Analysis of New Molecular Entity Utilization Patterns using the Sentinel Distributed Database

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Background

- The U.S. Food and Drug Administration's (FDA) Sentinel System routinely assesses utilization patterns of products containing new molecular entities (NMEs) – new active moieties that FDA had not previously approved, either as a single ingredient drug or as part of a combination product.[1] These data provide the FDA with information on drug use patterns and sample size availability before inferential studies are initiated using the Active Risk Identification and Analysis (ARIA) System.

Objectives

- To describe initiators of NMEs approved by the FDA from 2017 to 2021 and to characterize NME utilization patterns.
- To identify products with the highest utilization.

Methods

- **NME Assessment**: Five analyses conducted by year of NME approval using the Sentinel Distributed Database (SDD).
- **Study Populations**: Patients in the SDD who initiated any product containing NMEs approved from 2017 to 2021.
- Medical and drug coverage ≥ 183 days prior to index exposure was required (with gaps in coverage of up to 45 days allowed).
- **Characteristics Assessed**: Demographic; healthcare utilization; clinical[2] and lifestyle characteristics; and product utilization (i.e., median days supplied per dispensing, median cumulative exposure duration, and median all, first, second and subsequent episode duration, and all and first episodes' gaps duration).

Results

- A total of 260 products (containing 256 NMEs) were analyzed by year of approval (48 in 2017, 60 in 2018, 48 in 2019, 53 in 2020, and 51 in 2021).
- **Semaglutide** (2017), **bictegravir/emtricitabine/tenofovir alafenamide** (2018), **ubrogepant** (2019), **rimegepant** (2020), and **piflufolastat F-18** (2021) **had the highest number of initiators for each cohort**.
- **Semaglutide** – indicated for type 2 diabetes mellitus and chronic weight management[3] – had **982,602 initiators** (mean age 61 years, 57% female, mean of 23 filled prescriptions, Table 1) a median days' supply of 28 days, and a median cumulative exposure duration of 148 days (Table 2). Diabetes was the most frequently occurring health condition among this cohort.
- **Bictegravir/emtricitabine/tenofovir alafenamide** – indicated to treat HIV infection[3] – had **175,440 initiators** (mean age 47 years, 74% male, mean of 21 filled prescriptions), a median days' supply of 30 days, and a median cumulative exposure duration of 315 days.
- **Ubrogepant** – indicated for acute treatment of migraine[3] – had **111,136 initiators** (mean age 49 years, 87% female, mean of 29 filled prescriptions), a median days' supply of 30 days, and a median cumulative exposure duration of 58 days.
- **Rimegepant** – indicated for preventive and acute treatment of migraine[3] – had **71,338 initiators** (mean age 49 years, 86% female, mean of 51 filled prescriptions), a median days' supply of 30 days, and a median cumulative exposure duration of 48 days.
- **Piflufolastat F-18** – a radioactive diagnostic agent indicated for imaging in prostate cancer[3] – had **43,225 initiators** (mean age 74 years, 100% male, mean of 13 filled prescriptions), and a median days' supply and a median cumulative exposure duration of one day. Prostate cancer was the most frequently occurring health condition among this cohort.
- Depression was the most frequently occurring medical condition for initiators of several products: bictegravir/emtricitabine/tenofovir alafenamide, ubrogepant, and rimegepant.
- Semaglutide had the highest utilization of all products approved between 2017 and 2021 with > 6.2 million dispensings; rimegepant initiators had the highest healthcare utilization metrics (27 ambulatory encounters and 51 filled prescriptions in the SDD).

Conclusion

- Semaglutide had the highest utilization followed by the combination antiretroviral NME. Knowing the utilization of these NMEs provides opportunities to gauge sample size availability before initiating formal ARIA queries.

References

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Table 1. Characteristics of cohorts utilizing products — with the highest utilization — containing NMEs approved in the United States from 2017 to 2021[1, 2, 3]

NME	Semaglutide	Bictegravir/emtricitabine/ tenofovir alafenamide	Ubrogepant	Rimegepant	Piflufolastat F-18
Year of FDA Approval	2017	2018	2019	2020	2021
Number of initiators	982,602	175,440	111,136	71,338	43,225
Number of dispensings	6,246,642	2,430,596	525,555	286,197	45,606
Characteristics	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Age (years)	60.6 (11.0)	47.3 (12.6)	48.6 (13.0)	49.3 (13.3)	74.3 (7.1)
	n (%)	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Age					
0-17 years	459 (0)	966 (0.6)	514 (0.5)	356 (0.5)	0 (0.0)
18-24 years	5,849 (0.6)	8,703 (5.0)	5,841 (5.3)	3,660 (5.1)	*****
25-40 years	76,894 (7.8)	52,127 (29.7)	28,732 (25.9)	17,365 (24.3)	*****
41-64 years	458,381 (46.6)	94,953 (54.1)	58,815 (52.9)	37,752 (52.9)	*****
≥ 65 years	441,019 (44.9)	18,691 (10.7)	17,234 (15.5)	12,205 (17.1)	40,000 (92.5)
Sex					
Female	562,761 (57.3)	45,683 (26.0)	96,208 (86.6)	61,031 (85.6)	73 (0.2)
Male	419,841 (42.7)	129,757 (74.0)	14,928 (13.4)	10,307 (14.4)	43,152 (99.8)
Race					
American Indian or Alaska Native	6,643 (0.7)	1,406 (0.8)	287 (0.3)	144 (0.2)	49 (0.1)
Asian	13,561 (1.4)	2,114 (1.2)	795 (0.7)	431 (0.6)	473 (1.1)
Black or African American	76,901 (7.8)	61,711 (35.2)	4,750 (4.3)	2,586 (3.6)	3,814 (8.8)
Multi-racial	—	827 (0.5)	1,328 (1.2)	—	—
Native Hawaiian or Other Pacific Islander	1,535 (0.2)	283 (0.2)	65 (0.1)	29 (0.0)	79 (0.2)
Unknown	433,302 (44.1)	64,846 (37.0)	62,836 (56.5)	41,268 (57.8)	8,343 (19.3)
White	450,660 (45.9)	44,253 (25.2)	41,075 (37.0)	26,880 (37.7)	30,467 (70.5)
Hispanic Origin					
Yes	24,802 (2.5)	18,031 (10.3)	2,918 (2.6)	1,275 (1.8)	361 (0.8)
No	476,423 (48.5)	103,887 (59.2)	37,591 (33.8)	23,040 (32.3)	31,800 (73.6)
Unknown	481,377 (49.0)	53,522 (30.5)	70,627 (63.6)	47,023 (65.9)	11,064 (25.6)
Number of initiators by year					
2017	0 (0.0)	—	—	—	—
2018	33,697 (3.4)	35,808 (20.4)	—	—	—
2019	123,677 (12.6)	58,182 (33.2)	0 (0.0)	—	—
2020	178,605 (18.2)	46,465 (26.5)	35,062 (31.5)	15,363 (21.5)	—
2021	301,810 (30.7)	16,992 (9.7)	34,229 (30.8)	36,746 (51.5)	0 (0.0)
2022	344,813 (35.1)	16,347 (9.3)	37,267 (33.5)	19,229 (27.0)	40,586 (93.9)
2023	—	1,646 (0.9)	4,578 (4.1)	—	2,639 (6.1)
Most Frequently Occurring Health Condition among Cohort[4]	**Diabetes**	**Depression**	**Depression**	**Depression**	**Prostate Cancer**
	705,188 (71.8)	40,140 (22.9)	38,450 (34.6)	25,143 (35.2)	39,698 (91.8%)
Healthcare Utilization	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
Number of ambulatory encounters	11.2 (11.5)	9.1 (15.1)	14 (12.4)	26.8 (22.5)	15. 2 (11.9)
Number of filled prescriptions	23.4 (41.4)	20.5 (21.1)	28.7 (24.5)	50.7 (43.1)	12.5 (11.0)

1. Observation periods were as follows: January 1, 2017 - December 31, 2022, for all products approved in 2017; January 1, 2018 - May 31, 2023, for all products approved in 2018; January 1, 2019 - May 31, 2023, for all products approved in 2019; January 1, 2020 - December 31, 2022, for all products approved in 2020 and; January 1, 2021 - June 30, 2023, for products all approved in 2021.
2. ***** represents suppressed data due to small sample size or to ensure a small cell cannot be recalculated through the cells presented.
3. — represents that the characteristic/category was not applicable to the cohort for the product.
4. Refers to the most frequently occurring clinical condition among initiators of products — with the highest utilization — approved from 2017 to 2021.

Table 2. Dispensing and utilization patterns overall and by age and sex for products — with the highest utilization — containing NMEs approved in the United States from 2017 to 2021[1,2]

	Number of Dispensings	Median Days' Supply by Dispensing	Median Cumulative Exposure Duration (Days)	Median All Treatment Episode Duration (Days)	Median First Treatment Episode Duration (Days)	Median Second and Subsequent Episode Duration (Days)	Median All Episodes' Gaps Duration (Days)
Semaglutide							
Overall	6,246,642	28	148	37	56	30	11
Age							
0-17 years	2,309	28	112	30	30	30	14
18-24 years	28,165	28	101	30	30	30	13
25-40 years	434,376	28	119	30	32	30	11
41-64 years	3,066,749	28	156	31	50	30	10
≥ 65 years	2,715,043	28	146	42	56	30	11
Sex							
Female	3,466,988	28	140	31	50	30	11
Male	2,779,654	28	163	42	56	30	11
Bictegravir/emtricitabine/tenofovir alafenamide							
Overall	2,430,596	30	315	30	60	30	7
Age							
0-17 years	9,786	30	270	30	60	30	8
18-24 years	79,679	30	201	30	60	30	10
25-40 years	549,410	30	232	30	60	30	9
41-64 years	1,437,653	30	360	43	60	30	7
≥ 65 years	354,068	30	452	60	80	60	5
Sex							
Female	606,019	30	300	30	60	30	8
Male	1,824,577	30	323	30	60	30	7
Ubrogepant							
Overall	525,555	30	58	24	30	20	24
Age							
0-17 years	1,758	28	40	30	30	26	27
18-24 years	20,659	30	37	28	30	24	29
25-40 years	128,291	28	54	24	30	21	25
41-64 years	303,625	29	60	24	30	20	24
≥ 65 years	71,222	30	40	25	30	20	25
Sex							
Female	460,412	30	60	24	30	20	25
Male	65,143	30	48	24	30	20	23
Rimegepant							
Overall	286,197	30	48	24	30	17	23
Age							
0-17 years	1,088	30	37	27	30	22	24
18-24 years	12,229	30	38	28	30	24	26
25-40 years	71,513	30	54	25	30	18	23
41-64 years	161,786	30	56	24	30	16	22
≥ 65 years	39,581	28	32	24	30	17	22
Sex							
Female	247,882	30	50	24	30	17	23
Male	38,315	30	39	25	30	18	21
Piflufolastat F-18							
Overall	45,606	1	1	1	1	1	153
Age							
0-17 years	0	**	**	**	**	**	**
18-24 years	*****	*****	*****	*****	*****	**	**
25-40 years	*****	1	1	1	1	**	**
41-64 years	*****	1	1	1	1	1	151
≥ 65 years	42,212	1	1	1	1	1	153
Sex							
Female	73	1	1	1	1	**	**
Male	45,533	1	1	1	1	1	153

1. ** represents instances for which a number could not be determined due to lack of data
2. ***** represents suppressed data due to small sample size or to ensure a small cell cannot be recalculated through the cells presented.