Chronic frequent headache in the general population

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Chapter 7

Triptan use and overuse in the Netherlands – a national pharmaco-database analysis -

Submitted

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Abstract

We studied the prevalence and associated costs of triptan overuse in the Netherlands. Therefore, we used the Drug Information Project (GIP) database of the Health Care Insurance Board (CVZ), which registers prescribed drugs dispensed at pharmacies for patients insured by sickness funds (sample size n = 6.7 million, in the year 2005). We defined triptan overuse as intake of: 1) at least 120 defined daily doses (DDDs) per year (International Headache Society (IHS) criteria) and 2) at least 216 DDDs per year (stringent criteria). Among 85,172 triptan users (1.3% of all insured persons), 8,844 persons overused according to the IHS criteria (10.4%, 95% CI 10.2 to 10.6), and 2,787 persons according to stringent criteria (3.3%, 95% CI 3.2 to 3.4). The contribution of injections to overuse was negligible, indicating that triptan use in cluster headache patients did not bias results. Overusers were older than non-overusers. The risk of overuse differed per triptan. Compared to sumatriptan, the odds ratio (OR) for the risk of IHS-overuse was 0.11 (95% CI 0.08-017) for frovatriptan, 0.27 (95% CI 0.25-0.28) for rizatriptan, 0.48 (95% CI 0.40-0.57) for almotriptan, 0.68 (95% CI 0.62-0.74) for naratriptan, 0.83 (95% CI 0.72-0.95) for eletriptan and 0.86 (95% CI 0.80-0.93) for zolmitriptan. When corrected for duration of availability and number of users, the relative risk differences versus sumatriptan virtually disappeared, except for rizatriptan which remained to the triptan associated with the lowest risk of overuse. Similar results were obtained when using the stringent criteria. Total annual costs of triptans were 29.7 million Euros in 2005, with overusers accounting for 46% (IHS criteria) and 32% (stringent criteria) of total costs. Of the patients overusing triptans according to IHS criteria 30% used medication which can be prescribed as prophylaxis for migraine and according to the stringent criteria 32%. In conclusion, ten percent of triptan users are overusers, which accounts for half of total annual triptan costs. Rizatriptan is associated with the lowest risk of overuse.

Introduction

Triptans, selective serotonin $5HT_1$ agonists, are specific acute migraine drugs of which the efficacy is well established.[1-3] Because of their higher costs, triptans are prescribed only after analgesics and anti-emetics have been tried and failed (step care).[4,5] For migraine patients with severe disabling attacks, however, it is appropriate to prescribe triptans earlier in the course of treatment (stratified care).[6]

Some patients tend to overuse triptans and analgesics, leading to an increase in headache frequency until headaches become almost daily. This condition is called medication overuse headache (MOH).[7] MOH is an increasing problem worldwide; the prevalence of MOH in the general population is estimated to be 1-2%.[8] Clinical experience suggests a causal relationship between overuse of acute headache medication and chronic headache because withdrawal in MOH often results in dramatic improvement of headache frequency.[9] Based on clinical observations in headache clinics, triptans can induce headache when used two days a week or more.[10] In 2005, the International Headache Society (IHS) published revised criteria for triptan-overuse headache (TOH), which require a triptan intake on more than 10 days a month for more than 3 consecutive months. [7] With the increased availability of triptans and the now advocated, but unproven, patient instruction to treat attacks early, prevalence of triptan overuse is likely to increase.[11] This is an unfavourable situation because chronic frequent headache has a major impact on quality of life of the patient[12,13], and the cost of overuse for society is considerable.[14] It is also unnecessary since overuse of triptans can be prevented by restricting use and starting prophylactic medication in patients with high attack frequency.

To gain more insight into the magnitude and nature of the problem we studied the characteristics of triptan users in the Netherlands. Furthermore, we estimated the prevalence of overuse and the financial burden of overuse on health care resources.

Methods

Study Setting

Data were obtained from the Drug Information Project (GIP database) of the Health Care Insurance Board (CVZ). The CVZ is a public authority in the domain of drugs. As an independent non-profit governing body, it monitors conditions of the health insurance scheme

in the Netherlands. In 2005, more than 10 million persons (65% of the inhabitants in the Netherlands) were mandatorily insured on the grounds of the Sickness Fund Act. People were eligible for sickness fund insurance if they had a yearly income of less than € 33.000. The GIP registered prescribed drugs dispensed at pharmacies for all patients insured by sickness funds. All prescription drugs are coded according to the Anatomical, Therapeutic and Chemical (ATC) classification. [15] Data are available for 6.7 million people in 2005, covering 46% of the total Dutch population and 67% of the sickness fund insured patients. For migraine patients in the Netherlands, there were no financial restrictions in administering headache therapy (attack treatment or prophylaxis) in the study year 2005 if physicians prescribed the medication. In the Netherlands there was no over-the-counter sale of triptans in 2005. Each registered patient has an anonymous unique identification number, which allows observation of medication use over time per patient.

Definitions

We defined a triptan user as a patient for whom minimally one prescribed triptan was dispensed in 2005. We used two definitions for triptan overuse. One according to the IHS, i.e. intake on ≥10 days/month on a regular basis for > 3 consecutive months,[7] and a second more stringent definition based on studies in headache clinics, i.e. use of 18 single doses or more per month for > 3 consecutive months.[16] We converted these criteria into defined daily dose (DDD) per year, which is, according to the World Health Organization (WHO), the standardised dosage per day of a drug when prescribed for the registered indication (Table 1).[15] Accordingly, 'IHS triptan overuse' was defined as intake of at least 10 DDDs per month, or 120 DDDs per year and the 'stringent triptan overuse' as at least 18 DDDs per month, or 216 DDDs per year. In contrast to the IHS, which takes a 3-month period, our study carries a 12-month period for determining overuse.

Patients with cluster headache, but not so much those with migraine, may sometimes use very high quantities of subcutaneous injections of sumatriptan which could bias the results towards overuse of sumatriptan. To avoid such bias, we extracted the administration route and estimated the number of injection users.

Use of prophylactic medication was defined as minimally one dispensed prescription in 2005 of any medication registered for migraine prophylaxis. Since in the database the indication for the prophylactic prescription is not recorded, it is not known whether the medication was actually prescribed for migraine or for another comorbid disorder (e.g. propranolol, which can be prescribed for migraine, hypertension or other diseases).

Table 1 Defined daily dose per triptan according to the World Health Organisation.[15]

Triptan	Year of introduction in the Netherlands	Formulation	Defined daily dose (DDD)
Sumatriptan	1991 (1996*)	50-mg tablet	1 tablet
		100-mg tablet	½ tablet
		25-mg suppository	1 supp
		20-mg nasal spray	1 spray
		6-mg subcutaneous injection	1 injection
Naratriptan	1997	2.5 mg tablet	1 tablet
Zolmitriptan	1997	2.5 mg tablet	1 tablet
Rizatriptan	1998	5-mg tablet	2 tablets
		10-mg tablet	1 tablet
Eletriptan	2000	20-mg tablet	2 tablets
		40-mg tablet	1 tablet
Almotriptan	2000	12.5 mg tablet	1 tablet
Frovatriptan	2001	2.5 mg tablet	1 tablet

* First year of full availability of tablets without any surcharge.

Statistical analysis

Data was categorized and are presented as numbers with percentages. Differences between groups are presented with 95% confidence intervals (Δ, 95% CI). To assess the association with overuse of the various triptans relatively to sumatriptan, we calculated the odds ratios (OR) with sumatriptan as the reference. Because sumatriptan is the longest available and most widely prescribed triptan in the Netherlands, we chose sumatriptan as reference. We used the Mantel-Haenszel procedure to adjust for age.

Results

In 2005, 85,172 patients (1.3% of the total sample) received a triptan. Of these 31,841 (37.4%) received only one prescription in 2005 and 5,536 (6.5%) received a prescription for more than one type of triptan. Almost all triptans (95%) were prescribed by general practitioners (GP), and only 4% by specialists, mainly neurologists. Table 2 shows the characteristics of triptan users compared to the total population. The majority of triptan users were female and over thirty years old. Nineteen percent of triptan users used medication that can be prescribed as prophylactic medication for migraine.

Amongst the 85,172 triptan users, 8,844 persons overused according to the IHS criteria (10.4%; 95%CI: 10.2-10.6), and 2,787 persons according to the stringent criteria (3.3%; 95%CI: 3.2-3.4). Characteristics of overusers versus non-overusers are presented in table 3 (page 105). Percentages of overuse are similar in females and males. Overusers are older than non-overusers; in both overuse groups 60% of patients are in the fifth and sixth decade of life. Prophylactic medication is more frequently dispensed in overusers (according to IHS criteria 30.4 % and according to stringent criteria 32.1 %) than in non-overusers (17.9%).

As there are four different routes of administration for sumatriptan we studied the relative prevalences. In the total sample, 6.7% used more than one route of administration, in the non-overusers this was 5.5%. Of the 45,639 patients who used sumatriptan, exclusive use of tablets was the formulation most commonly prescribed: 64% of the total sample, 62% of the non-overusers, 76% of the IHS overusers, and 74% of stringent overusers. Exclusive use of injections was found in 9.8% of all sumatriptan users, for 10.3% of sumatriptan non-overusers, for 6.6% of the IHS sumatriptan overusers and for 4.6% of stringent sumatriptan overusers.

Table 2 Characteristics of triptan users compared to the total population.

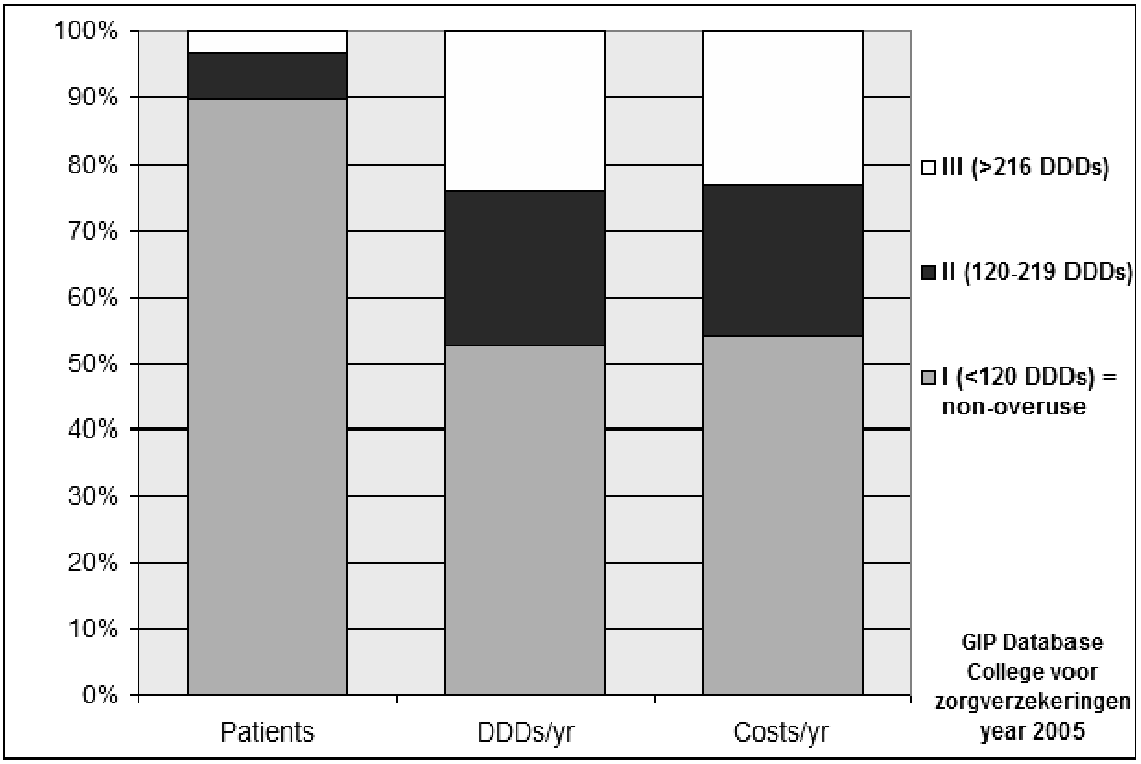
	Total population N = 6,704,627 n (%)		Triptan users N = 85,172 n (%)	
Females	3,665,773	(55)	71,047	(83)
Age < 20	685,352	(19)	1,916	(3)
20 – 29	459,630	(13)	9,616	(14)
30 – 39	586,641	(16)	16,620	(23)
40 – 49	588,504	(16)	21,628	(30)
50 – 59	503,518	(14)	14,615	(21)
60 – 69	365,634	(10)	4,926	(7)
≥ 70	476,494	(13)	1,726	(2)
Males	3,038,854	(45)	14,125	(17)
Age < 20	719,131	(24)	871	(6)
20 – 29	447,465	(15)	1,782	(13)
30 – 39	486,320	(16)	3,499	(25)
40 – 49	433,975	(14)	3,644	(26)
50 – 59	371,537	(12)	2,725	(19)
60 – 69	297,714	(10)	1,194	(9)
> 70	282,712	(9)	410	(3)
Prophylactic medication*	437.354	(6.5)	16.327	(19.2)
Propranolol	54,254	(0.8)	6,267	(7.4)
Metoprolol	339,244	(5.1)	6,985	(8.2)
Pizotiphen	4,028	(0.1)	1,400	(1.6)
Flunarizine	2,803	(0.0)	218	(0.3)
Valproic acid	30,228	(0.5)	1,713	(2.0)
Clonidine	13,363	(0.2)	747	(0.9)
Topiramate	3,325	(0.0)	1,084	(1.3)

Source: GIP database, College voor Zorgverzekeringen. *Medication which can be prescribed as prophylactic therapy for migraine. Amitriptyline is not registered and not prescribed as migraine prophylaxis in the Netherlands. Methysergide can only be prescribed for a short period to prevent adverse events and was therefore excluded.

Table 4 (page 106) shows differences in use of triptan type between non-overusers and overusers. Sumatriptan is the most prescribed triptan. The majority of triptan users and overusers used only one triptan. Some triptans have different dosages (Table 1). In patients overusing sumatriptan, the 100 mg tablets are more often prescribed than the 50 mg tablets (ratio 50:100mg: 1:2.7 in IHS overusers and 1:5.3 in stringent overusers). For all sumatriptan users the 50 mg to 100 mg ratio is 1:1.

Overuse was observed for all triptans, but the risk of overuse differed per triptan. Compared to sumatriptan, the odds ratio (OR) for the risk of IHS overuse was 0.11 (95% CI 0.08-0.17) for frovatriptan, 0.27 (95% CI 0.25-0.28) for rizatriptan, 0.48 (95% CI 0.40-0.57) for almotriptan, 0.68 (95% CI 0.62-0.74) for naratriptan, 0.83 (95% CI 0.72-0.95) for eletriptan and 0.86 (95% CI 0.80-0.93) for zolmitriptan. When corrected for duration of availability the relative risk differences versus sumatriptan virtually disappeared, except for rizatriptan which remained to the triptan associated with the lowest risk of overuse. Compared to sumatriptan the risk in the IHS group was three times smaller (OR 0.34, 95% 0.32 – 0.37). Similar results were obtained when using the stringent criteria (Table 5, page 107), the risk of overuse was nearly eight times smaller for rizatriptan compared to that for sumatriptan (corrected OR 0.17, 95% CI 0.15-0.20).

The costs of triptan use and overuse are shown in Figure 1. Total costs of triptan use in our study (85,172 triptan users, 6.7 million total population) were 29.7 million Euros in 2005, i.e. 349 Euro per triptan users and 4.43 Euros per inhabitant. Patients overusing triptans according to the IHS criteria account for 46% of total costs and according to the stringent criteria for 23% of total costs, i.e. 1,543 Euros per IHS overuser and 2,468 Euros per stringent overuser.



DDD: daily defined dose. I= non-overuse, II + III = overuse according to IHS criteria, III = overuse according to Stringent criteria.

Figure 1 *Relative costs of triptan use and overuse.*

Discussion

We analysed the prescription and dispense data for triptans in the year 2005 by using an unique database of the National Health Care Insurance Board, which covers medication use of 6.7 million people, nearly half of the total population in the Netherlands. Triptans were used by 1.3% of all persons, of which 10% were overusing triptans accounting for almost half of the total costs. Remarkably, the risk of overuse differed per triptan,with rizatriptan and possibly frovatriptan being associated with the lowest risk.

The results from our analysis appear robust and representative. We use an extensive and unbiased, nation-wide, population-based database with an accurate count of actual dispense of triptans at pharmacies. Although we couldn't measure the actual use of triptans by the patient, it seems very unlikely that large proportions of patients would not use medication that was dispensed. Furthermore, our results are in agreement with a population-based study in Denmark where 5% of sumatriptan users used > 30 DDDs per month and was responsible for

38% of the total sumatriptan consumption.[17] A French study estimated that 25-30% of the triptan users are overusing these drugs.[18]

We calculated the average triptan consumption over a 12 month period rather than only over three month periods because use and overuse of acute antimigraine medication are known to fluctuate substantially. Of the 9,120 IHS overusers in the first quarter, only 5,891 (65%) were overusers in the second quarter, 5,732 (63%) in the third, and 5,860 (64%) in the last quarter. By using dispense of 120 DDDs or more over a 12-month period as cut-off criterion, we found 8,844 IHS overusers. This appears a better estimate of true long-term consistent triptan overuse.

The most striking finding of our study was that risk of overuse appears to differ among triptans. In particular, use of frovatriptan and rizatriptan was associated with remarkably lower proportions of overusers compared to the reference agent sumatriptan and the other triptans. Several confounding factors could potentially explain this finding and need to be discussed first before assuming that rizatriptan and frovatriptan are indeed associated with a lower risk of overuse.

A possible confounding factor could be that we used DDDs for the threshold for overuse rather than total amount of mg. In 2001, the DDD for sumatriptan was changed from 100 mg to 50 mg (http://www.whocc.no/atcddd/).[15] Thus, if patients continued using the 100 mg rather than the 50 mg dose, the threshold for overuse could have been artificially lowered. This could, however, not be confirmed by the number of dispensed DDDs per patient in 2005. For sumatriptan 52 DDDs in average per patient were prescribed with an average prescription size of 14.8 DDDs. The average DDDs per patient and prescription size of sumatriptan is comparable to the other triptans. Respectively, the numbers for naratriptan are 47 and 13.8, for zolmitriptan 50 and 13.9, for rizatriptan 27 and 9.7, for almotriptan 34 and 10.7, for eletriptan 45 and 12.4, and for frovatriptan 20 and 9.6.

Secondly, high use of subcutaneous sumatriptan by cluster headache patients could have biased the results towards overuse of sumatriptan. However, use of the subcutaneous formulation of sumatriptan made up for only 8.8% of the total sumatriptan overuse in the IHS

group and for only 5.7% in the stringent group. This is less than in the non-overuse group (10.5%), making a major impact of overuse of subcutaneous sumatriptan unlikely.

A third potential confounding factor is the difference in duration of availability of the various triptans (Table 1). This might have led to preferential use of the earlier available agents by the most disabled patients who potentially could have a higher risk of overuse. Sumatriptan was the first available triptan (1991), but because of complicated reimbursement issues in the Netherlands, the oral formulation became fully reimbursed only in 1996. Sales for sumatriptan really started only then. Overuse before that time was rare in the Netherlands. The other triptans were always fully reimbursed from the date of introduction. When corrected for duration of availability (for sumatriptan from year of full reimbursement), the risk differences for naratriptan, zolmitriptan, eletriptan, and almotriptan compared to sumatriptan almost disappeared, but remained for frovatriptan and rizatriptan. Although we cannot fully exclude that the later introduction of rizatriptan and frovatriptan has contributed to their lower association with overuse, it seems unlikely to have been a major contributor, especially not in the case of rizatriptan.

Taken together, rizatriptan and frovatriptan were associated with substantially lower proportions of overusers in 2005. We consider this a true benefit for rizatriptan, but find it too early to arrive at the same conclusion for frovatriptan. Frovatriptan is the most recently introduced triptan, 10 years later than sumatriptan, and was marketed as a triptan with a slower and lower onset of efficacy. This would not seem a profile well suited for many highly disabled migraine patients. Indeed, the absolute numbers for users (N=957) and overusers (N=17) of frovatriptan in 2005 were extremely small compared to those for sumatriptan (N= 41,352 and N= 5,554), rizatriptan (N=25,796 and N=1,026) and the other triptans. The small numbers make meaningful assessment of true risk of overuse difficult.

We can only speculate why rizatriptan, and possibly frovatriptan, are associated with a lower risk of overuse. Risk of overuse may be influenced by the initial efficacy of the agent (how fast does it completely stop the migraine symptoms) and the subsequent duration of action (absence of recurrence of the symptoms precluding redosing). In a large meta-analysis of 53 controlled trials with all available triptans, use of rizatriptan was associated with the highest rates for initial efficacy (pain free at two hours post dose) and sustained effect (24 hrs

sustained pain free)[1]. The differences with the other triptans were, however, in absolute terms hardly large enough to explain the remarkable reduction in risk of overuse for rizatriptan in the present study.

Overusers account for almost half of the total costs of triptans. These costs can be greatly reduced if physicians would monitor their prescriptions better and would consider prophylactic treatment earlier in case of increasing headache frequency to prevent overuse. Once overuse is established, withdrawal of overused medication is the most appropriate therapy.[19]

A limitation of our study is firstly the lack of information on the indication for the prescribed drug, as we already noted for cluster headache. The prophylactic medication for instance, can be prescribed for other disorders than migraine (e.g. propranolol for hypertension, among other diagnoses). The reported use of migraine prophylaxis may therefore be slightly overestimated. Secondly, we do not have information on the number of headache days of the triptan users. It is likely though that patients who overuse triptans have chronic frequent headache (CFH), which is defined as headache on at least 15 days per month and leads to a considerable decrease in quality of life.[13] CFH is more prevalent in people with a low educational level.[20,21] Given the nature of our sickfund-based database our patients had a relatively lower socio-economic status, which could imply that the prevalence of triptan overuse is slightly overestimated. However, the database covers 6.7 million people and represents 65% of the Dutch population in 2005 and data from these patients are generally no different from those in the general population.[22]

To our knowledge, this is the first large study reporting the prevalence of overuse of all currently available triptans in the general population. Although the overall prevalence of triptan overuse is low, overuse accounts for a large percentage of total costs of migraine therapy. The risk of overuse differs per triptan. Rizatriptan had the lowest risk of overuse.

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Table 3 Characteristics of triptan overusers compared to non-overusers

	Total		Non-overusers		Overusers							
	N = 85,172		< 120 DDDs/yr N = 76,328		IHS criteria: ≥120 DDD/yr N = 8,844		Difference IHS-overusers vs non-overusers (95% CI)		Stringent criteria* ≥216 DDD/yr N = 2,787		Difference stringent-overusers vs non-overusers (95% CI)	
Female, n (%)	71,047	(83)	63,622	(83)	7,425	(84)	1%	(-0.2 to 1.4)	2,294	(82)	-1%	(-2.5 to 0.4)
Mean age, y (SD)	43	(13)	42	(13)	47	(11)	5 yrs	(4.7 to 5.3)	48	(11)	6 yrs	(5.2 to 6.2)
Age, n (%)												
< 20	2,787	(3)	2,765	(4)	22	(0)	-3%	(-3.5 to -3.2)	6	(0)	-3%	(-3.6 to -3.1)
20 - 29	11,398	(13)	10,913	(14)	485	(6)	-9%	(-9.3 to -8.3)	113	(4)	-10%	(-11.0 to -9.4)
30 - 39	20,119	(24)	18,439	(24)	1,680	(19)	-5%	(-6.0 to -4.3)	515	(19)	-6%	(-7.1 to 4.2)
40 - 49	25,272	(30)	22,275	(29)	2,997	(34)	5%	(3.7 to 5.7)	964	(35)	5%	(3.6 to 7.2)
50 - 59	17,340	(20)	14,861	(20)	2,479	(28)	9%	(7.6 to 9.5)	789	(28)	9%	(7.2 to 10.6)
60 - 69	6,120	(7)	5,210	(7)	910	(10)	4%	(2.8 to 4.1)	298	(11)	4%	(2.8 to 5.1)
≥70	2,136	(2)	1,865	(2)	271	(3)	1%	(0.3 to 1.0)	102	(4)	1%	(0.6 to 2.0)
Prophylaxis, n (%)†												
Propranolol	6,267	(7.4)	5,287	(6.9)	980	(11.1)	4%	(3.5 to 4.8)	326	(11.7)	5%	(3.6 to 6.0)
Metoprolol	6,985	(8.2)	5,868	(7.7)	1,117	(12.6)	5%	(4.2 to 5.7)	352	(12.6)	5%	(3.7 to 6.2)
Pizotifeen	1,400	(1.6)	1,133	(1.5)	267	(3.0)	2%	(1.2 to 1.9)	106	(3.8)	2%	(1.7 to 3.1)
Flunarizine	218	(0.3)	165	(0.2)	53	(0.6)	0%	(0.2 to 0.6)	17	(0.6)	0%	(0.2 to 0.8)
Valproic acid	1,713	(2.0)	1,352	(1.8)	361	(4.1)	2%	(1.9 to 2.8)	123	(4.4)	3%	(1.9 to 3.5)
Clonidine	747	(0.9)	628	(0.8)	119	(1.3)	1%	(0.3 to 0.8)	38	(1.4)	1%	(0.2 to 1.0)
Topiramate	1,084	(1.3)	757	(1.0)	327	(3.7)	3%	(2.3 to 3.1)	130	(4.7)	4%	(2.9 to 4.5)
Any of the above	16,327	(19.2)	13,635	(17.9)	2,692	(30.4)	13%	(11.6 to 13.6)	895	(32.1)	14%	(12.5 to 16.0)

Source: GIP Database/College voor Zorgverzekeringen. * Stringent-overusers are a subgroup of IHS-overusers. † Medication which can be prescribed as prophylactic medication for migraine, but may have been prescribed for other co-morbid disorders.

Table 4 Triptan use in non-overusers versus overusers

	Total	Non-overusers		Overusers		
		< 120 DDDs/yr	IHS criteria: ≥120 DDDs/yr	Difference IHS-overusers – non-overusers	Stringent criteria* ≥216 DDDs/yr	Difference stringent-overusers – non-overusers
	N = 85,172	N = 76,328	N = 8,844	(95% CI)	N = 2,787	(95% CI)
Single triptan use	79,636 (94)	71,837 (94)	7,799 (88)	-6% (-6.6 to -5.3)	2,416 (87)	-7% (-8.8 to -6.2)
Sumatriptan	41,352 (52)	35,798 (50)	5,554 (71)	21% (20 to 22)	1,952 (81)	31% (29 to 33)
Naratriptan	3,798 (5)	3,437 (5)	361 (5)	0% (-0.6 to 0.4)	86 (4)	-1% (-1.9 to -0.4)
Zolmitriptan	4,983 (6)	4,397 (6)	586 (8)	1% (0.8 to 2.0)	134 (6)	-1% (-1.4 to 0.4)
Rizatriptan	25,796 (32)	24,770 (35)	1,026 (13)	-21% (-22 to -21)	182 (8)	-27% (-28 to -26)
Eletriptan	1,455 (2)	1,289 (2)	166 (2)	0% (0.0 to 0.7)	37 (2)	0% (-0.7 to 0.3)
Almotriptan	1,295 (2)	1,206 (2)	89 (1)	-1% (-0.8 to -0.3)	23 (1)	-1% (-1.1 to -0.2)
Frovatriptan	957 (1)	940 (1)	17 (0.2)	-1% (-1.2 to -0.9)	2 (0.1)	-1% (-1.3 to -1.0)
Multiple triptans	5,536 (6)	4,491 (6)	1,045 (12)	6% (5.3 to 6.6)	371 (13)	7% (6.2 to 8.8)

Values are numbers (%). * Stringent-overusers are a subgroup of IHS-overusers. Source: GIP Database/College voor Zorgverzekeringen

Table 5 The association with overuse for all triptans relative to sumatriptan tablets.

	Total	Non-overuse		Overuse							
		< 120 DDD/yr		IHS criteria: >120 DDD/yr		Odds (95%CI)		Stringent criteria* >216 DDD/yr		Odds (95%CI)	
	N = 85,172	n	(%)	n	(%)			n	(%)		
Sumatriptan	41,352	35,798	(87)	5,554	(13)	1.00	(ref)	1,952	(5)	1.00	(ref)
Naratriptan	3,798	3,437	(91)	361	(10)	0.68	(0.62-0.74)	86	(2)	0.46	(0.38-0.55)
Zolmitriptan	4,983	4,397	(88)	586	(12)	0.86	(0.80-0.93)	134	(3)	0.56	(0.48-0.65)
Rizatriptan	25,796	24,770	(96)	1,026	(4)	0.27	(0.25-0.28)	182	(1)	0.13	(0.12-0.15)
Eletriptan	1,295	1,206	(93)	89	(7)	0.48	(0.40-0.57)	23	(2)	0.35	(0.25-0.50)
Almotriptan	1,455	1,289	(89)	166	(11)	0.83	(0.72-0.95)	37	(3)	0.53	(0.40-0.69)
Frovatriptan	957	940	(98)	17	(2)	0.11	(0.08-0.17)	2	(0)	0.04	(0.01-0.13)

Values are numbers (%).*Stringent-overusers are a subgroup of IHS-overusers. Source: GIP Database/College voor Zorgverzekeringen.