# Triptans Step Therapy and Quantity Limit Program Summary

This step therapy and quantity limit criteria applies to Commercial, GenPlus, and Health Insurance Marketplace.
Quantity limit only applies to NetResults A series and NetResults F series.

**OBJECTIVE**
The intent of the Triptans Step Therapy (ST) program is to encourage the use of cost-effective generic triptans before brand triptan products and to accommodate for use of brand triptan products when the more cost-effective generics cannot be used due to documented intolerance, FDA labeled contraindication, or hypersensitivity or previous trial and failure; or if the brand agent is a recommended first-choice agent for the diagnosis. The program allows continuation of therapy with a brand triptan product when there is documentation that the patient is receiving the requested agent. Requests for brand triptan products will be reviewed when patient-specific documentation has been provided.

The intent of the Triptans Quantity Limit (QL) program is to provide automatic approval for patients with three or fewer migraine or cluster headaches per month (two headache days per episode) and to require individual evaluation through the prior authorization process for patients who have more headaches per month and exceed this limit. Additionally, the intent of the quantity limit and PA criteria together is to ensure that patients and prescribers address the current guidelines for the prevention and treatment of migraine and/or cluster headache. Requests for larger quantities will be evaluated through the Clinical Review process when the prescriber provides evidence that dosing with higher quantities is appropriate for the patient. The quantity limit edit applies to both generic and brand triptan products.

**TARGET AGENTS (brands only)**
**Amerge®** (naratriptan)[a]
**Axert®** (almotriptan)[a]
**Frova®** (frovatriptan)[a]
**Imitrex® (**sumatriptan)[a]
**Maxalt®, Maxalt® MLT** (rizatriptan)[a]
**Onzetra Xsail™** (sumatriptan)
**Relpax®** (eletriptan)[a]
**Sumatriptan** (brand products)
**Sumavel DosePro®** (sumatriptan)
**Treximet™** (sumatriptan/naproxen)
**Zecuity** (sumatriptan iontophoretic transdermal system)
**Zembrace SymTouch™** (sumatriptan injection)
**Zomig®, Zomig® ZMT** (zolmitriptan)[a]
a – available as a generic; used as prerequisite not target in step therapy program

**QUANTITY LIMIT TARGET AGENTS - RECOMMENDED LIMITS**

| Brand (generic) | GPI | Quantity Limit per Month |
|---|---|---|
| **Amerge® (naratriptan) Tablets** | | |
| 1 mg[a] | 67406050100310 | 18 tablets (2 packages of 9) |

| Brand (generic) | GPI | Quantity Limit per Month |
|---|---|---|
| 2.5 mg[a] | 67406050100320 | 18 tablets (2 packages of 9) |
| **Axert® (almotriptan) Tablets** | | |
| 6.25 mg [a] | 67406010100320 | 12 tablets (2 packages of 6) |
| 12.5 mg [a] | 67406010100330 | 12 tablets (1 package of 12) |
| **Frova® (frovatriptan) Tablets** | | |
| 2.5 mg[a] | 67406030100320 | 18 tablets (2 packages of 9) |
| **Imitrex® (sumatriptan) Injection** | | |
| 4 mg STATdose® system[a] | 6740607010D510 | 12 doses (6 packages) |
| 4 mg STATdose® refill[a] | 6740607010E210 | 12 doses (6 packages) |
| 6 mg STATdose® system[a] | 6740607010D520 | 12 doses (6 packages) |
| 6 mg STATdose® refill[a] | 6740607010E220 | 12 doses (6 packages) |
| 6mg/0.5mL single dose vial (5 x 0.5 mL/package)[a] | 67406070102010 | 5 mL (2 packages) |
| **Sumatriptan injection** | | |
| 4 mg/0.5 mL vial[a] | 67406070102005 | 12 doses (12 vials) |
| 6 mg/0.5 mL syringe[b] | 6740607010E520 | 12 doses (12 syringes) |
| **Imitrex®, Sumatriptan (sumatriptan) Nasal Spray** | | |
| 5 mg[a] | 67406070002010 | 12 units (2 packages of 6) |
| 20 mg[a] | 67406070002040 | 12 units (2 packages of 6) |
| **Imitrex® (sumatriptan) Tablets** | | |
| 25 mg[a] | 67406070100305 | 18 tablets (2 packages of 9) |
| 50 mg[a] | 67406070100310 | 18 tablets (2 packages of 9) |
| 100 mg[a] | 67406070100320 | 18 tablets (2 packages of 9) |
| **Maxalt® (rizatriptan) MLT Tablets** | | |
| 5 mg[a] | 67406060107220 | 18 tablets (1 package of 18) |
| 10 mg[a] | 67406060107230 | 18 tablets (1 package of 18) |
| **Maxalt® (rizatriptan) Tablets** | | |
| 5 mg[a] | 67406060100310 | 18 tablets (1 package of 18) |
| 10 mg[a] | 67406060100320 | 18 tablets (1 package of 18) |
| **Onzetra Xsail™ (sumatriptan) nasal powder** | | |
| 11 mg nosepiece | 6740607010G420 | 32 nosepieces (2 kits of 16) |
| **Relpax® (eletriptan) Tablets** | | |
| 20 mg[a] | 67406025100320 | 12 tablets (2 packages of 6) |
| 40 mg[a] | 67406025100340 | 12 tablets (2 packages of 6) |
| **Sumatriptan Injection** | | |
| 6 mg/0.5 mL single dose injection device | 6740607010D520 | 12 doses (6 packages of 2) |
| **Sumavel™ DosePro™ (sumatriptan) Injection** | | |
| 4 mg/0.5 mL single dose injection device | 6740607010D810 | 12 doses (2 packages of 6) |
| 6 mg/0.5 mL single dose injection device | 6740607010D820 | 12 doses (2 packages of 6) |
| **Treximet™ (sumatriptan/naproxen) Tablets** | | |
| 10/60 mg | 67992002600305 | 9 tablets (1 package of 9) |
| 85/500 mg | 67992002600320 | 18 tablets (2 packages of 9) |
| **Zecuity® (sumatriptan) Iontophoretic Transdermal System** | | |
| 6.5 mg/4 hours | 67406070105920 | 12 transdermal systems |
| **Zembrace SymTouch™ (sumatriptan injection)** | | |
| 3 mg/0.5 ml pens | 6740607010D505 | 24 pens (12 ml) |
| **Zomig® (zolmitriptan) Nasal Spray** | | |
| 2.5 mg/100 microliters | 67406080002010 | 12 units (2 packages of 6) |
| 5 mg/100 microliters | 67406080002020 | 12 units (2 packages of 6) |
| **Zomig® (zolmitriptan) Tablets** | | |
| 2.5 mg [a] | 67406080000320 | 12 tablets (2 packages of 6) |

| Brand (generic) | GPI | Quantity Limit per Month |
|---|---|---|
| 5 mg [a] | 67406080000330 | 12 tablets (4 packages of 3) |
| **Zomig® (zolmitriptan) ZMT Tablets** | | |
| 2.5 mg [a] | 67406080007220 | 12 tablets (2 packages of 6) |
| 5 mg [a] | 67406080007230 | 12 tablets (4 packages of 3) |

a - available as a generic, included in quantity limit program
b – available as generic only, included in quantity limit program

**PRIOR AUTHORIZATION CRITERIA FOR APPROVAL**
Quantities above the program set limit for **Generic Triptans** will be approved when ONE of the following is met:

1. ALL of the following:
    a. The patient has a diagnosis of migraine headache
    **AND**
    b. ONE of the following:
        i. The patient is currently using migraine prophylactic medication
        **OR**
        ii. The patient has a documented intolerance, FDA labeled contraindication, hypersensitivity, or treatment failure to prophylactic migraine medication
    **AND**
    c. The patient has been evaluated for and does not have medication overuse headache
    **AND**
    d. ONE of the following:
        i. The patient is not currently taking another triptan product or an ergotamine product
        **OR**
        ii. The patient's current triptan product or ergotamine product will be discontinued prior to starting the requested agent

**OR**

2. BOTH of the following:
    a. The patient has a diagnosis of cluster headache
    **AND**
    b. The requested product is an injection or nasal spray

**Length of Approval:** 12 months
[For a diagnosis of migraine, the quantity requested up to the FDA-labeled maximum dose allowed per 24 hours will be approved.]

**Brand Triptan Products** will be approved when BOTH of the following are met:

1. ONE of the following:
    a. The patient's medication history includes use of a generic triptan in the past 90 days
    **OR**
    b. There is documentation that the patient is currently using the requested brand triptan product
    **OR**
    c. The prescriber states the patient is using the requested brand triptan product AND is at risk if therapy is changed
    **OR**
    d. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to generic triptan agent(s)

**AND**

2. ONE of the following:

a. The quantity is within the program quantity limit
   **OR**
b. ALL of the following:
   i. The patient has a diagnosis of migraine headache
      **AND**
   ii. ONE of the following:
      a) The patient is currently using migraine prophylactic medication
         **OR**
      b) The patient has a documented intolerance, FDA labeled contraindication, hypersensitivity, or treatment failure to prophylactic migraine medication
      **AND**
   iii. The patient has been evaluated for and does not have medication overuse headache
      **AND**
   iv. ONE of the following:
      a) The patient is not currently taking another triptan product or an ergotamine product
         **OR**
      b) The patient's current triptan product or ergotamine product will be discontinued prior to starting the requested agent

   **OR**
c. BOTH of the following:
   i. The patient has a diagnosis of cluster headache
      **AND**
   ii. The requested product is an injection or nasal spray

**Length of Approval:** 12 months
[For a diagnosis of migraine, the quantity requested up to the FDA labeled maximum dose allowed per 24 hours will be approved.]

**FDA APPROVED INDICATIONS AND DOSAGE [1-13,14,23,24]**

| Agents | Acute treatment, migraine attacks with/without aura (adults) | Acute treatment, migraine headaches (adolescents[a]) | Acute treatment, cluster headache episodes (adults) | Dosage and Administration Schedule[b] |
|---|---|---|---|---|
| **Amerge** (naratriptan) 1 mg, 2.5 mg tablets | ✓ | | | Initial dose: 1 mg or 2.5 mg<br>Min time before repeat dose: 4 hours<br>Max dose/24 hours: 5 mg |
| **Axert** (almotriptan) 6.25 mg, 12.5 mg tablets | ✓ | ✓ | | Initial dose: 6.25 mg or 12.5 mg<br>Min time before repeat dose: 2 hours<br>Max dose/24 hours: 25 mg |
| **Frova** (frovatriptan) 2.5 mg tablet | ✓ | | | Initial dose: 2.5 mg<br>Min time before repeat dose: 2 hours<br>Max dose/24 hours: 7.5 mg |
| **Imitrex, Sumatriptan** 25 mg, 50 mg, 100 mg tablets | ✓ | | | Initial dose: 25 mg to 100 mg<br>Min time before repeat dose: 2 hours<br>Max dose/24 hours: 200 mg |
| **Imitrex** (sumatriptan) nasal spray 5 mg, or 20 mg/spray | ✓ | | | Initial dose: 5 mg or 10 mg (1-2 sprays) or 20 mg (1 spray)<br>Min time before repeat dose: 2 hours<br>Max dose/24 hours: 40 mg |
| **Imitrex, Sumavel, Sumatriptan** (sumatriptan) injectable 4 mg or 6 mg subcutaneous | ✓ | | ✓ | Initial dose: 4 mg or 6 mg SC<br>Min time before repeat dose: 1 hour<br>Max dose/24 hours: 12 mg |
| **Maxalt, Maxalt MLT** (rizatriptan) 5 mg or 10 mg tablets | ✓ | | | Initial dose: 5 mg or 10 mg<br>Min time before repeat dose: 2 hours<br>Max dose/24 hours: 30 mg |
| **Onzetra Xsail™** (sumatriptan nasal powder) 11 mg nosepiece | ✓ | | | Initial dose: 22 mg<br>Min time before repeat dose: 2hours<br>Max dose/24 hours: 44 mg |
| **Relpax** (eletriptan) 20 mg, 40 mg tablets | ✓ | | | Initial dose: 20 mg or 40 mg<br>Min time before repeat dose: 2 hours<br>Max dose/24 hours: 80 mg |

| Agents | Acute treatment, migraine attacks with/without aura (adults) | Acute treatment, migraine headaches (adolescents[a]) | Acute treatment, cluster headache episodes (adults) | Dosage and Administration Schedule[b] |
|---|---|---|---|---|
| **Treximet** (sumatriptan/naproxen) 85/500 mg tablets<br>10/60 mg tablets | ✓ | | | Adults:<br>Initial dose: One 85/500 mg tablet<br>Min time before repeat dose: 2 hours<br>Max Dose/24 hours: Two 85/500 mg tablets<br><br>Pediatric:<br>Recommended dose: 10/60 mg<br>Maximum dose: 85/500 mg |
| **Zecuity** (sumatriptan) 6.5 mg/4 hours iontophoretic transdermal system | ✓ | | | Initial dose: 1 transdermal system applied to skin of upper arm or thigh<br>Min time before repeat: 2 hours<br>Max dose/24 hours: 2 transdermal systems |
| **Zembrace SymTouch™** (sumatriptan injection) 3 mg/0.5 mL | ✓ | | | The recommended dose of Zembrace SymTouch is 3 mg injected subcutaneously.<br><br>The maximum cumulative dose that may be given in 24 hours is 12 mg; one 3 mg injection may be given up to four times a day with each injection at least 1 hour apart. |
| **Zomig, Zomig ZMT** (zolmitriptan) 2.5 mg or 5 mg tablets | ✓ | | | Initial dose: 2.5 mg or 5 mg<br>Min time before repeat dose: 2 hours<br>Max dose/24 hours: 10 mg |
| **Zomig** (zolmitriptan nasal spray) 2.5 mg/spray; 5mg/spray | ✓ | ✓ | | Initial dose: 2.5 mg;<br>Maximum single dose: 5 mg<br>Min time before repeat dose: 2 hours<br>Max dose/24 hours: 10 mg |

a - (12-17 years of age [whose attacks usually last ≥4 hours])
b - Min=minimum; Max=maximum

All products in the above chart are indicated for the acute treatment of migraine attacks with or without aura in adults.[1-13,14,23,24]

- Use only after a clear diagnosis of migraine has been established
- These products are not intended for prophylactic therapy of migraine attacks, or for management of hemiplegic or basilar migraine.

While the incidence is rare, the triptans have been associated with angina, myocardial infarction (MI), cardiac arrhythmias, hypertension, or stroke, particularly when they were used in patients with vascular risk factors. Triptans should be used with extreme caution in these patients or those with a suspected history of coronary artery disease. Triptans should not be used in patients with uncontrolled hypertension, ischemic heart disease, peripheral vascular disease, or cerebrovascular disease. Triptans should not be used within 24 hours of treatment with another 5-HT1 agonist, or an ergotamine-containing or ergot-type medication like dihydroergotamine or methysergide.[1-13,14,23,24]

**CLINICAL RATIONALE**

The Medical Letter Treatment Guidelines (2017) – Drugs for Migraine state that a triptan is the drug of choice for moderate to severe migraine. The short-acting oral serotonin (5-HT1B/1D) receptor agonists (triptans) sumatriptan (Imitrex, and others), almotriptan (Axert, and generics), eletriptan (Relpax), rizatriptan (Maxalt, and generics), and zolmitriptan (Zomig, and generics are similar in efficacy. Onset of pain relief generally occurs 30-60 minutes after administration. The longer-acting oral triptans naratriptan (Amerge, and generics) and frovatriptan (Frova, and generics) have a slower onset of action and lower initial response rate than other triptans, but they are better tolerated. Patients with migraine who have nausea or vomiting may not be able to take an oral triptan. Intranasal triptan formulations have a more rapid onset of action than oral tablets, but their efficacy is partially dependent on GI absorption of the portion of the dose that is swallowed. Use of sumatriptan nasal powder (Onzetra Xsail) results in a faster rise in sumatriptan plasma concentrations and higher peak concentrations than use of a similar dose of sumatriptan nasal spray, suggesting that a larger portion of the dose is absorbed intranasally with the powder. Subcutaneously administered sumatriptan relieves pain faster (in about 10 minutes) and more effectively than other triptan formulations, but it causes more adverse effects. [19]

The American Academy of Neurology and the American Headache Society guidelines (2012, reaffirmed 2015) on pharmacologic treatment for episodic migraine prevention in adults state that frovatriptan is established as effective and should be offered for short-term menstrually associated migraine (MAMs) prevention (Strong Evidence). Naratriptan and zolmitriptan are probably effective and should be considered for short-term MAMs prevention (Moderate Evidence).[16]

The Institute for Clinical Systems Improvement Guideline Diagnosis and Treatment of Migraine Headache states that triptans are considered to have equal efficacy and are more effective at halting migraine pain at mild levels than if the headache is more severe. Clinicians should consider using subcutaneous sumatriptan or intranasal zolmitriptan as a first line option for the treatment of cluster headaches.[17]

National Institute for Health and Clinical Excellence (NICE) Clinical Guidance: Diagnosis and management of headaches in young people and adults 2012 state that for migraine headache with or without aura (acute treatment), an oral triptan or an oral triptan with an NSAID is recommended taking into account the person's preference, comorbidities, and risk of adverse events. For people whom oral preparations are ineffective or not tolerated, a nasal triptan is recommended. For cluster headache acute treatment, use of 100% oxygen and/or subcutaneous or nasal triptan are recommended. [18]

The American Academy of Neurology 2010 Guideline: Acute and preventive pharmacologic treatment of cluster headache state that sumatriptan subcutaneous injection and zolmitriptan nasal spray are recommended for acute treatment of cluster headaches.[15]

American Headache Society (2015): The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies: The specific medications – triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan [oral, nasal spray, injectable, transcutaneous patch], zolmitriptan [oral and nasal spray]) are effective (Level A). The evidence base for medication efficacy should be considered along with potential medication side effects, potential adverse events, patient-specific contraindications to use of a particular medication, and drug-to-drug interactions when deciding which medication to prescribe for acute therapy of a migraine attack.[22]

American Headache Society (2016): Treatment of Cluster Headaches: Since the publication of the 2010 American Academy of Neurology review, there are no new data from randomized, double-blind, controlled trials that contribute to determining the efficacy or safety for a number of acute treatments, including specifically sumatriptan and zolmitriptan. For acute treatment, sumatriptan subcutaneous, zolmitriptan nasal spray, and high flow oxygen remain the treatments with a Level A recommendation.[25]

Triptan Formulations
Reviews evaluating sumatriptan oral tablet, nasal spray, and subcutaneous injection vs. placebo or other treatments found the NNT for a pain-free response at two hours was 6.1 for the 50 mg tablet, 4.7 for the 100 mg tablet, 2.3 for the 6 mg SC injection, and 4.7 for the nasal spray. [20]

A systematic review and meta-analysis of 74 RCTs of oral triptans vs placebo or other triptans for acute treatment of migraine has shown that all seven triptans are superior to placebo, with significantly greater odds of being pain free at two hours compared with placebo. Though this meta-analysis found differences in efficacy between the various tablet formulations of triptans, in clinical practice differences between patients seem more important than the differences between drugs. The response of individuals with migraine to a specific acute drug is unpredictable. If a patient does not respond well to one triptan, other triptans should be tried in subsequent attacks. [20]

Oral formulations are appropriate when nausea is mild to moderate and vomiting is absent at the time of treatment. Because comparative studies do not clearly establish superiority of one oral triptan over another, a specific agent may be chosen on the basis of formulary availability and previous therapeutic trials. Subcutaneous sumatriptan is the fastest and most efficacious. It is indicated for migraine accompanied by severe nausea or vomiting, for migraines already established by the time of awakening, or in patients who do not respond consistently to oral or nasal preparations.[21]

For additional clinical information see Prime Therapeutics Formulary Chapter 10.4A: Migraine Products: Triptans.

**REFERENCES – Clinical Rationale**


1. Amerge Tablets prescribing information. GlaxoSmithKline. November 2016.
2. Axert Tablets prescribing information. Janssen-Ortho, LLC. May 2017.
3. Frova prescribing information. Endo Pharmaceuticals, Inc. November 2016.
4. Imitrex Injection prescribing information. GlaxoSmithKline. December 2017
5. Imitrex Nasal Spray prescribing information. GlaxoSmithKline. December 2017
6. Imitrex Tablets prescribing information. GlaxoSmithKline. December 2017
7. Maxalt Tablets/Maxalt-MLT Tablets prescribing information. Merck & Co, Inc. June 2015.
8. Relpax Tablets prescribing information. Pfizer, Inc. September 2015.
9. Treximet prescribing information. GlaxoSmithKline. May 2016.
10. Zomig Tablets, Zomig-ZMT Orally Disintegrating Tablets prescribing information. AstraZeneca Pharmaceuticals LP. September 2012.
11. Zomig Nasal Spray prescribing information. Impax Laboratories, Inc. June 2015.

12. Alsuma prescribing information. King Pharmaceuticals. June 2014.
13. Sumavel DosePro Prescribing Information. Zogenix, Inc. June 2016.
14. Zecuity prescribing information. NuPathe Inc. March 2014.
15. Francis GJ, Becker WJ, Prinsheim T. Acute and preventive treatment of cluster headache. *Neurology* 2010;75:463-473.
16. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: American Academy of Neurology/American Headache Society. *Neurology* 2012;78:1337-1345.
17. ICSI. Health care guideline: diagnosis and treatment of headache (updated 2013) Accessed 2/8/2017
18. National Institute for Health and Clinical Excellence (NICE). Headaches: diagnosis and management of headaches in young people and adults. Guideline #150 2012. Accessed November 2012 @ www.nice.org.uk/cg150
19. Drugs for migraine. Medical Letter Treatment Guidelines. 2017; 59(1514):27-32.
20. Pringsheim T, Becker W. Triptans for symptomatic treatment of migraine headache. BMJ 2014;348:g2285 doi: 10.11361bmj.g2285.
21. MacGregor E, Cotton D, Taichman D, Williams S. In the clinic: migraine. Ann Intern Med. Nov. 2013;ITC1-ITC15.
22. The acute treatment of migraine in adults: the American Headache Society evidence assessment of migraine pharmacotherapies. 2015. Available at http://www.headachejournal.org/SpringboardWebApp/userfiles/headache/file/HEAD%20Acute%20Guidelines.pdf.
23. Zembrace SymTouch prescribing information. Promius Pharma LLC. March 2017.
24. Onzetra Xsail prescribing information. Avanir Pharmaceuticals. January 2016.
25. Treatment of cluster headache: the American Headache Society evidence-based guidelines. Headache. 2016 Jul;56(7):1093-106. doi: 10.1111/head.12866.

**ADDITIONAL INFORMATION - Migraine Frequency and Prophylactic Therapy**

Following appropriate management of acute migraine, patients should be evaluated for initiation of preventive therapy. Factors that should prompt consideration of preventive therapy include the occurrence of two or more migraines per month with disability lasting three or more days per month; failure of, contraindication for, or adverse events from acute treatments; use of abortive medication more than twice per week; and uncommon migraine conditions (e.g., hemiplegic migraine, migraine with prolonged aura, migrainous infarction). Risk of medication overuse headache is also a factor that should be considered.[15] Patient preference and cost also should be considered.[1]

For continuous prophylaxis, beta-blockers are commonly used; propranolol and timolol are FDA approved, but metoprolol, nadolol, and atenolol also have been effective. Antiepileptic drugs such as valproate and topiramate have been effective in decreasing migraine frequency in 50% of patients; gabapentin has been used with varying degrees of success. Calcium channel blockers are also used but the evidence for their effectiveness is weak. Tricyclic antidepressants can prevent migraine in some patients but often cause sedation, dry mouth and weight gain. In small double-blind studies, lisinopril and candesartan have reduced migraine frequency.[2] A Cochrane review (2004)[3] of anticonvulsants for migraine prophylaxis states that valproic acid/sodium valproate has proven efficacy for this use. This review suggested that gabapentin needed further evaluation and that topiramate had reasonable evidence to support its use.[3]

In 2012, the American Academy of Neurology (AAN) updated its guidelines for migraine prevention.[13,14] Strongly recommended agents include divalproex sodium/sodium valproate, topiramate, metoprolol, propranolol, and timolol; medications listed as probably effective include amitriptyline, venlafaxine, atenolol, and nadolol; and those possibly effective are lisinopril, candesartan, clonidine, guanfacine, carbamazepine, nebivolol and pindolol. Certain NSAIDs are also listed as probably effective (fenoprofen, ibuprofen, ketoprofen, naproxen) or possibly effective (flurbiprofen, mefenamic acid).[13,14]

Based on published data from a 1989 survey[4] the median frequency of migraine attacks is 1.5 per month, and the median duration of an attack is 24 hours; at least 10% of patients have weekly attacks, and 20% have attacks lasting two to three days.[4] Additional surveys from the mid to late 1990's have confirmed these data.[5-8] Survey results continue to report a median attack duration of 24 hours; 54% to 63% of patients report monthly attacks and 13% to 25% report weekly attacks.[5-8]

Evidence-based guidelines and published practice parameters from the American Academy of Neurology (AAN) for the pharmacologic management of migraine headaches suggest that acute therapy should be limited to no more than two headache days per week to guard against medication-overuse headache.[9] AAN guidelines recommend preventive treatment where the frequency of attacks has increased the use of acute medications to a level that would increase the potential for medication overuse headaches.[10] Medication overuse headache is now included in the International Classification of Headache Disorders.[11,12] According to this classification, medication overuse headache can be diagnosed when headaches occur on 15 or more days per month, the pain is characterized as bilateral, dull, and of light to moderate intensity, drug intake includes ergots, triptans and opioids for ten or more days per month or analgesics are used for 15 or more days per month for at least three months, and the headache disappears after withdrawal.[11,12]

**REFERENCES – Additional Information section**


1. Snow V, Weiss K, Wall EM, et al. Pharmacologic Management of Acute Attacks of Migraine and Prevention of Migraine Headache. *Ann Intern Med.* 2002; 137:840-849.
2. Drugs for migraine. Medical Letter Treatment Guidelines. 2013; 11(136):107-112.
3. Chronicle E, Mulleners W. Anticonvulsant drugs for migraine prophylaxis. Cochrane Database of Systematic Reviews. 2004, Issue 3. Art. No.: CD003226. DOI: 10.1002/14651858. CD003226.pub2.
4. Stewart WF, Lipton RB, Celentano DD, Reed ML. Prevalence of migraine headache in the United States: relation to age, income, race and other sociodemographic factors. *JAMA* 1992;267:64-9.
5. 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*. 2001;41:646-57.
6. Lipton RB, Scher AI, Kolodner K, et al. Migraine in the United States: epidemiology and patterns of health care use. *Neurology*. 2002;58:885-94.
7. Steiner TJ, Scher AI, Stewart WF, et al. The prevalence and disability burden of adult migraine in England and their relationships to age, gender and ethnicity. *Cephalalgia*. 2003;23:519-27.
8. Hu XH, Markson LE, Lipton RB, Stewart WF, Berger ML. Burden of migraine in the United States; disability and economic costs. *Arch Intern Med*. 1999;159:813-8.
9. Matchar DB, Young WB, Rosenberg JH, Pietrzak MP, Silbertein SD, Lipton RB, Ramadan NM. Evidence-based guidelines for migraine headache in the primary care setting: Pharmacological management of acute attacks. American Academy of Neurology. 2000. Available at: http://www.aan.com/professionals/practice/pdfs.g10087.pdf. Accessed July 31, 2008.
10. Ramadan NM, Silberstein SD, Freitag FG, Gilbert TT, Frishberg BM. Evidence-Based Guidelines for Migraine Headache in the Primary Care Setting: Pharmacological Management of Prevention of Migraine. American Academy of Neurology. 2000. Available at: http://www.aan.com/professionals/practice/pdfs/gl0090.pdf. Accessed May 22, 2009.
11. The International Classification of Headache Disorders, 3rd edition. Headache Classificatoin Committee of the International Headache Society (HIS). Accessed 2/16/2015. http://www.ihs-classification.org/_downloads/mixed/International-Headache-Classification-III-ICHD-III-2013-Beta.pdf
12. Limmroth V, Katsarava Z. Medication overuse headache. *Current Opinion in Neurology*. 2004;17(3):301-306

13. Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: American Academy of Neurology/American Headache Society. *Neurology* 2012;78:1337-1345.
14. Holland S, Silberstein SD, Freitag F, et al. Evidence-based guideline update: NSAIDs and other complementary treatments for episodic migraine prevention in adults: American Academy of Neurology/American Headache Society. *Neurology* 2012;78:1346-1353.
15. Preventative treatment of migraine in adults. UptoDate. Last updated Oct 13, 2016. Accessed 2/10/2017.