

Prevalence and Characteristics of Patients with Migraine Unsuitable for Triptan Treatment: A Systematic Literature Review

Objective



This systematic review was conducted to identify and evaluate published evidence on the incidence, prevalence, and characteristics of patients with migraine unsuitable for acute treatment with triptans for any reason.

Conclusions



There is a marked uncertainty as to the total population of patients unsuitable for triptans, representing an important evidence gap.

Although prevalence estimates of triptan unsuitability were not found, the identified literature does highlight a large group of patients with migraine who cannot or do not persist with triptans, despite ongoing migraines.

In addition to those who discontinue triptans, many patients are prescribed triptans despite having clear contraindications, which may be further exacerbated by the over-the-counter availability of triptans in some countries.

As with all research areas explored in this SLR, further research is needed to determine more precisely the prevalence of this triptan unsuitable population.

Lipton RB¹, Gendolla A³, Abraham L⁴, Jenkins A⁵, Telford J⁴, Hygge Blakeman K⁴, Saccone P⁴, Engh A⁴, Pustulka I⁶, Fotheringham I⁷

Background

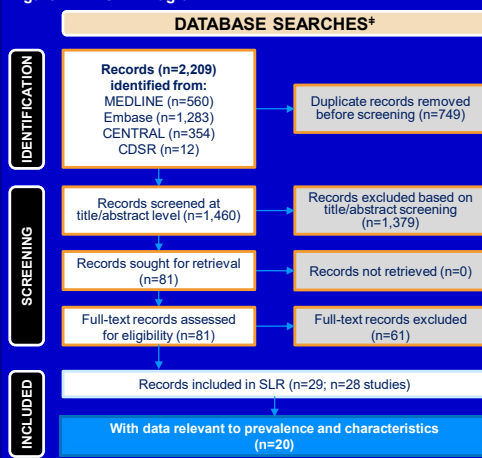
- Migraine is a neurological condition with symptoms such as moderate-to-severe headache pain accompanied by nausea, vomiting, phonophobia, and photophobia. Globally, migraine is the third most common disease and second leading cause of years lived with disability.¹
- Triptans are widely used in the acute treatment of migraine,² but for some patients with migraine they are associated with clinical challenges such as insufficient efficacy, tolerability concerns, and contraindications (primarily cardiovascular disease).^{3,4}
- Definitions are evolving to describe the triptan-unsuitable patient population more precisely, and there is debate about the prevalence and characteristics of patients for whom triptan therapy is not appropriate.

Results

SEARCH RESULTS

- A total of 1460 unique records were screened by two independent reviewers, resulting in a total of 20 studies reported on the prevalence of migraine patients potentially unsuitable for triptans.^{8,27}

Figure 1. PRISMA Diagram



INSUFFICIENT RESPONSE TO TRIPTANS (4 STUDIES)

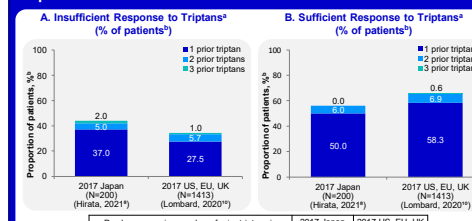
- Based on four studies⁸⁻¹¹ reporting data from patient surveys on triptan response, between 10% and 44% of patients who try triptans have insufficient response, although definitions of insufficient response varied.
- Among all patients who tried triptans, 34%–44% reported insufficient response; 6.7%–7.0% had insufficient response and had tried 2–3 prior triptans (2 studies; Fig. 2A).
- Most patients who achieved a sufficient response did so during treatment with their first triptan; very few became sufficient responders during treatment with a second or third triptan (2 studies; Fig. 2B).
- Among patients with 2–3 prior triptans, 67%–54% reported insufficient response (2 studies; data not shown).

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Materials and Methods

- Searches of Medline and Embase were performed, identifying evidence on patients with migraine who were potentially unsuitable for acute treatment with triptans for any reason.
- Searches covered January 2012 to August 2022.
- Study design, patient characteristics, and outcomes data were extracted and compiled.
- This analysis focused on publications describing the incidence, prevalence, and characteristics of patients unsuitable for triptans.

Figure 2. Patients With Insufficient and Sufficient Response to Triptans

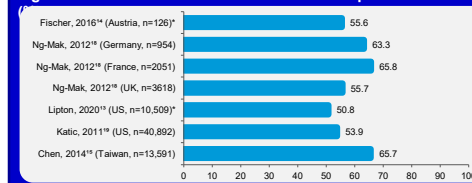


- Triptan insufficient responders were those patients who reported achieving pain freedom within 2 hours of taking their acute medication in 45% of their most recent five migraine attacks.
- Population all had triptan as their sole acute prescribed medication. Results from Adelphi Migraine DSP.

TRIPATAN DISCONTINUATION OR FAILURE (10 STUDIES)

- Ten studies¹²⁻²² reported on patients who were intolerant to triptans, discontinued triptans, and/or switched to another class of acute medications. Seven of these studies analyzed prescription refill data from Europe, the UK, the US, and Asia, showing that 51% to 86% of patients with migraine who started a new triptan discontinued it by the time of first refill (Fig. 3; 5 studies); even more discontinued by 2 years of follow-up (43%–100% across 5 studies; data not shown).
- Fewer than 21% of patients from Europe and Asia persisted on the index triptan at the end of a 2-year follow-up (6 studies; data not shown).

Figure 3. Patients Who Did Not Refill Index Triptan at First Refill



- * Study population (n) = patients with a newly prescribed triptan.
- ** Fischer 2016* rate was reported at first follow-up with median time to first follow-up 24 weeks. Ng-Mak 2012** rate was reported after 1-year follow-up.

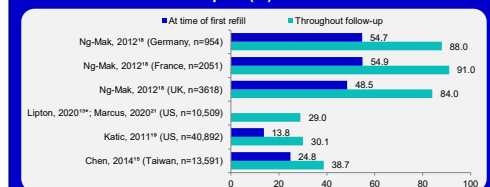
- After discontinuing their index triptan, fewer than 20% of patients tried a subsequent triptan (6 studies; data not shown), and most patients either switched to a different class of acute medication (up to 53% across 6 studies; data not shown) or received no subsequent prescriptions for acute migraine (29%–91% across 5 studies; Fig. 4).

Definition of Triptan Suitability

There are no universally established criteria to determine whether a patient should be considered unsuitable for triptan therapy. Clinical guidelines vary among countries regarding how many triptans should be tried before a patient should no longer be treated with triptans. However, based on guidelines and literature available at the time of the SLR (August 2022),^{5,7} we operationally defined patients as unsuitable for triptans using the following categories, for the purpose of identifying and categorizing clinical evidence in the SLR:

- Triptan unsuitable based on prior response:** patients who have taken at least one triptan but have had an inadequate/insufficient/no response over multiple attacks, or for whom triptans have stopped working.
- Triptan unsuitable due to intolerance or discontinuation:** patients who have taken triptans and have experienced adverse events that stop them from subsequently using triptans or who have discontinued using triptans due to unrelated reasons.
- Triptan unsuitable due to contraindications:** patients who have comorbidities that mean they are not suitable for triptans (e.g., cardiovascular risk factors).

Figure 4. Patients Who Discontinued All Acute Migraine Treatments After Index Triptan (%)



- * Study population (n) = patients with a newly prescribed triptan.
- ** Lipton 2020*** did not report the number of patients that discontinued all migraine treatments.

CONTRAINDICATIONS TO TRIPTANS (12 STUDIES)

- Twelve studies^{4,10,12,14,15,19,21,23-27} reported on patients with identified triptan contraindications (4 studies) or potential/preempted triptan contraindications (8 studies).
- Despite disparate methods and definitions across the 12 studies, data from large real-world studies consistently suggest that 10.0%–14.5% of patients with migraine have clear contraindications, primarily CV disease (Table 1 – blue shading).
- Additionally, results from 2 of the 5 studies suggest that many more patients may have CV risk factors/comorbidities that may make use of triptans inadvisable (Table 1 – gray shading).
- Despite the risks, patients with existing contraindications to triptans are often treated with triptans; up to 20% of patients receiving triptans had contraindications (data not shown).

Table 1. Patients With Migraine^a and Triptan Contraindications (%)

Study	Study/ Database	Patients with migraine, n	Contraindication definition	Patients with contraindication, n	%
Lipton, 2013 ^b	AMPP 2009 (patient surveys)	5,991	CV events (MI, TIA, stroke, angina, coronary angioplasty, coronary stenting, claudication, or coronary artery bypass surgery)	592	10
Buse, 2017 ^c		6,723	CV event, condition, or procedure	781	11.6
Lipton, 2017 ^d		6,723	≥1 CV risk factors	4729	70.3
Doddick, 2020 ^e	Optum CDMA and IBM Watson Health Market Scan (Claims database)	233,386	≥1 contraindication listed in the triptan label or considered as "other significant CV disease" in triptan label	29,148	12.5
Gendolla, 2022 ^f	German SHI	2,923,979 ^g	Adapted from the summary of product characteristics of all triptans available in Germany	425,089	14.5

- * Study population = all patients with migraine (regardless of current/prior treatment). Omitted data from Martinez-Piia 2021^d, due to smaller sample size (n=941). ^b In Gendolla 2022^f, sample size (n) and data is for total extrapolated German statutory health insurance population for 2019.
- Abbreviations: CV, cardiovascular; MI, myocardial infarction; SHI, Statutory Health Insurance; SPC, Summary of Product Characteristics; TIA, transient ischemic attack.

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