Response to Pharmac's proposed declining of inactive application for zolmitriptan

This submission is from Migraine Foundation Aotearoa New Zealand, a charity established in 2022 with the mission to raise awareness of the impact of migraine disease and support people living with migraine in Aotearoa New Zealand (NZ).

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Thank you for the opportunity to provide feedback on Pharmac's Proposal to decline inactive funding applications, issued 18 December 2023, which includes a funding application for the migraine-specific treatment zolmitriptan. Zolmitriptan is currently on the 'cost saving or cost neutral' priority list for funding applications.

Migraine Foundation Aotearoa New Zealand was established in 2022 and is the only charity in New Zealand with the mission to raise awareness of the impact of migraine disease and support people living with migraine in Aotearoa New Zealand (NZ).

We strongly oppose the proposal to decline the funding application for zolmitriptan.

Background to the zolmitriptan application

This application was made in September 2007 for zolmitriptan nasal spray and was recommended to be declined by PTAC in 2007, primarily because of cost, as at this time zolmitriptan was more expensive than sumatriptan, the only triptan then available in NZ. From the meeting notes:

> Members considered that it was possible that listing zolmitriptan nasal spray could further grow the market for antimigraine drugs.

Given that the Committee recommended declining the application, we can infer that the Committee disapproved of any measure to 'grow the market for antimigraine drugs'. This displays a complete and callous disregard for the disability and impact of migraine on people's lives, implying that migraine is not worth treating and people with migraine should not be provided evidence-based medication options to treat migraine attacks. This demonstrates an inadequate consideration of 'Need' and 'Benefit', from Pharmac's Factors for Consideration.

Migraine disease is estimated to globally affect one in seven people (Stovner et al., 2022) and 642,000 people in NZ (Global Burden of Disease Collaborative Network, 2020). From the 2016 and 2019 Global Burden of Disease studies, migraine is the second highest cause of "years of life lived with disability" (YLD) worldwide but the top cause of YLD among people aged 15-49 years old.(Steiner et al., 2020) Prevalence of migraine is similar for Māori, Pacific people and NZ European (15.7%, 16.0% and 14.4% respectively).(Migraine Foundation Aotearoa New Zealand, 2022)

PTAC re-considered the application for zolmitriptan nasal spray and tablets in 2008, after additional information from the applicant (AstraZeneca) had been supplied to address some of PTAC's concerns. The Committee recommended that zolmitriptan 2.5mg and 5mg tablets be listed without restrictions if cost-neutral and the nasal spray be listed if cost neutral compared to sumatriptan injection, with the possibility of a Special Authority restricting access e.g. to patients with severe vomiting or non-response to other triptans. At this meeting, the Committee also noted that around 30% of patients do not respond to the first triptan that they try, but they may respond to a different triptan, as each of the seven triptans have slightly different properties. It follows that patients should have more than the current two options, to accommodate differing clinical and patient characteristics. For example, if sumatriptan doesn't work, then the option of zolmitriptan may be preferable for patients with severe nausea or vomiting or for people who find the taste of rizatriptan intolerable.

In 2013, the zolmitriptan application went through the 'Options Compared' process and is currently on the cost-neutral or cost-saving priority list. The patent for zolmitriptan expired in 2012. In December 2023, Pharmac proposed to decline the application. The justification for this decline was because an application for the listing of triptans was declined in March 2022. Note that no migraine consumer group was consulted on the decision to decline this application. Migraine Foundation Aotearoa New Zealand was only established in April 2022.

Concerning the application for the listing of additional triptans, this was reviewed by the Neurological Subcommittee in 2013. This was a comparison of triptans undertaken by Pharmac staff, comparing rate of onset of action, to help the Committee decide whether a third triptan should be funded. At that time, zolmitriptan was available in NZ (as a pharmacy-only medicine) but not funded. The Committee did not recommend listing another triptan but did consider that there may be benefit from funding a nasally-administered triptan (such as zolmitriptan). The reasons for not recommending another funded triptan are not explicit but appear to be:

1. there were relatively few studies comparing the triptans head to head; although they also noted that the most effective triptans (including zolmitriptan) were similar in effectiveness to sumatriptan so it is unclear what additional research was required or why
2. the triptans with the most rapid onset of action, sumatriptan and rizatriptan, were already funded
3. the addition of further triptans may exacerbate the problem of 'triptan overuse'.

MFANZ feedback on the zolmitriptan application

We note that since the 2013 Neurological Committee meeting, further evidence has been published regarding the effectiveness and tolerability of zolmitriptan, for example (Cameron et al., 2015; Chiang et al., 2023; Li et al., 2023; Ruscheweyh, Dresler, et al., 2023; Ruscheweyh, Gossrau, et al., 2023; Vanderpluym et al., 2021). We also note that the overview from Pharmac of all the triptans focused on the pharmacokinetic properties of the triptans, particularly the rate of onset of action. A recent publication that reviewed randomised controlled trials of acute migraine medication found that only subcutaneous sumatriptan and nasal zolmitriptan had real-world evidence for an onset of action within 30 minutes (Tfelt-Hansen & Diener, 2021) (and note randomised controlled trial from (Dodick, 2005) which found responses to zolmitriptan nasal spray as early as 15 minutes after administration and in addition to the very fast onset of action, produced significantly higher sustained headache response and pain-free rates at 24 hours post-dose compared with placebo.) Zolmitriptan also comes as orally disintegrating tablets, which many patients prefer over a conventional tablet (Dowson, 2002).

Other relevant literature includes evidence of the efficacy of zolmitriptan nasal spray for paediatric patients (McKeage, 2016; Lewis, 2007), as this has been FDA-approved for use in patients aged 12 years and older. In this critical age group, zolmitriptan nasal spray has demonstrated both high tolerability and rapid, substantial efficacy in alleviating symptoms during acute migraine episodes. Also, although this is outside the scope of treatment for migraine, zolmitriptan nasal spray is also effective in treating cluster headache (Hedlund et al., 2009), and funding of zolmitriptan would add another funded acute treatment for this patient group.

We note that the application for the listing of triptans does not appear to have been a comprehensive review of triptans that adequately addressed Pharmac's Four Factors for Consideration. It is noted in the Subcommittee meeting notes (7.5) that Pharmac staff "provided a comprehensive overview of the pharmacokinetics (including the rate of action) of the various triptans." In its decision to decline this application, the Subcommittee appears to consider rapidity of onset of action to be the primary criteria for funding a triptan, which disregards the other Factors of Need, Benefit and Suitability. It is not at all clear why other triptans were declined for funding due to a less rapid onset of action than sumatriptan or rizatriptan, longer acting and less rapid onset triptans, such as frovatriptan, have been shown to be preferable for treatment of menstrual migraine, a more prolonged and severe form of migraine affecting women at the time of menstruation (Grøtta Vetvik & Anne MacGregor, 2021). A lack of consideration for providing the most appropriate treatment for menstrual migraine gives the impression that the Committee lacked understanding of the impact of menstrual migraine and lacked consideration for women's health issues.

If Migraine Foundation Aotearoa NZ had had the opportunity to be consulted on this application before it was declined, we would have raised serious concerns about the lack of transparency and poor process taken in the review of this application. We note that the efficacy of zolmitriptan is well established and was accepted by the Committee at this time.

The availability of zolmitriptan at the time of this meeting may have influenced the Committee's decision not to recommend this to be funded, given that it was accessible (although unfunded). However, zolmitriptan is no longer available in NZ, reportedly preempted by supply issues around the time of the COVID-19 pandemic. There is now even more need for an additional triptan to be made available and funded in NZ.

Clinical guidelines recommend that patients should try three different triptans (Olesen et al., 2022) before being considered refractory to triptans (Sacco et al., 2022), that choice of triptan should be individualised (Zhao et al., 2023) and non-oral routes of administration should be used for people with severe nausea or vomiting (Ailani et al., 2021). In NZ, we are unable to classify any migraine patient as refractory to triptans since there are only two triptans to try, choice is limited compared to other countries, and sumatriptan injection is the only non-oral formulation available, which provides limited options for people with severe nausea and vomiting with migraine who are averse to injections.

Triptan overuse can cause medication overuse headache (MOH), a headache that occurs on 15 days or more a month for at least three months. Triptans are implicated in causing MOH if taken for 10 or more days a month for more than three months. Concerning the issue of triptan overuse, the Committee provided no evidence for the statement that additional triptans may exacerbate this problem, and we are unaware of any literature that supports this idea, which makes this an unacceptable reason to decline the application. There is no evidence that triptan overuse or MOH is either less or more of a problem in NZ compared to countries that have access to more than two triptans. We would like to see the evidence from the Committee that increasing the number of triptans available for prescription leads to an increased prevalence of MOH.

Regardless of this, overuse of triptans, as a risk factor for MOH, needs to be addressed through improved education of clinicians and patients about the recommended limits to triptan use (Braunstein et al., 2015) and correct prescribing practices (Ashina et al., 2023) , not through restricting access to different types of triptan. It is inappropriate to propose addressing an issue of poor adherence to best practice by limiting access to medication that has proven efficacy and may benefit patients who are unable to tolerate or do not respond to other options. In fact, acute medication overuse can be seen not only as a failure of prescribing practice but as a failure of migraine management overall (Green, 2021) and the best response is to improve access to both effective migraine treatments and to knowledgeable health professionals who are able to provide holistic, effective and ongoing migraine healthcare.

We do not have prevalence data on triptan overuse or MOH or chronic migraine in NZ. However, we can estimate the proportion of people with migraine using triptans using administrative data (PHARMS data from the Ministry of Health). In 2020, nearly 63,000 people were dispensed a triptan or around 10% of people with migraine in NZ (estimated at 642,000 from the Global Burden of Disease study). This suggests, at a population level, a significant undertreatment of migraine, given that around 10% of people with migraine have chronic migraine (headache on 15 days or more per month), and a similar proportion have high-frequency episodic migraine (migraine on 8-14 days per

month (Lipton et al., 2022), both of which would presumably merit treatment with the only migraine-specific acute medication currently available in NZ. A cohort study from Denmark up until 2019 found that the prevalence of triptan use was around 1.5% (which is roughly the prevalence of chronic migraine), corresponding to only 12% of the migraine population (i.e. most people with migraine in Denmark were not using any migraine-specific acute treatment) (Davidsson et al., 2021). The prevalence of triptan overuse, defined as purchase of at least 20 daily doses of triptans per month for 3 consecutive months, was 56 of every 1000 triptan users (Davidsson et al., 2021). (For comparison, a French study found a triptan overuse prevalence of 2.3% (Braunstein et al., 2015); 5.9% from an Austrian study (Zebenholzer et al., 2018)). Note that in Denmark all seven triptans are available for use, compared with NZ where only sumatriptan and rizatriptan are available. This study, and many others, highlight that the major issue with triptans is not overuse but underuse, and there remains a significant unmet need for effective acute treatment of migraine (Baratta et al., 2023; Ezzati et al., 2022; Hirata et al., 2023; Lipton et al., 2022; Ruscheweyh, Gossrau, et al., 2023) (Baratta et al., 2023; Ezzati et al., 2022; Hirata et al., 2023; Lipton et al., 2022; Ruscheweyh, Gossrau, et al., 2023).

We have a snapshot of triptan use from a small online survey (n=530) from 2022, which collected data from a non-representative and self-selected sample of people with migraine in NZ.[1] This was a sample skewed to people with more severe and disabling migraine, with 20% of the sample having chronic migraine (headache on 15 days or more a month). From this survey, around a third of respondents were currently taking a triptan (33% for sumatriptan, 32% for rizatriptan), higher than the estimated use of triptans in the whole NZ migraine population. Over a third had never used a triptan (39% for sumatriptan, 36% for rizatriptan); although 25% would like to try sumatriptan and 19% would like to try rizatriptan, suggesting a significant level of under-treatment. Just under a third had previously used a triptan and stopped (27% for sumatriptan and 32% for rizatriptan), indicating a failure of existing migraine-specific acute treatment options. The reasons for stopping were because of side effects (9% for sumatriptan and 7% for rizatriptan), because they didn't work (11% for sumatriptan and 13% for rizatriptan) or another reason, not specified (10% for sumatriptan, 11% for rizatriptan). For people currently taking a triptan, 71% of those with chronic migraine reported taking a triptan on 10 days or more in the last month, and 15% of those with episodic migraine (note that a diagnosis of MOH requires 10 days or more use for three consecutive months, so this is not an estimate of MOH but indicates a risk of developing MOH). This is consistent with the findings internationally that the prevalence of MOH is high in people with chronic headache (Fischer & Jan, 2023) and that 40-50% of all patients with chronic headache overuse medications (Diener et al., 2022), noting again that this sample was not representative of the whole migraine population but represented a group with a high level of migraine disability.

[1] For more information about the survey and results see here https://www.migrainefoundation.org.nz/migraine-in-new-zealand-survey-2022-insights/

Pharmac's reasons for declining an application

Pharmac states that inactive applications may be declined when:

- our expert clinical advisors have recommended that the funding application be declined
- other medicines for the same condition are now funded making the funding application no longer relevant
- our expert clinical advisors have recommended that the medicine would provide no additional benefits over other treatments we already fund, or it may be harmful
- no company is willing to supply the medicine in New Zealand

None of these are a satisfactory reason to decline the zolmitriptan application. The application has not been recommended for decline – in 2008, PTAC made a cost-neutral recommendation. The decline of the other triptan application does not justify declining this one, for reasons noted above and also because this application has not been reviewed by the Neurological Advisory Committee. There would be benefit from having a third triptan funded in NZ, as previously outlined. PTAC actually recommended funding a triptan with a nasal spray formulation, so this is in direct conflict with the proposal to decline. There are pharmaceutical companies able to supply the medicine in NZ, as evidenced by zolmitriptan previously being available (although not currently).

Our recommendations

- We strongly oppose the proposal to decline the zolmitriptan application. Pharmac has not provided sufficient justification to do this.
- Pharmac should revisit the evidence for comparative efficacy of zolmitriptan, including real-world data. There is a large amount of relevant new literature that needs to be considered before declining this application. This should include a review of zolmitriptan nasal spray for paediatric patients aged 12 to 17 years, a demographic notably underserved in terms of rigorously evaluated migraine abortive treatments.
- Pharmac should revisit the cost-benefit analysis and reassess whether zolmitriptan is now cost-saving rather than cost-neutral compared to the other triptans.
- Pharmac should re-engage with pharmaceutical companies around the cost and supply of zolmitriptan, particularly the nasal spray formulation.
- Pharmac should consider seeking advice on this application from the Neurological Advisory Committee. An additional triptan, especially one with a nasal spray formulation, would address a significant need for more migraine treatment options.

References

Ailani, J., Burch, R. C., & Robbins, M. S. (2021). The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache: The Journal of Head and Face Pain*, *61*(7), 1021–1039. https://doi.org/10.1111/HEAD.14153

Ashina, S., Terwindt, G. M., Steiner, T. J., Lee, M. J., Porreca, F., Tassorelli, C., Schwedt, T. J., Jensen, R. H., Diener, H. C., & Lipton, R. B. (2023). Medication overuse headache. *Nature Reviews. Disease Primers*, *9*(1), 5. https://doi.org/10.1038/S41572-022-00415-0

Baratta, F., Allais, G., Gnavi, R., Scarinzi, C., Enri, L. R., Rolando, S., Spadea, T., Costa, G., Benedetto, C., Mana, M., Giaccone, M., Mandelli, A., Manzoni, G. C., Bussone, G., & Brusa, P. (2023). Triptans utilization in Italian population: A real-life study in community pharmacies. *PLOS ONE*, *18*(9), e0291323. https://doi.org/10.1371/JOURNAL.PONE.0291323

Braunstein, D., Donnet, A., Pradel, V., Sciortino, V., Allaria-Lapierre, V., Lantéri-Minet, M., & Micallef, J. (2015). Triptans use and overuse: A pharmacoepidemiology study from the French health insurance system database covering 4.1 million people. *Cephalalgia*, *35*(13), 1172–1180. https://doi.org/10.1177/0333102415570497

Cameron, C., Kelly, S., Hsieh, S. C., Murphy, M., Chen, L., Kotb, A., Peterson, J., Coyle, D., Skidmore, B., Gomes, T., Clifford, T., & Wells, G. (2015). Triptans in the Acute Treatment of Migraine: A Systematic Review and Network Meta-Analysis. *Headache: The Journal of Head and Face Pain*, *55*(S4), 221–235. https://doi.org/10.1111/HEAD.12601

Chiang, C.-C., Fang, X., Horvath, Z., Cadiou, F., Urani, A., Poh, W., Narimatsu, H., Cheng, Y., & Dodick, D. W. (2023). Simultaneous Comparisons of 25 Acute Migraine Medications Based on 10 Million Users' Self-Reported Records From a Smartphone Application. *Neurology*, 10.1212/WNL.0000000000207964. https://doi.org/10.1212/WNL.0000000000207964

Davidsson, O. B., Olofsson, I. A., Kogelman, L. J. A., Andersen, M. A., Rostgaard, K., Hjalgrim, H., Olesen, J., & Hansen, T. F. (2021). Twenty-five years of triptans – a nationwide population study. *Cephalalgia*, *41*(8), 894–904. https://doi.org/10.1177/0333102421991809

Diener, H.-C., Kropp, P., Dresler, T., Evers, S., Förderreuther, S., Gaul, C., Holle-Lee, D., May, A., Niederberger, U., Moll, S., Schankin, C., & Lampl, C. (2022). Management of medication overuse (MO) and medication overuse headache (MOH) S1 guideline. *Neurological Research and Practice*, *4*, 37. https://doi.org/10.1186/s42466-022-00200-0

Dodick D, Brandes J, Elkind A, Mathew N, Rodichok L. Speed of onset, efficacy and tolerability of zolmitriptan nasal spray in the acute treatment of migraine: a randomised, double-blind, placebo-controlled study. CNS Drugs. 2005;19(2):125-36. doi: 10.2165/00023210-200519020-00003.

Dowson AJ, MacGregor EA, Purdy RA, Becker WJ, Green J, Levy SL. Zolmitriptan orally disintegrating tablet is effective in the acute treatment of migraine. Cephalalgia. 2002 Mar;22(2):101-6. doi: 10.1046/j.1468-2982.2002.00319.x.

Ezzati, A., Buse, D. C., Fanning, K. M., Reed, M. L., Martin, V. T., & Lipton, R. B. (2022). Predictors of treatment-response to acute prescription medications in migraine: Results from the American Migraine Prevalence and Prevention (AMPP) Study. *Clinical Neurology and Neurosurgery*, *223*, 107511. https://doi.org/10.1016/J.CLINEURO.2022.107511

Fischer, M. A., & Jan, A. (2023). Medication-Overuse Headache. *StatPearls*. https://www.ncbi.nlm.nih.gov/books/NBK538150/

Global Burden of Disease Collaborative Network. (2020). *Global Burden of Disease Study 2019 (GBD 2019) Results*.

Green, M. W. (2021). Medication overuse headache. In *Current Opinion in Neurology* (Vol. 34, Issue 3, pp. 378–383). Lippincott Williams and Wilkins. https://doi.org/10.1097/WCO.0000000000000925

Grøtta Vetvik, K., & Anne MacGregor, E. (2021). Menstrual migraine: a distinct disorder needing greater recognition. *Lancet Neurology*, *20*(4), 304–315. https://doi.org/10.1016/S1474-4422(20)30482-8

Hedlund, C., Rapoport, A. M., Dodick, D. W., & Goadsby, P. J. (2009). Zolmitriptan Nasal Spray in the Acute Treatment of Cluster Headache: A Meta-Analysis of Two Studies. *Headache: The Journal of Head and Face Pain*, *49*(9), 1315–1323. https://doi.org/10.1111/J.1526-4610.2009.01518.X

Hirata, K., Komori, M., Kaname Ueda, ·, Anthony, ·, Zagar, J., Kim, Y., Jaffe, D. H., Matsumori, Y., & Takeshima, T. (2023). Outcomes and Factors Associated with Insufficient Effectiveness of Acute Treatments of Migraine in Japan: Results of the ObserVational survey of the Epidemiology, tReatment, and Care Of MigrainE (OVERCOME [Japan]) Study. *Drugs - Real World Outcomes 2023*, 1–14. https://doi.org/10.1007/S40801-023-00368-0

Lewis DW, Winner P, Hershey AD, Wasiewski WW; Adolescent Migraine Steering Committee. Efficacy of zolmitriptan nasal spray in adolescent migraine. Pediatrics. 2007 Aug;120(2):390-6. doi: 10.1542/peds.2007-0085

Li, G., Duan, S., Zhu, T., Ren, Z., Xia, H., Wang, Z., Liu, L., & Liu, Z. (2023). Efficacy and safety of intranasal agents for the acute treatment of migraine: a systematic review and network meta-analysis. *The Journal of Headache and Pain*, *24*(1), 129. https://doi.org/10.1186/S10194-023-01662-6

Lipton, R. B., Nicholson, R. A., Reed, M. L., Araujo, A. B., Jaffe, D. H., Faries, D. E., Buse, D. C., Shapiro, R. E., Ashina, S., Cambron-Mellott, M. J., Rowland, J. C., & Pearlman, E. M. (2022). Diagnosis, consultation, treatment, and impact of migraine in the US: Results of the OVERCOME (US) study. *Headache*, *62*(2), 122–140. https://doi.org/10.1111/HEAD.14259

McKeage, K. (2016). Zolmitriptan Nasal Spray: A Review in Acute Migraine in Pediatric Patients 12 Years of Age or Older. *Pediatric Drugs*, *18*(1), 75–81. https://doi.org/10.1007/S40272-015-0160-2/FIGURES/1

Migraine Foundation Aotearoa New Zealand. (2022). *New Zealand health survey data – a decade to be released.* . Https://www.migrainefoundation.org.nz/Blog/Post/93215/New-Zealand-Health-Survey-Data--a-Decade-to-Be-Released/.

Olesen, A., Winther Schytz, H., Rye Ostrowski, S., Topholm, M., Nielsen, K., Erikstrup, C., Mikkelsen, S., Birger Pedersen, O., Olesen, J., Folkmann Hansen, T., & Ameri Chalmer, M. (2022). Low adherence to the guideline for the acute treatment of migraine. *Nature Scientific Reports*, *12*(8487). https://doi.org/10.1038/s41598-022-12545-2

Ruscheweyh, R., Dresler, T., Förderreuther, S., Gaul, C., Gossrau, G., Jürgens, T. P., Ruschil, V., Straube, A., & Scheidt, J. (2023). What do patients' efficacy and tolerability ratings of acute migraine medication tell us? Cross-sectional data from the DMKG Headache Registry. *Https://Doi.Org/10.1177/03331024231174855*, *43*(5), 033310242311748. https://doi.org/10.1177/03331024231174855

Ruscheweyh, R., Gossrau, G., Dresler, T., Freilinger, T., Förderreuther, S., Gaul, C., Kraya, T., Neeb, L., Ruschil, V., Straube, A., Scheidt, J., & Jürgens, T. P. (2023). Triptan non-response in specialized headache care: cross-sectional data from the DMKG Headache Registry. *The Journal of Headache and Pain*, *24*(1), 135. https://doi.org/10.1186/s10194-023-01676-0

Sacco, S., Lampl, C., Amin, F. M., Braschinsky, M., Deligianni, C., Uludüz, D., Versijpt, J., Ducros, A., Gil-Gouveia, R., Katsarava, Z., Martelletti, P., Ornello, R., Raffaelli, B., Boucherie, D. M., Pozo-Rosich, P., Sanchez-del-Rio, M., Sinclair, A., Maassen van den Brink, A., & Reuter, U. (2022). European Headache Federation (EHF) consensus on the definition of effective treatment of a migraine attack and of triptan failure. *The Journal of Headache and Pain 2022 23:1*, *23*(1), 1–10. https://doi.org/10.1186/S10194-022-01502-Z

Steiner, T. J., Stovner, L. J., Jensen, R., Uluduz, D., & Katsarava, Z. (2020). Migraine remains second among the world's causes of disability, and first among young women: findings from GBD2019. *Journal of Headache and Pain*, *21*(137). https://doi.org/10.1186/s10194-020-01208-0

Stovner, L. J., Hagen, K., Linde, M., & Steiner, T. J. (2022). The global prevalence of headache: an update, with analysis of the influences of methodological factors on prevalence estimates. *The Journal of Headache and Pain 2022 23:1*, *23*(1), 1–17. https://doi.org/10.1186/S10194-022-01402-2

Vanderpluym, J. H., Halker Singh, R. B., Urtecho, M., Morrow, A. S., Nayfeh, T., Torres Roldan, V. D., Farah, M. H., Hasan, B., Saadi, S., Shah, S., Abd-Rabu, R., Daraz, L., Prokop, L. J., Murad, M. H., & Wang, Z. (2021). Acute Treatments for Episodic Migraine in Adults: A Systematic Review and Meta-analysis. *JAMA*, *325*(23), 2357–2369. https://doi.org/10.1001/JAMA.2021.7939

Zebenholzer, K., Gall, W., & Wöber, C. (2018). Use and overuse of triptans in Austria – a survey based on nationwide healthcare claims data. *The Journal of Headache and Pain*, *19*(1). https://doi.org/10.1186/S10194-018-0864-0

Zhao, Y. J., Idu Jion, Y. B., Ho, K. H., Wong, P. S., Lo, Y. L., Chan, Y. C., Ang, L. L., Yeo, S. N., Soh, S. B., Wu, T. S., & Yuan Ong, J. J. (2023). Approach to headache disorders and the management of migraine: consensus guidelines from the Headache Society of Singapore, first edition (2023). *Singapore Medical Journal*. https://doi.org/10.4103/singaporemedj.SMJ-2022-195