective

To describe characteristics of initiators of GLP-1RA and GIP/GLP-1RA products in the United States, focusing on approved indication for weight management and for T2D

Methods

- Study Population: Initiators of GLP-1RA products of all ages in the U.S. within four commercial and two public insurers in the FDA Sentinel Distributed Database
- Study period: January 1, 2008 – latest available data (cut-off date: May 31, 2024)
- Index date: Date of first dispensing of a GLP-1RA product in 365 days
- Drug utilization: Initiators by calendar year, cumulative duration of use (dispensed days' supply), number of non-overlapping treatment episodes
- Baseline characteristics (based on diagnosis, procedure or dispensing codes) assessed in 365 days before index date

Results

- 3,321,029 initiators of GLP-1RAs and 374,607 initiators of GIP/GLP-1RAs identified
- Roughly 7% of all initiators started a weight management product
- Use of semaglutide and tirzepatide have increased rapidly since approval (Figure 1)
- Overall, 58.8% of initiators were female, and the mean age was 59.3 years
- 39.7% had evidence of T2D and obesity; 36.2% had T2D only; 15.1% had obesity only

Figure 1. GLP-1RA Initiation by Calendar Year*

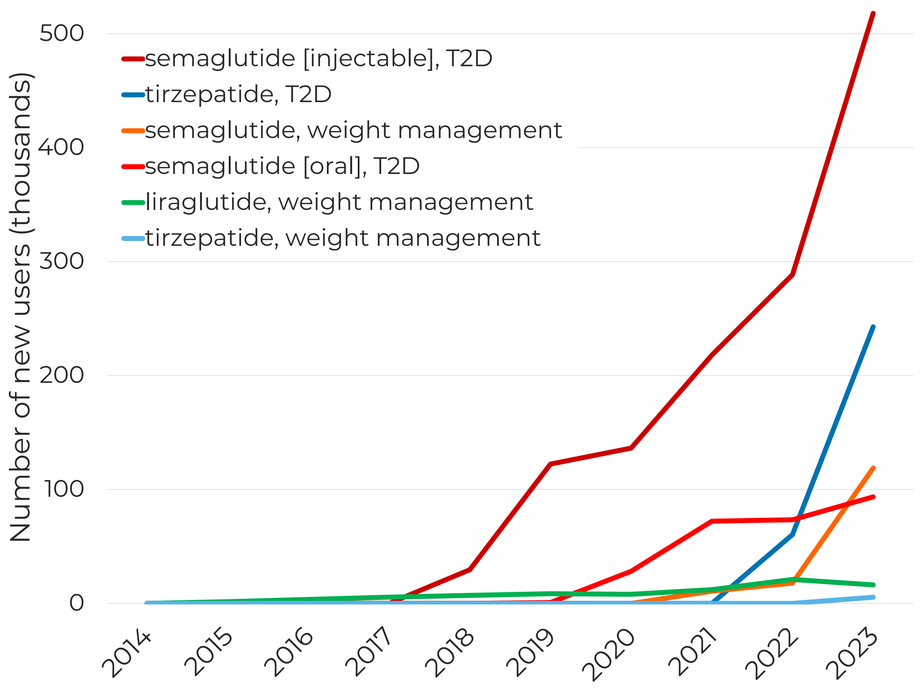

*Figure only includes years for which complete data was available

Table 1. Characteristics of Initiators of GLP-1 RA Products by FDA Approved Indication for Weight Management and for T2D

	GLP-1 RA Approved for Weight Management			Select GLP-1 RA Approved for T2D Treatment		
	Liraglutide	Semaglutide	Tirzepatide	Semaglutide	Semaglutide	Tirzepatide
Formulation	Injection	Injection	Injection	Tablet	Injection	Injection
Number of new users	84,064	163,331	27,069	277,037	1,364,127	349,937
Characteristics						
Age (Mean ± SD) (years)	45.3 ± 11.0	46.4 ± 11.0	47.2 ± 10.7	63.4 ± 10.8	60.9 ± 10.9	59.1 ± 10.7
Female (%)	82.2	78.4	76.4	54.4	59.2	61.0
Obesity (%)	77.7	78.6	78.9	51.6	61.2	67.5
T2D[a] (%)	11.0	6.9	4.9	86.7	77.9	76.8
Cross-classification of T2D and obesity						
T2D only (%)	2.1	1.1	0.1	43.0	31.1	24.4
Obesity only (%)	68.8	72.8	78.5	7.9	14.4	15.0
T2D and obesity (%)	8.9	5.8	0.4	43.7	46.8	52.4
Neither obesity nor T2D (%)	20.2	20.3	21.1	5.4	7.8	8.1
Type 1 diabetes (T1D)[b] (%)	0.6	0.5	0.4	0.3	0.9	0.7
Hypertension (%)	41.6	40.8	39.3	81.3	78.9	76.7
Hyperlipidemia (%)	38.3	41.8	44.5	80.4	76.9	77.1
Obstructive sleep apnea (%)	17.3	17.1	18.1	19.8	25.7	28.1
Ischemic heart disease (%)	3.6	3.9	3.9	21.9	23.2	20.5
Smoking (%)	11.1	9.4	9.6	19.6	22.1	19.6
Prior T2D product use						
Metformin (%)	15.6	11.3	10.7	68.7	60.6	54.8
Sulfonylureas (%)	1.3	0.4	0.1	31.0	22.8	17.1
DPP-4 inhibitors (%)	1.0	0.2	0.1	19.8	13.1	7.2
SGLT-2 inhibitors (%)	1.8	1.0	0.5	29.4	21.5	25.5
LIA insulin(%)	1.8	0.8	0.3	16.1	26.9	22.9
Short/rapid insulin (%)	1.5	0.8	0.5	7.7	15.2	13.7
Exposure information						
Average # episodes	3.02	2.36	1.22	2.40	3.24	2.07
First treatment exposure duration (days)						
Median (IQR)	30 (30, 60)	30 (28, 84)	28 (22, 46)	30 (30, 90)	56 (28, 98)	52 (28, 112)
Mean ± SD	66.7 ± 93.6	81.5 ± 100.1	33.9 ± 21.7	99.0 ± 150.2	104.9 ±162.1	88.6 ± 98.3
Cumulative duration of exposure (days)						
Median (IQR)	92 (48, 210)	112 (52, 250)	32 (22, 56)	120 (55, 300)	174 (80, 364)	119 (55, 241)
Mean ± SD	177.5 ± 219.4	164.3 ± 152.0	38.6 ± 24.7	220.9 ± 248.2	283.4 ± 309.5	158.5 ± 128.3

[a] Defined as ≥1 T2D and no T1D codes in the year prior to initiation. [b] >50% of T1D or T2D code days during [-365, -5] were T1D codes (Source: Klompas M, et al. 2013. doi: 10.2337/dc12-0964)
DPP-4 = dipeptidyl peptidase-4; IQR = interquartile range; LIA = long or intermediate-acting; SD = standard deviation; SGLT-2 = sodium-glucose cotransporter-2

- Initiators of weight management products appeared younger (age range: 45-48 years) and included a higher proportion of females (76-82%) than the initiators of T2D products (age range 59-64 years, 54-61% females) (Table 1)
- 78-79% of initiators of weight management products had diagnosis of obesity at baseline (vs. 51-68% of initiators of T2D products)
- One in five initiators of weight management products had no diagnoses for T2D or obesity (vs. <10% of initiators of T2D products)
- Less than 12% of initiators of weight management products had a diagnosis of T2D at baseline (vs. 76-87% of initiators of T2D products)
  - Prior use of metformin, sulfonylureas, DPP-4 and SGLT-2 inhibitors was infrequent in initiators of weight management products
  - Metformin was the most observed prior T2D medication among initiators of T2D products
- Prevalence of hypertension and hyperlipidemia were lower in initiators of weight management products (vs. initiators of T2D products)
- Median cumulative days of exposure (and average number of episodes) ranged from 32 days (1.22 episodes; tirzepatide, weight management) to 174 days (3.24 episodes; semaglutide [injectable], T2D), partially reflecting time available on the market (Figure 1)

Conclusions

- In these 3.69 million initiators of GLP-1RA or GIP/GLP-1RA, baseline characteristics, evidence of T2D or obesity diagnoses, comorbidities, and concurrent drug use differed, depending on a product's indication (for weight management or for T2D treatment)
- **Limitations:** Characteristics of initiators of newer GLP-1RA products may change as the market uptake has not stabilized

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- The contents are those of the authors and do not necessarily represent the official views of, nor an endorsement by, FDA/HHS or the U.S. Government
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