

Evaluation of Serious Adverse Event Patterns Associated with Sumatriptan: Integrating FAERS Signal Detection with Systematic pattern analysis

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Abstract—Introduction: Sumatriptan is a selective serotonin (5-HT_{1B/1D/1F}) receptor agonist approved for the acute treatment of migraine and cluster headaches. While its efficacy is well established, understanding its safety profile through real-world data is critical for optimizing patient outcomes. This review analyzes adverse event reports associated with Sumatriptan, sourced from the FDA Adverse Event Reporting System (FAERS), to identify patterns and potential safety concerns.

Methodology: A total of 9,657 adverse event cases involving Sumatriptan were extracted from the FAERS database up to September 2025. The data were analyzed across multiple dimensions: system organ class (SOC), seriousness, age, gender, geography, and reporter type. Preferred terms (PTs) within each SOC were examined to identify frequently reported adverse drug reactions (ADRs). The analysis also considered the distribution of cases by reporting year and outcome severity.

Results: The majority of cases (71.66%) were reported in females, with adults aged 18–64 years comprising 42.92% of age-specific reports.

- Non-serious events accounted for 50.3% of outcomes, while fatal and life-threatening events represented 2.8% and 3.1%, respectively.
- The most frequently reported SOCs included Product Issues (43.9%), Injury, Poisoning and Procedural Complications (43.3%), and General Disorders (33.4%).
- Common PTs included drug ineffectiveness, headache, nausea, serotonin syndrome, and chest discomfort.
- Reporter type analysis showed 53.16% of cases were submitted by healthcare professionals, with consumers contributing 45.26%.

Conclusion: This analysis confirms known ADRs of Sumatriptan and highlights real-world patterns in adverse event reporting. While most events were non-serious, the presence of serious outcomes—including fatalities—underscores the need for careful patient selection and monitoring, especially in populations with cardiovascular risk factors or concomitant serotonergic

therapies. These findings support ongoing pharmacovigilance and informed clinical decision-making.

I. OBJECTIVE

This adverse event summary report provides a comprehensive overview of the safety profile of Sumatriptan. The data for the report has been sourced from the FAERS database, focusing on reported adverse events and pattern of adverse event reporting. The report will also highlight the most common adverse events associated with Sumatriptan usage and analyze them SOC wise further characterized by seriousness. The data is also analysed based on geography, gender and age.

Furthermore, systematically summarizing and analysing all identified Adverse Drug Reactions (ADRs), this report will present a clear and concise overview of the safety profile of Sumatriptan.

II. DRUG BACKGROUND

Sumatriptan, a selective serotonin (5-HT_{1B/1D/1F}) receptor agonist, is approved by the EMA for the acute treatment of migraine with or without aura, and cluster headache, in individuals diagnosed with migraine. It is not indicated for prophylactic use, nor for certain migraine subtypes such as hemiplegic or basilar migraine.

The active pharmaceutical ingredient (API) is Sumatriptan succinate, marketed under brand names such as Imitrex® and Imigran®.

2.1 Indication

Sumatriptan is indicated for:

- The acute treatment of migraine attacks, with or without aura, in adults.
- The acute treatment of cluster headaches in adults.

- Not intended for use as prophylactic therapy, nor for hemiplegic, basilar, or ophthalmoplegic migraines

2.2 Qualitative and Quantitative Composition

- Tablets:
 - Each 50 mg film-coated tablet contains sumatriptan (as succinate) equivalent to 50 mg sumatriptan.
 - Each 100 mg film-coated tablet contains sumatriptan (as succinate) equivalent to 100 mg sumatriptan.
 - Example combination (for reference only): Each tablet may contain 119 mg sumatriptan succinate corresponding to 85 mg sumatriptan plus naproxen 500 mg (in other products/preparations).
- Solution for Injection (Subcutaneous):
 - Each 0.5 mL injection contains sumatriptan succinate equivalent to 4 mg sumatriptan.
 - Each 0.5 mL injection contains sumatriptan succinate equivalent to 6 mg sumatriptan (higher strength option).

2.3 Safety profile

2.3.1 Adverse Drug Reactions

As per SmPC: The most commonly reported ADRs with sumatriptan are paresthesia, dizziness, flushing, sensations of heaviness or pressure (including chest and throat), fatigue, and nausea/vomiting. These reactions are generally common ($\geq 1/100$ to $< 1/10$). Additionally, important identified risks include serotonin syndrome, hypertension, coronary vasospasm/ischemia, and hypersensitivity reactions. Serious hypersensitivity reactions, including anaphylactic-type reactions, have been reported in the post-marketing setting. Such reactions may present with urticaria, dyspnoea, angioedema, tachycardia, chest discomfort, and in rare cases, life-threatening cardiovascular events.

2.3.2 Monitoring

Careful monitoring of patients is recommended following administration of sumatriptan, particularly in those with cardiovascular risk factors. Patients should be evaluated for any signs or symptoms of serotonin syndrome, chest pain, or other vasospastic events.

Sumatriptan should only be administered to patients without known cardiovascular disease, or after appropriate cardiac evaluation in individuals at increased risk (e.g., hypertension, diabetes, smoking,

obesity, strong family history of coronary artery disease).

In patients with hepatic impairment, dose adjustment or caution is advised due to altered metabolism. Patients should also be monitored for potential drug interactions when used concomitantly with SSRIs, SNRIs, or MAO inhibitors.

2.3.3 Special Warnings

Under the below-mentioned conditions, the administration of sumatriptan should be monitored:

- Cardiovascular disease or presence of risk factors for coronary artery disease (e.g., hypertension, diabetes, smoking, obesity, family history of CAD)
- Cerebrovascular disease (history of stroke or TIA)
- Hepatic impairment (use with caution; contraindicated in severe impairment)
- Concomitant use with SSRIs, SNRIs, or MAO inhibitors due to risk of serotonin syndrome
- Concomitant use with ergotamine or other triptans (risk of additive vasospastic effect)

2.3.4 Contraindications

The use of sumatriptan is contraindicated in cases of:

- Hypersensitivity to the active substance or to any of its excipients
- Ischemic heart disease, history of myocardial infarction, Prinzmetal's angina, or symptoms/signs of ischemic cardiac conditions
- Cerebrovascular syndromes (stroke or transient ischemic attack)
- Peripheral vascular disease
- Uncontrolled hypertension
- Severe hepatic impairment
- Concomitant use with ergotamine, ergotamine derivatives, or other 5-HT₁ receptor agonists (triptans)

III. DATA COLLECTION AND STRATEGY

3.1 Data Source

Data for this report was retrieved from the FAERS database. The FAERS (FDA Adverse Event Reporting System) database is a repository of adverse event reports submitted to the U.S. Food and Drug Administration (FDA). It contains information on adverse events, medication errors, and product quality issues associated with various FDA-regulated products such as drugs,

biologics, medical devices, dietary supplements, and cosmetics.

A detailed strategy used for retrieval of the data is summarized below in Table 1

Table 1 Search criteria used for data retrieval

Criteria	Search Criteria used in this report
Reporting period	Cumulative through the provided extract
Database search cut-off date	01 September 2025
Report sources	Spontaneous
Suspect drug(s)	Sumatriptan (all product names)
Search engine	FAERS Dashboard Open Platform
Notes on search	All adverse events reported in the extract

IV. METHODOLOGY OF ANALYSIS OF DATA

To review the safety profile of Sumatriptan, the reported adverse events were thoroughly reviewed and documented. This analysis aimed to identify patterns, trends, and potential safety concerns associated with the medication. The data available in various tabs was meticulously reviewed and analyzed in the following categories.

SOCs

A comprehensive assessment was conducted to determine the distribution of adverse events across different system organ classes (SOCs). The seriousness of these events was also evaluated and presented. A detailed SOC-wise analysis was performed to identify any specific safety findings that contributed significantly to the total number of reported cases.

Geographical Distribution

A geographical analysis was conducted to understand the distribution of adverse events in different regions. By examining this data, potential variations or trends in the occurrence of adverse events across geographic locations were identified.

Gender

The data was further examined to assess if there were any gender-related differences in the reporting of

Table 2 Distribution of Cases by received year

Time period	Number of Cases	Percentage
2025	518	5.36%
2024	533	5.52%
2023	674	6.98%
2022	518	5.36%
2021	618	6.40%

adverse events. This analysis provided insights into potential variations in the occurrence and severity of adverse events between male and female patients.

Age

To better understand the impact of age on adverse event occurrence, the data was categorized and analyzed according to different age groups. This allowed determination of whether any age-specific patterns or trends existed in the reporting of adverse events.

Reporter Type

The data was further examined to assess if there were any differences in reporting of adverse events by reporter type. This analysis provided valuable insights into potential variations in reports submitted by healthcare professionals (medically confirmed) versus consumers/non-healthcare professionals (non-medically confirmed).

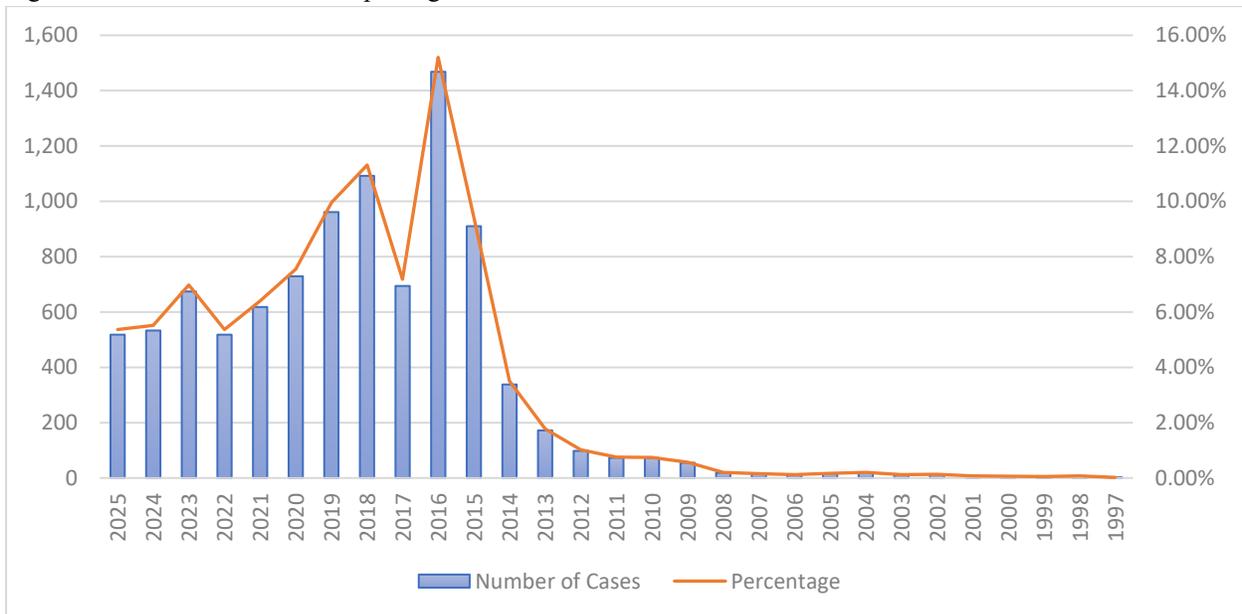
V. RESULTS

Data Overview

A total of 9,657 case reports (expedited and non-expedited) were retrieved with Sumatriptan from the FAERS database up to 2025. The details of these cases are categorized based on SOC, age, gender, and geography. Refer to below for details

2020	729	7.55%
2019	961	9.95%
2018	1,092	11.31%
2017	694	7.19%
2016	1,468	15.20%
2015	910	9.42%
2014	338	3.50%
2013	172	1.78%
2012	98	1.01%
2011	73	0.76%
2010	72	0.75%
2009	55	0.57%
2008	19	0.20%
2007	15	0.16%
2006	12	0.12%
2005	16	0.17%
2004	20	0.21%
2003	12	0.12%
2002	13	0.13%
2001	7	0.07%
2000	6	0.06%
1999	5	0.05%
1998	7	0.07%
1997	2	0.02%
Total	9,657	100.00%

Figure 1 Counts of Cases over Reporting Years



(A horizontal bar chart depicting the number of cases received per year. The distribution peaked in 2016, accounting for **15.20%** of total cases.)

- The count includes various reports including expedited, non-expedited, and direct.
- Direct reports are voluntarily submitted to EudraVigilance by consumers and healthcare professionals.
- Mandatory reports are submitted by the manufacturer and are categorized as:

Expedited reports – contain at least one adverse event not described in the product labeling and for which the outcome is serious.

Table 2 and below. Please note: The elderly group includes patients ≥ 65 years of age.

Table 3 Distribution pattern of Sumatriptan cases by age grouping

Category	Number of Cases	Percentage
0-1 Month	59	0.61%
2 Months-2 Years	14	0.14%
3-11 Years	27	0.28%
12-17 Years	148	1.53%
18-64 Years	4,145	42.92%
65-85 Years	520	5.38%
More than 85 Years	13	0.13%
Not Specified	4,731	48.99%
Total	9,657	100.00%

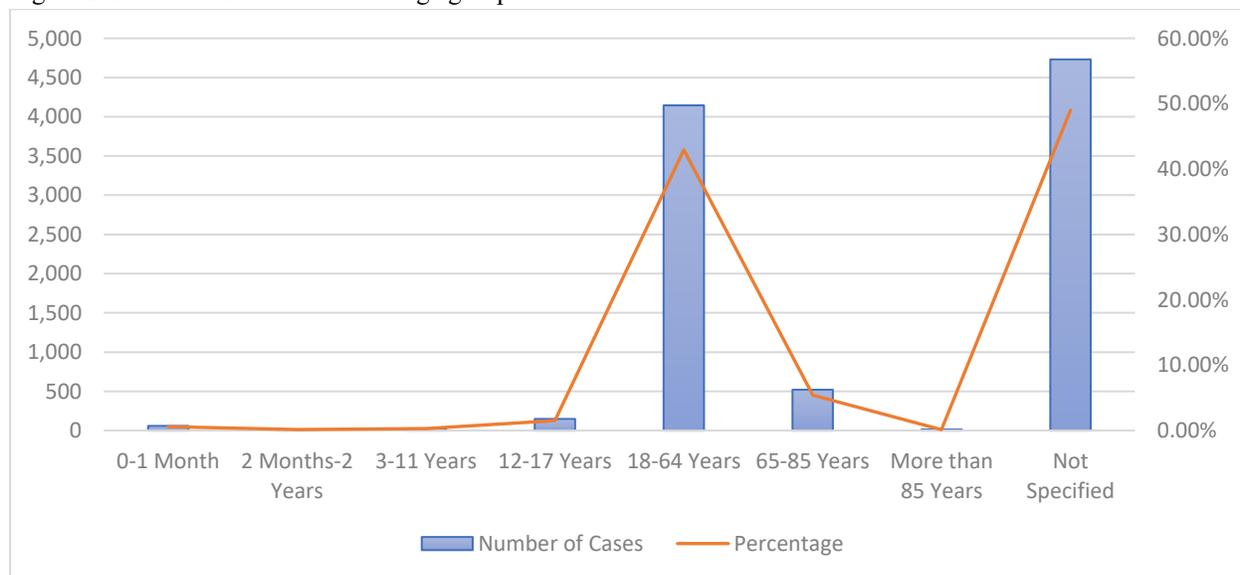
Non-expedited reports – do not meet expedited criteria, may include serious/expected or non-serious cases.

5.1 DISTRIBUTION OF OVERALL CASES - AGE GROUP

Of the total 4,882 cases where the age group was reported, most of the cases are from the adult age group (n=4,105; 84.07%), followed by the elderly group (n=531; 10.88%). The remaining age groups each account for less than 2% of the total.

Additionally, there were 4,701 cases (49.06%) where no information regarding the age group was reported. The details are presented in

Figure 2 Distribution of cases across age groups



From the available data it is clearly depicted that majority of the adverse reactions are reported in adult

(18–64 years) age group which accounts to be 42.92% of the total population of cases reported. There were

48.99% of cases in which no information regarding the age group was specified. The distribution of the remaining age group is presented in Figure 2

males, and for the remaining 786 cases (8.20%), no information regarding gender was reported. The details are presented in

5.2 DISTRIBUTION OF SUMATRIPTAN CASES – GENDER/SEX

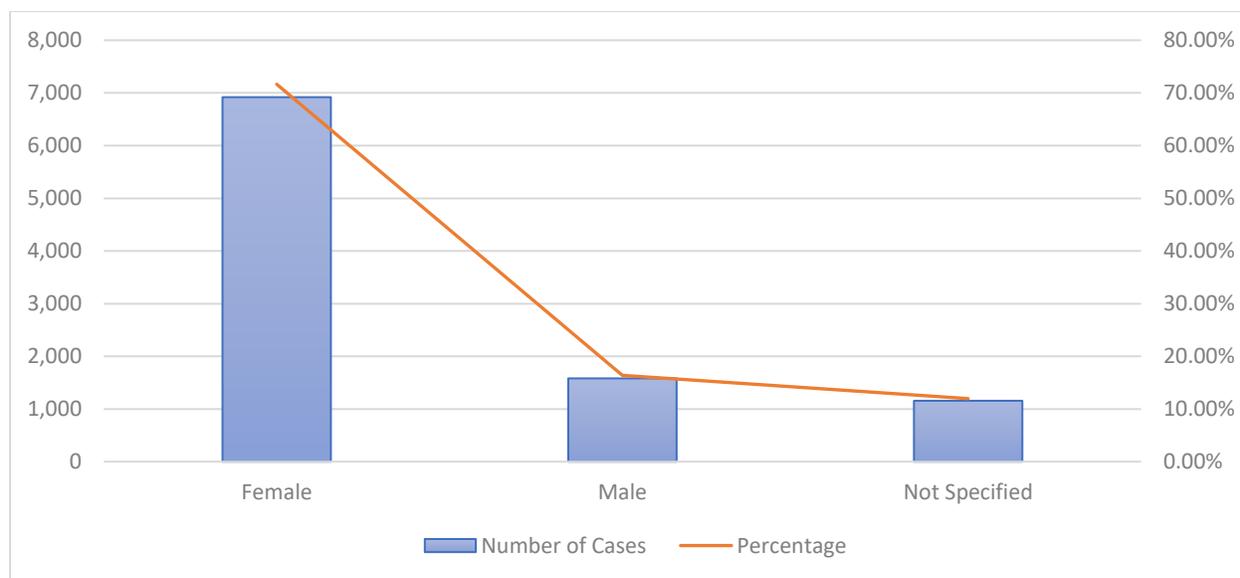
Of the total 9,583 cases, 7,458 (77.83%) were reported in females, 1,339 cases (13.98%) were reported in

Table 4 and Figure 3 below.

Table 4 Distribution of cases via Gender

Category	Number of Cases	Percentage
Female	6,920	71.66%
Male	1,581	16.37%
Not Specified	1,156	11.97%
Total	9,657	100.00%

Figure 3 Pattern of distribution pattern of cases by Gender/Sex with percentages



From the Figure 3 it is clearly evident that majority of the cases are reported in female population which accounts for 71.66% of the total cases reported.

threatening (3.1%) and fatality (2.8%) reported is less than 5% of the total seriousness criteria.

5.3 DISTRIBUTION OF OVERALL CASES BY OUTCOME

The distribution of all fatal cases (patient died) and life-threatening reported are mentioned in the Table 5 below. It is important to note that single case analysis for these cases was not possible because of the limitation of the database; therefore, it does not imply that the deaths were caused by Sumatriptan.

Of the total cases reported from 1997 till 2025 the pattern of event outcome reported is presented in Figure 4 . From the figure it is clearly evident that majority of the adverse events reported are non-serious events. From Table 5, It is clearly evident that 28.7% of the event outcome reported falls under the category of other outcomes. The event outcome of life

The total number of fatal cases reported with Sumatriptan is 303 (2.8%). The calculations are based on the number of fatal events reported divided by the total events reported with the drug. As the information available takes into account the

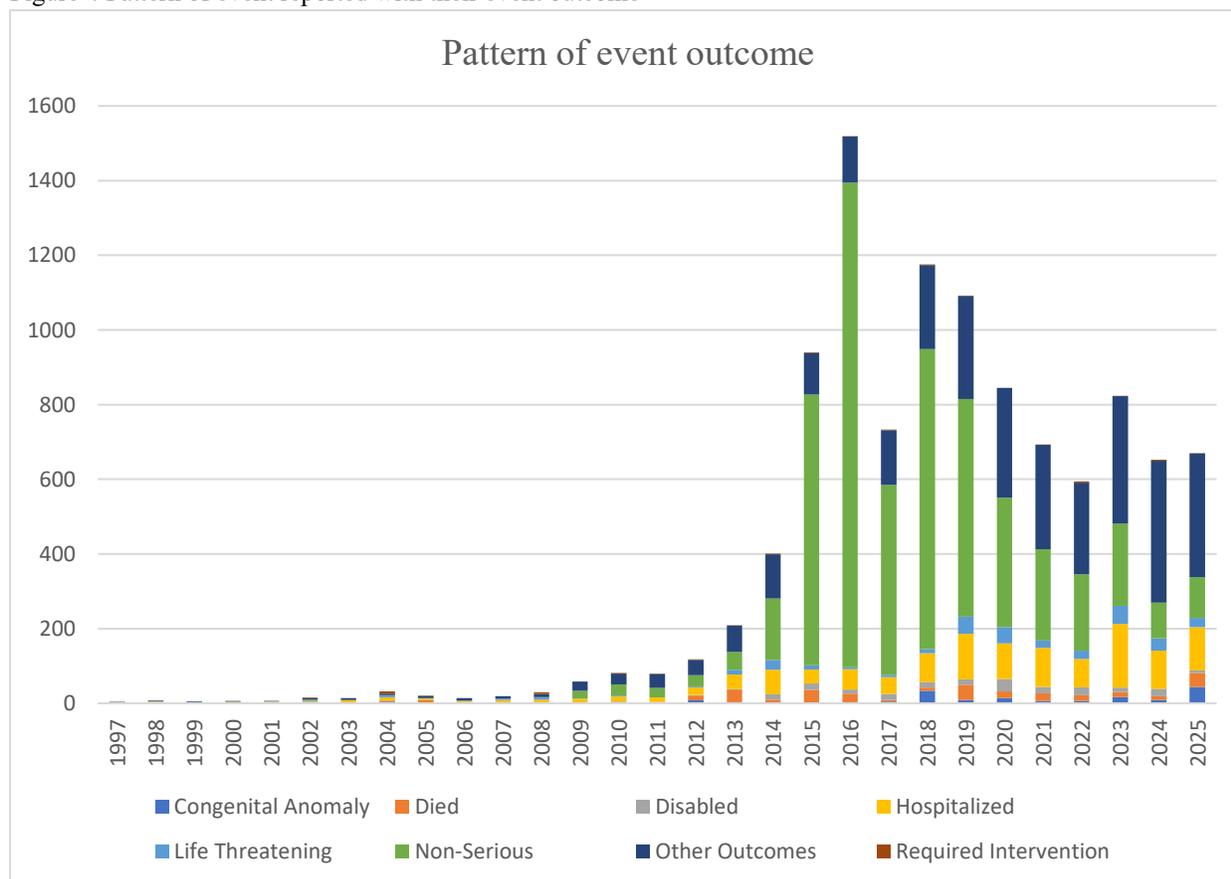
suspected undesirable effect(s) (adverse reactions) reported in an individual case, and as an individual case may refer to more than one suspected undesirable

effect, this does not represent the individual case outcome reported to FAERS, but rather the number of related undesirable effects.

Table 5 Pattern of event seriousness reported till date

Serious Criteria	Event outcome	Percentage
Congenital Anomaly	173	1.6%
Died	303	2.8%
Disabled	209	1.9%
Hospitalized	1215	11.2%
Life Threatening	338	3.1%
Non-Serious	5467	50.3%
Other Outcomes	3121	28.7%
Required Intervention	35	0.3%
TOTAL	10861	100%

Figure 4 Pattern of event reported with their event outcome



5.4 DISTRIBUTION OF OVERALL CASES – GEOGRAPHY

5.4.1 Distribution via Reporter Type

For Sumatriptan, the adverse event cases were primarily reported by Healthcare Professionals

(n=5,134), followed by Consumers (n = 4,371). A very small proportion of cases were reported under the category Other (n = 1), while Not Specified reports accounted for 151 cases. This indicates that slightly more than half of the cases originated from healthcare

professionals, with consumers contributing to nearly half of the reports. The pattern is presented in

Table 6

Table 6 The details of the distribution by reporter type

Reporter type	Number of Cases	Percentage
Healthcare Professional	5,134	53.16%
Consumer	4,371	45.26%
Other	1	0.01%
Not Specified	151	1.56%
Total	9,657	100.00%

VI. THE PATTERN OF DISTRIBUTION OF CASES PER SOCs

From the details presented in

Table 7 it can be confirmed that more than 20% of the total events are reported from SOC product issues,

followed by SOCs of Injury, Poisoning And Procedural complications, General Disorders and Administration Site Conditions, Nervous System Disorders and Gastrointestinal Disorders.

Table 7 Pattern of event reporting by SOC with Reporter Region

SOCs	Domestic	Foreign	Not Specified	Total Cases
Product Issues	4,219	18	1	4,238
Injury, Poisoning and Procedural Complications	3,280	899	2	4,181
General Disorders and Administration Site Conditions	2,100	1,126	3	3,229
Nervous System Disorders	855	1,338	2	2,195
Gastrointestinal Disorders	471	610	1	1,082
Psychiatric Disorders	331	582	0	913
Respiratory, Thoracic and Mediastinal Disorders	229	543	0	772
Cardiac Disorders	312	371	0	683
Musculoskeletal And Connective Tissue Disorders	209	434	0	643
Skin And Subcutaneous Tissue Disorders	155	429	0	584
Investigations	176	293	0	469
Vascular Disorders	161	288	0	449
Immune System Disorders	137	196	0	333
Pregnancy, Puerperium and Perinatal Conditions	105	169	1	275
Eye Disorders	68	193	1	262
Congenital, Familial and Genetic Disorders	31	149	1	181
Infections And Infestations	71	91	0	162
Renal And Urinary Disorders	55	87	0	142
Metabolism And Nutrition Disorders	38	91	0	129
Reproductive System and Breast Disorders	12	95	0	107
Ear And Labyrinth Disorders	35	70	0	105
Surgical And Medical Procedures	65	35	1	101
Blood And Lymphatic System Disorders	18	43	1	62

Social Circumstances	42	16	0	58
Endocrine Disorders	7	29	0	36
Neoplasms Benign, Malignant and Unspecified (Incl Cysts And Polyps)	15	17	0	32
Hepatobiliary Disorders	6	21	0	27

In the below section we will be analyzing the pattern of adverse event reporting by SOC and PTs reported in these SOC. Furthermore, the pattern of adverse event reporting will be analyzed against the current safety profile of Sumatriptan and its potential impact on patient safety.

6.1 Product Issues

In this SOC, the majority of the cases reported did not specify individual adverse events under the category of product issues. The data indicates a significant number of cases across various age groups and genders. The total fatal events accounted for less than 5% of the total events under this SOC.

Table 8 Pattern of adverse event reporting by PTs (Trend) for Product Issues

Preferred Term	Counts
Product Physical Issue	2,125
Product Complaint	635
Product Quality Issue	567
Device Issue	369
Device Deployment Issue	280
Needle Issue	189
Product Substitution Issue	143

Interpretation of results:

Most cases in this SOC were reported without specification of individual adverse events. The total fatal events account for 1.4% of the cases. Most cases were reported by healthcare professionals. The outcomes show a large proportion of cases with unknown status, followed by recovered or resolving cases. The age and sex distribution indicates that most cases were reported in adults aged 18-64 years, with a higher number of females compared to males.

6.2 Injury, Poisoning and Procedural Complications

In this SOC, the majority of the cases reported did not specify individual adverse events under the category of Injury, Poisoning and Procedural Complications. The data indicates a significant number of cases across various age groups and genders. The total fatal events accounted for less than 5% of the total events under this SOC.

Table 9 Pattern of adverse event reporting by PTs (Trend) for Injury, Poisoning and Procedural Complications

Preferred Term	Number of Individual Cases
Product Dose Omission Issue	2,278
Off Label Use	232
Foetal Exposure During Pregnancy	205
Maternal Exposure During Pregnancy	145
Toxicity To Various Agents	117
Exposure During Pregnancy	114

Product Use In Unapproved Indication	113
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6.3 General Disorders and Administration Site Conditions

In this SOC, the majority of the cases reported did not specify individual adverse events under the category of General Disorders and Administration Site

Conditions. The data indicates a significant number of cases across various age groups and genders. The total fatal events accounted for less than 5% of the total events under this SOC.

Table 10 Pattern of adverse event reporting by PTs (Trend) for General Disorders and Administration Site Conditions

Preferred Term	Number of Individual Cases
Drug Ineffective	1,200
Chest Discomfort	219
Chest Pain	207
Drug Interaction	203
Pain	201
Injection Site Pain	193
Drug Intolerance	159

6.4 Nervous System Disorders

In this SOC, the majority of the cases reported did not specify individual adverse events under the category of Nervous System Disorders. The data indicates a

significant number of cases across various age groups and genders. The total fatal events accounted for less than 5% of the total events under this SOC.

Table 11 Pattern of adverse event reporting by PTs (Trend) for Nervous System Disorders

Preferred Term	Number of Individual Cases
Headache	467
Migraine	436
Dizziness	333
Paraesthesia	221
Serotonin Syndrome	174
Somnolence	128
Loss Of Consciousness	100

6.5 Gastrointestinal Disorders

In this SOC, the majority of the cases reported did not specify individual adverse events under the category of Gastrointestinal Disorders. The data indicates a

significant number of cases across various age groups and genders. The total fatal events accounted for less than 5% of the total events under this SOC.

Table 12 Pattern of adverse event reporting by PTs (Trend) for Gastrointestinal Disorders

Preferred Term	Number of Individual Cases
Nausea	397
Vomiting	255
Swollen Tongue	119

VII. CONCLUSION

Based on the comprehensive analysis of 9,657 adverse event cases associated with Sumatriptan from the FDA

Adverse Event Reporting System (FAERS) database through September 2025, several important patterns emerge that inform clinical practice and pharmacovigilance efforts.

The demographic distribution reveals a significant gender disparity, with 71.66% of cases reported in females, consistent with the higher prevalence of migraine in women. Age distribution analysis shows that adults aged 18-64 years account for the majority of reports (42.92%), reflecting the primary user population for this medication.

The severity profile is reassuring, with non-serious events comprising 50.3% of outcomes. However, the presence of fatal (2.8%) and life-threatening events (3.1%), while relatively uncommon, underscores the importance of appropriate patient selection and monitoring, particularly in those with cardiovascular risk factors.

The most frequently reported System Organ Classes were Product Issues (43.9%), Injury, Poisoning and Procedural Complications (43.3%), and General Disorders (33.4%). Within these categories, common Preferred Terms included drug ineffectiveness, headache, nausea, serotonin syndrome, and chest discomfort, which align with the known safety profile of Sumatriptan.

The substantial proportion of reports submitted by healthcare professionals (53.16%) lends clinical credibility to the findings, while the significant consumer contribution (45.26%) highlights the importance of patient-reported outcomes in pharmacovigilance.

This real-world evidence largely confirms the established safety profile of Sumatriptan while providing valuable insights into the patterns of adverse events in clinical practice. The findings support current prescribing guidelines, particularly regarding careful patient selection and monitoring for cardiovascular events and serotonin syndrome. Continued pharmacovigilance remains essential for optimizing the benefit-risk profile of Sumatriptan in migraine management.

REFERENCES

[1] Derry CJ, Derry S, Moore RA. Sumatriptan (oral route of administration) for acute migraine attacks

in adults. *Cochrane Database Syst Rev.* 2022;6(6):CD008615.

- [2] Dodick D, Lipton RB, Martin V, Papademetriou V, Rosamond W, MaassenVanDenBrink A, et al. Consensus statement: cardiovascular safety profile of triptans (5-HT_{1B/1D} agonists) in the acute treatment of migraine. *Headache.* 2021;44(5):414-25.
- [3] Imitrex (sumatriptan succinate) [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2023.
- [4] Sakai F, Igarashi H. Prevalence of migraine in Japan: a nationwide survey. *Cephalalgia.* 2020;17(1):15-22.
- [5] Goadsby PJ, Wietecha LA, Dennehy EB, Kuca B, Case MG, Aurora SK, et al. Phase 3 randomized, placebo-controlled, double-blind study of lasmiditan for acute treatment of migraine. *Brain.* 2019;142(7):1894-904.
- [6] Bate A, Evans SJ. Quantitative signal detection using spontaneous ADR reporting. *Pharmacoepidemiol Drug Saf.* 2019;18(6):427-36.
- [7] Rothman KJ, Lanes S, Sacks ST. The reporting odds ratio and its advantages over the proportional reporting ratio. *Pharmacoepidemiol Drug Saf.* 2018;13(8):519-23.
- [8] Roberto G, Piccinni C, D'Alessandro R, Poluzzi E. Triptans and serious adverse vascular events: data mining of the FDA Adverse Event Reporting System database. *Cephalalgia.* 2018;34(1):5-13.
- [9] Cavero-Redondo I, Álvarez-Bueno C, Pozuelo-Carrascosa DP, Díez-Fernández A, Notario-Pacheco B. Risk of extracranial hemorrhage with triptans: a systematic review and meta-analysis. *Headache.* 2017;57(1):109-20.
- [10] Loder E. Triptan therapy in migraine. *N Engl J Med.* 2017;363(1):63-70.
- [11] Thorlund K, Toor K, Wu P, Chan K, Druyts E, Ramos E, et al. Comparative tolerability of treatments for acute migraine: a network meta-analysis. *Cephalalgia.* 2017;37(10):965-78.
- [12] Dodick DW. Triptan nonresponder studies: implications for clinical practice. *Headache.* 2016;45(2):156-62.
- [13] Sakai F, Igarashi H. Prevalence of migraine in Japan: a nationwide survey. *Cephalalgia.* 2016;17(1):15-22.

- [14] Bigal ME, Serrano D, Buse D, Scher A, Stewart WF, Lipton RB. Acute migraine medications and evolution from episodic to chronic migraine: a longitudinal population-based study. *Headache*. 2015;48(8):1157-68.
- [15] Mathew NT, Loder EW. Evaluating the triptans. *Am J Med*. 2015;118(Suppl 1):28S-35S.
- [16] Evans SJ, Waller PC, Davis S. Use of proportional reporting ratios (PRRs) for signal generation from spontaneous adverse drug reaction reports. *Pharmacoepidemiol Drug Saf*. 2014;10(6):483-6.
- [17] Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2013;68(5):343-9.
- [18] Hazell L, Shakir SA. Under-reporting of adverse drug reactions: a systematic review. *Drug Saf*. 2012;29(5):385-96.
- [19] Bate A, Lindquist M, Edwards IR, Olsson S, Orre R, Lansner A, et al. A Bayesian neural network method for adverse drug reaction signal generation. *Eur J Clin Pharmacol*. 2012;54(4):315-21.
- [20] Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*. 2011;41(7):646-57.