

## Supplementary Material

**Article Title:** A Retrospective Observational Study to Understand Medication Utilization and Lines of Treatment in Patients With Insomnia Disorder

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### **DISCLAIMER**

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## **Appendix 1. SUPPLEMENTARY METHODS**

### *Lines of treatment analysis*

Within the selection period from 1 January 2020 to 30 June 2021, the most recent claim for any insomnia drug of interest was defined as the index claim, and the date of the index claim was defined as the index date. The analysis period was variable for each patient and included the history from the first claim of any insomnia drug in the drug plan to the index claim. The 12 months prior to the first insomnia drug claim in the drug plan were used to determine the patients' activity in the plan and the first line of treatment (look-back period). The three-month period following the index claim was used to determine the patients' activity in the plan and the current line of treatment (look-forward period).

## SUPPLEMENTARY TABLES & FIGURES

**Supplementary Table 1. List of study outcomes**

Analysis	Outcome	Description
Insomnia medication utilization	Patient demographic characteristics	Reported patient distribution by age, sex, province and polypharmacy separately in 2018, 2019 and 2020 analysis year
	Insomnia medications claimed	Reported number and proportion of patients who claimed 1, 2, 3, 4, 5 or 5+ types of insomnia medication(s) in 2018, 2019 and 2020 analysis year
	Patients on insomnia medication	Reported number and proportion of patients who claimed insomnia medication(s) in 2018, 2019 and 2020 analysis year
	Duration of supply per patient	Reported the total number of days supply of insomnia medication(s) a patient had in 2018, 2019 and 2020 analysis year
	Prescribing daily dose per patient	Reported the daily dose (mg) of insomnia medication(s) a patient had in 2018, 2019 and 2020 analysis year
	Daily units per patient	Reported the daily units of insomnia medication(s) a patient had in 2018, 2019 and 2020 analysis year
	Drug cost per patient	Reported the total drug cost (including ingredient cost and markup) of insomnia medication(s) a patient had in 2018, 2019 and 2020 analysis year
Inappropriate medication usage	Patients with inappropriate medication usage	Reported number of patients with each type of inappropriate medication usage in 2018, 2019 and 2020
	Total cost on inappropriate medication usage	Reported total drug cost (including ingredient cost and pharmacy markup) on inappropriate medication usage in 2018, 2019 and 2020. For each drug claim, only the portion of cost defined as inappropriate use was included into the calculation.
Lines of treatment	Patient demographic characteristics	Reported patient distribution by age, sex, province, and polypharmacy in the 12 months look-back period
	Treatment history per patient	Reported number of years a patient had from the first drug used for insomnia to the most recent one
	Treatment lines	Reported the average number of treatment lines a patient had and proportion of patients by number of treatment lines

**Supplementary Table 2. Patient distribution by number of medications used for insomnia by payer and age groups**

Payer	Age	Number of Insomnia Medications	Patients, N (%)		
			Year 2018	Year 2019	Year 2020
Private (PDP)	Total	<b>Total</b>	607,473 (100.0%)	593,241 (100.0%)	574,618 (100.0%)
		1 Insomnia Medication	405,100 (66.7%)	395,619 (66.7%)	379,595 (66.1%)
		2 Insomnia Medications	143,458 (23.6%)	140,387 (23.7%)	137,972 (24.0%)
		3 Insomnia Medications	41,792 (6.9%)	40,873 (6.9%)	40,910 (7.1%)
		4 Insomnia Medications	12,041 (2.0%)	11,724 (2.0%)	11,539 (2.0%)
		5 Insomnia Medications	3,646 (0.6%)	3,294 (0.6%)	3,317 (0.6%)
		>5 Insomnia Medications	1,436 (0.2%)	1,344 (0.2%)	1,285 (0.2%)
	18-64	<b>Total</b>	479,025 (100.0%)	456,196 (100.0%)	439,333 (100.0%)
		1 Insomnia Medication	314,463 (65.6%)	299,024 (65.5%)	283,085 (64.4%)
		2 Insomnia Medications	115,054 (24.0%)	109,952 (24.1%)	108,609 (24.7%)
		3 Insomnia Medications	34,697 (7.2%)	33,306 (7.3%)	33,739 (7.7%)
		4 Insomnia Medications	10,325 (2.2%)	9,872 (2.2%)	9,842 (2.2%)
		5 Insomnia Medications	3,197 (0.7%)	2,855 (0.6%)	2,916 (0.7%)
		>5 Insomnia Medications	1,289 (0.3%)	1,187 (0.3%)	1,142 (0.3%)
	≥65	<b>Total</b>	128,448 (100.0%)	137,045 (100.0%)	135,285 (100.0%)
		1 Insomnia Medication	90,637 (70.6%)	96,595 (70.5%)	96,510 (71.3%)
		2 Insomnia Medications	28,404 (22.1%)	30,435 (22.2%)	29,363 (21.7%)
		3 Insomnia Medications	7,095 (5.5%)	7,567 (5.5%)	7,171 (5.3%)
		4 Insomnia Medications	1,716 (1.3%)	1,852 (1.4%)	1,697 (1.3%)
		5 Insomnia Medications	449 (0.3%)	439 (0.3%)	401 (0.3%)
		>5 Insomnia Medications	147 (0.1%)	157 (0.1%)	143 (0.1%)
Public ( )	Total	<b>Total</b>	3,248 (100.0%)	3,981 (100.0%)	4,099 (100.0%)
		1 Insomnia Medication	1,288 (39.7%)	1,526 (38.3%)	1,609 (39.3%)
		2 Insomnia Medications	976 (30.0%)	1,280 (32.2%)	1,320 (32.2%)
		3 Insomnia Medications	561 (17.3%)	710 (17.8%)	694 (16.9%)
		4 Insomnia Medications	258 (7.9%)	302 (7.6%)	309 (7.5%)
		5 Insomnia Medications	110 (3.4%)	106 (2.7%)	112 (2.7%)
		>5 Insomnia Medications	55 (1.7%)	57 (1.4%)	55 (1.3%)
	18-64	<b>Total</b>	1,825 (100.0%)	1,848 (100.0%)	1,765 (100.0%)
		1 Insomnia Medication	500 (27.4%)	496 (26.8%)	458 (25.9%)
		2 Insomnia Medications	580 (31.8%)	578 (31.3%)	559 (31.7%)
		3 Insomnia Medications	390 (21.4%)	438 (23.7%)	407 (23.1%)
		4 Insomnia Medications	213 (11.7%)	211 (11.4%)	209 (11.8%)
		5 Insomnia Medications	94 (5.2%)	80 (4.3%)	88 (5.0%)
		>5 Insomnia Medications	48 (2.6%)	45 (2.4%)	44 (2.5%)
	≥65	<b>Total</b>	1,423 (100.0%)	2,133 (100.0%)	2,334 (100.0%)
		1 Insomnia Medication	788 (55.4%)	1,030 (48.3%)	1,151 (49.3%)
		2 Insomnia Medications	396 (27.8%)	702 (32.9%)	761 (32.6%)

	3 Insomnia Medications	171 (12.0%)	272 (12.8%)	287 (12.3%)
	4 Insomnia Medications	45 (3.2%)	91 (4.3%)	100 (4.3%)
	5 Insomnia Medications	16 (1.1%)	26 (1.2%)	24 (1.0%)
	>5 Insomnia Medications	7 (0.5%)	12 (0.6%)	11 (0.5%)

**Supplementary Table 3. Drug utilization of top 5 medications used for insomnia among ODB patients by age group**

Age Group	Insomnia Drug	Patients, N (%)	Duration of supply per patient per year (Days), Mean (SD)	Units per day per patient, Mean (SD)	Daily dose per patient (mg), Mean (SD)	Drug Cost per patient per year, Mean (SD)
Total Population	<b>Year 2018</b>					
	<b>Total</b>	<b>3,248 (100.0%)</b>	<b>510.5 (420.6)</b>	<b>3.6 (3.5)</b>	<b>39.1 (63.0)</b>	<b>\$312.9 (937.7)</b>
	Zopiclone	1,233 (38.0%)	238.0 (160.4)	1.4 (0.8)	10.2 (6.5)	\$165.9 (151.3)
	Lorazepam	1,037 (31.9%)	174.5 (156.5)	1.8 (1.1)	1.7 (1.2)	\$16.2 (20.0)
	Trazodone	746 (23.0%)	212.2 (156.5)	1.5 (0.8)	98.7 (64.4)	\$26.3 (28.3)
	Clonazepam	838 (25.8%)	253.2 (149.4)	2.3 (1.5)	1.6 (1.6)	\$32.7 (33.2)
	Quetiapine	843 (26.0%)	350.6 (259.7)	2.0 (1.3)	168.9 (195.6)	\$189.9 (280.0)
	<b>Year 2019</b>					
	<b>Total</b>	<b>3,981 (100.0%)</b>	<b>492.6 (409.4)</b>	<b>3.4 (2.9)</b>	<b>31.9 (51.2)</b>	<b>\$283.2 (804.2)</b>
	Zopiclone	2,538 (63.8%)	218.0 (122.5)	1.3 (0.7)	9.2 (5.4)	\$138.8 (149.2)
	Lorazepam	1,040 (26.1%)	174.1 (156.8)	1.8 (1.9)	1.7 (2.0)	\$15.8 (19.3)
	Trazodone	802 (20.1%)	210.0 (164.5)	1.4 (0.9)	95.0 (65.7)	\$25.9 (31.1)
	Clonazepam	862 (21.7%)	259.5 (148.6)	2.4 (1.9)	1.6 (1.6)	\$31.7 (32.0)
	Quetiapine	887 (22.3%)	348.4 (259.5)	2.1 (1.4)	161.0 (162.7)	\$143.9 (208.0)
	<b>Year 2020</b>					
	<b>Total</b>	<b>4,099 (100.0%)</b>	<b>535.0 (408.5)</b>	<b>3.3 (2.9)</b>	<b>30.0 (53.9)</b>	<b>\$307.7 (773.8)</b>
	Zopiclone	2,988 (72.9%)	256.3 (125.7)	1.3 (0.6)	9.1 (5.0)	\$158.4 (162.7)
	Lorazepam	1,007 (24.6%)	189.7 (162.4)	1.8 (1.5)	1.8 (1.7)	\$17.2 (19.8)
Trazodone	752 (18.3%)	227.3 (165.4)	1.4 (1.0)	98.3 (73.4)	\$28.0 (32.9)	
Clonazepam	837 (20.4%)	259.9 (141.9)	2.4 (1.9)	1.6 (2.6)	\$31.7 (31.7)	
Quetiapine	857 (20.9%)	371.1 (262.6)	2.1 (1.4)	157.0 (162.8)	\$150.3 (216.1)	
Age 18-64	<b>Year 2018</b>					
	<b>Total</b>	<b>1,825 (100.0%)</b>	<b>611.1 (449.4)</b>	<b>4.4 (4.1)</b>	<b>46.1 (71.2)</b>	<b>\$456.5 (1207.7)</b>
	Zopiclone	862 (47.2%)	248.7 (170.3)	1.5 (0.9)	10.6 (7.3)	\$180.7 (163.0)
	Lorazepam	585 (32.1%)	172.5 (161.1)	1.8 (1.1)	1.9 (1.3)	\$17.1 (21.8)
	Trazodone	425 (23.3%)	222.3 (152.3)	1.5 (0.8)	109.7 (70.0)	\$30.4 (30.9)
	Clonazepam	578 (31.7%)	263.5 (152.7)	2.4 (1.6)	1.8 (1.8)	\$36.9 (35.7)
	Quetiapine	617 (33.8%)	347.5 (256.0)	2.1 (1.3)	183.7 (212.4)	\$202.8 (292.6)
	<b>Year 2019</b>					
	<b>Total</b>	<b>1,848 (100.0%)</b>	<b>608.8 (454.2)</b>	<b>4.3 (3.4)</b>	<b>42.4 (62.3)</b>	<b>\$429.7 (1111.2)</b>
Zopiclone	1,037 (56.1%)	235.2 (135.0)	1.4 (0.9)	10.4 (6.8)	\$170.4 (200.2)	

	Lorazepam	544 (29.4%)	177.1 (166.0)	1.9 (2.4)	2.0 (2.5)	\$17.3 (21.0)	
	Trazodone	411 (22.2%)	225.6 (165.1)	1.5 (0.8)	105.6 (66.7)	\$29.9 (31.2)	
	Clonazepam	576 (31.2%)	266.9 (150.7)	2.5 (1.7)	1.7 (1.8)	\$35.4 (34.6)	
	Quetiapine	616 (33.3%)	344.4 (261.4)	2.1 (1.5)	177.9 (175.2)	\$155.2 (221.3)	
	<b>Year 2020</b>						
	<b>Total</b>	<b>1,765 (100.0%)</b>	<b>651.3 (464.6)</b>	<b>4.4 (3.3)</b>	<b>41.9 (64.7)</b>	<b>\$458.1 (1090.6)</b>	
	Zopiclone	1,080 (61.2%)	252.9 (132.9)	1.4 (0.9)	10.4 (6.7)	\$184.3 (231.1)	
	Lorazepam	527 (29.9%)	193.6 (170.5)	1.9 (1.4)	1.9 (1.7)	\$18.7 (21.5)	
	Trazodone	400 (22.7%)	238.0 (161.6)	1.5 (0.8)	106.9 (68.5)	\$31.0 (31.2)	
	Clonazepam	557 (31.6%)	262.8 (143.8)	2.5 (1.7)	1.7 (1.8)	\$34.8 (34.6)	
	Quetiapine	571 (32.4%)	378.6 (262.5)	2.1 (1.4)	175.8 (174.0)	\$167.7 (231.5)	
	<b>Age ≥65</b>	<b>Year 2018</b>					
<b>Total</b>		<b>1,423 (100.0%)</b>	<b>381.5 (339.7)</b>	<b>2.6 (2.0)</b>	<b>30.0 (49.0)</b>	<b>\$128.8 (276.6)</b>	
Zopiclone		371 (26.1%)	213.2 (131.4)	1.3 (0.5)	9.2 (3.9)	\$131.6 (112.7)	
Lorazepam		452 (31.8%)	177.2 (150.5)	1.8 (1.1)	1.6 (1.1)	\$15.0 (17.3)	
Trazodone		321 (22.6%)	198.9 (161.2)	1.4 (0.7)	84.1 (52.9)	\$21.0 (23.4)	
Clonazepam		260 (18.3%)	230.3 (139.2)	1.9 (1.2)	1.2 (1.0)	\$23.5 (24.5)	
Quetiapine		226 (15.9%)	359.1 (270.0)	1.9 (1.3)	128.4 (131.8)	\$154.7 (239.6)	
<b>Year 2019</b>							
<b>Total</b>		<b>2,133 (100.0%)</b>	<b>391.8 (335.0)</b>	<b>2.6 (2.2)</b>	<b>22.7 (36.7)</b>	<b>\$156.2 (320.6)</b>	
Zopiclone		1,501 (70.4%)	206.2 (111.6)	1.2 (0.5)	8.4 (3.9)	\$117.0 (93.8)	
Lorazepam		496 (23.3%)	170.8 (146.3)	1.7 (1.1)	1.5 (1.1)	\$14.2 (17.2)	
Trazodone		391 (18.3%)	193.5 (162.4)	1.4 (1.1)	83.8 (62.9)	\$21.7 (30.5)	
Clonazepam		286 (13.4%)	244.5 (143.3)	2.1 (2.1)	1.2 (1.3)	\$24.3 (24.2)	
Quetiapine		271 (12.7%)	357.5 (255.6)	2.0 (1.3)	122.5 (121.9)	\$118.2 (171.8)	
<b>Year 2020</b>							
<b>Total</b>		<b>2,334 (100.0%)</b>	<b>447.1 (334.5)</b>	<b>2.5 (2.2)</b>	<b>21.0 (41.8)</b>	<b>\$193.9 (349.8)</b>	
Zopiclone		1,908 (81.7%)	258.2 (121.5)	1.2 (0.5)	8.3 (3.4)	\$143.7 (103.2)	
Lorazepam		480 (20.6%)	185.4 (153.1)	1.8 (1.6)	1.6 (1.6)	\$15.5 (17.6)	
Trazodone		352 (15.1%)	215.2 (169.0)	1.4 (1.2)	88.5 (77.4)	\$24.5 (34.5)	
Clonazepam		280 (12.0%)	254.4 (138.4)	2.1 (2.1)	1.4 (3.6)	\$25.7 (23.9)	
Quetiapine	286 (12.3%)	356.0 (262.8)	1.9 (1.2)	119.7 (130.5)	\$115.6 (176.9)		

**Supplementary Table 4. Demographic summary of Patients in Lines of Treatment**

Demographics	Categories	Patients, N (%)
<b>Total</b>	-	<b>240,820 (100.0%)</b>
<b>Age</b>	Median (IQR)	54 (45, 62)
	Mean (SD)	54 (14)
<b>Age group</b>	18-64	192,973 (80.1%)
	≥65	47,847 (19.9%)
<b>Sex</b>	Female	148,689 (61.7%)
	Male	91,548 (38.0%)
	Unknown	583 (0.2%)

<b>Payer</b>	Public (ODB)	2,761 (1.1%)
	Private (PDP)	238,059 (98.9%)
<b>Province among patients in private payer</b>	BC	19,261 (8.0%)
	AB	22,449 (9.3%)
	SK	6,457 (2.7%)
	MB	7,820 (3.2%)
	ON	91,791 (38.1%)
	QC	61,451 (25.5%)
	NB	12,341 (5.1%)
	NS	8,439 (3.5%)
	PEI	1,745 (0.7%)
	NL	5,179 (2.2%)
	YT	380 (0.2%)
	NT	66 (0.0%)
	NU	45 (0.0%)
Unknown	635 (0.3%)	
<b>Polypharmacy</b>	0-4	62,681 (26.0%)
	5-7	79,409 (33.0%)
	8-10	54,212 (22.5%)
	11-13	27,602 (11.5%)
	14-16	11,182 (4.6%)
	17-19	4,018 (1.7%)
	20+	1,716 (0.7%)

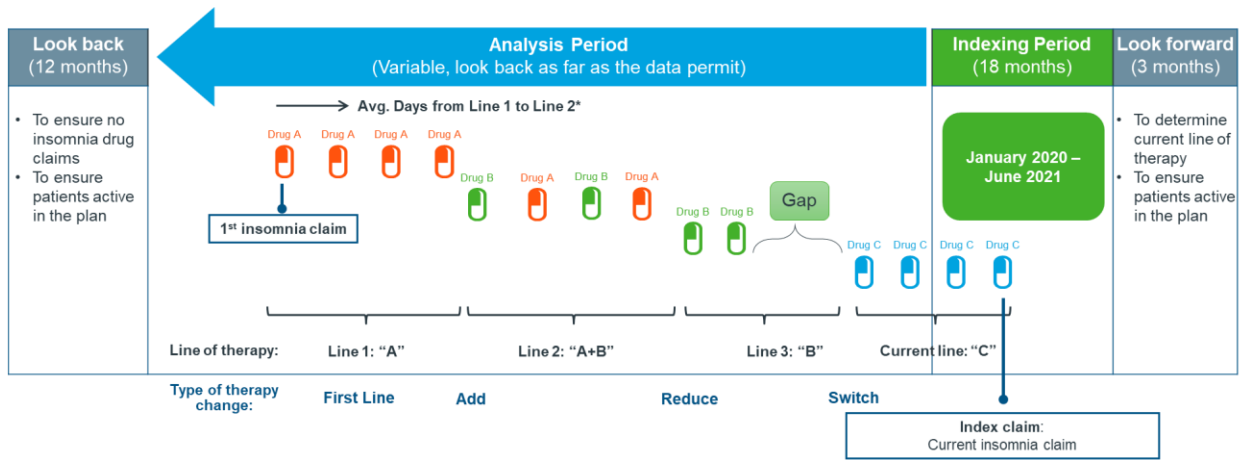
### Supplementary Table 5. Summary of Insomnia Treatment History and Lines of Treatment

Lines of Treatment	Value
<b>Total Patients</b>	240,820 (100.0%)
<b>Insomnia Treatment History (Year)</b>	
Mean (SD)	5.1 (5.2)
Median (IQR)	3.5 (0.7, 8.0)
<b>Lines</b>	
Mean (SD)	6.4 (14.3)
Median (IQR)	2.0 (1.0, 5.0)
<b>Patients by Number of Lines</b>	
1 Line	81,317 (33.8%)
2 Lines	41,848 (17.4%)
3 Lines	29,160 (12.1%)
4 Lines	16,966 (7.0%)
5 Lines	12,675 (5.3%)
6 Lines	8,612 (3.6%)
7 Lines	6,675 (2.8%)
8 Lines	4,989 (2.1%)
9 Lines	4,229 (1.8%)
10 Lines	3,375 (1.4%)
11 Lines	2,796 (1.2%)

12 Lines	2,379 (1.0%)
13 Lines	2,051 (0.9%)
14 Lines	1,730 (0.7%)
15 Lines	1,558 (0.6%)
16 Lines	1,398 (0.6%)
17 Lines	1,168 (0.5%)
18 Lines	1,044 (0.4%)
19 Lines	974 (0.4%)
20 Lines	954 (0.4%)
>20 Lines	14,922 (6.2%)



## Supplementary Figure 1. Study design of line-of-treatment analysis



Longitudinal analysis of the insomnia patients' whole treatment history was performed as per the scheme shown above.