Gemeinsamer Bundesausschuss

Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

und

Schriftliche Beteiligung der wissenschaftlich-medizinischen Fachgesellschaften und der Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2022-B-305 Lasmiditan

Stand: Januar 2023

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA

Lasmiditan
[Akutbehandlung der Kopfschmerzphase von Migräne-Attacken mit oder ohne Aura]

Kriterien gemäß 5. Kapitel § 6 VerfO	
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	Siehe Übersicht „II. Zugelassene Arzneimittel im Anwendungsgebiet“.
Sofern als Vergleichstherapie eine nicht-medikamentöse Behandlung in Betracht kommt, muss diese im Rahmen der GKV erbringbar sein.	nicht angezeigt
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	Anlage III zur Arzneimittelrichtlinie: Übersicht über Verordnungseinschränkungen und -ausschlüsse in der Arzneimittelversorgung durch die Arzneimittel-Richtlinie und aufgrund anderer Vorschriften (§ 34 Absatz 1 Satz 6 und Absatz 3 SGB V): 36. Migränemittel-Kombinationen: Verordnungsausschluss verschreibungspflichtiger Arzneimittel nach dieser Richtlinie.
Die Vergleichstherapie soll nach dem allgemein anerkannten Stand der medizinischen Erkenntnisse zur zweckmäßigen Therapie im Anwendungsgebiet gehören.	Siehe systematische Literaturrecherche

II. Zugelassene Arzneimittel im Anwendungsgebiet

Wirkstoff **ATC-Code** **Handelsname**	**Anwendungsgebiet** (Text aus Fachinformation)
Zu bewertendes Arzneimittel:	
Lasmiditan N02CC08 RAYVOW®	<u>Anwendungsgebiet laut Zulassung vom 17.08.2022:</u> RAYVOW ist angezeigt zur Akutbehandlung der Kopfschmerzphase von Migräne-Attacken mit oder ohne Aura bei Erwachsenen.
Nicht-steroidale Antirheumatika (NSAR) und NSAR-haltige Kombinationen	
Diclofenac M01AB05 Voltaren® K Migräne	Akute Behandlung der Kopfschmerzphase bei Migräneanfällen mit und ohne Aura.
Ibuprofen M01AE01 Aktren® Spezial	Symptomatische Behandlung von – leichten bis mäßig starken Schmerzen wie Kopfschmerzen, Zahnschmerzen und Regelschmerzen – Fieber Akute Kopfschmerzen bei Migräne mit und ohne Aura.
Acetylsalicylsäure N02BA01 Aspirin® Migräne	Akute Behandlung der Kopfschmerzphase von Migräneanfällen mit und ohne Aura.
Weitere Analgetika und Antipyretika sowie Kombinationen	
Paracetamol/ Acetylsalicylsäure/ Coffein N02BE51 Doloversa®	Für Erwachsene und Jugendliche ab 12 Jahren: – zur akuten Behandlung von leichten bis mäßig starken Kopfschmerzen bei Migräneattacken mit oder ohne Aura, – zur Behandlung von Spannungskopfschmerzen.
Paracetamol/ Metoclopramid N02BE51	Migränerton® wird angewendet bei Erwachsenen und Jugendlichen ab 14 Jahren (43 kg). Behandlung von Kopfschmerzen mit Schwindel, Übelkeit und Erbrechen bei Migräneanfall.

II. Zugelassene Arzneimittel im Anwendungsgebiet	
Migränerton®	
Phenazon N02BB01 Migräne-Kranit®	Akute Behandlung der Kopfschmerzen von Migräneanfällen mit und ohne Aura. Leichte bis mäßig starke Schmerzen.
Selektive Serotonin-5HT$_1$-Rezeptoragonisten	
Sumatriptan N02CC01 Imigran®	Akute Behandlung von Migräneanfällen mit und ohne Aura.
Naratriptan N02CC02 Naramig®	Akute Behandlung der Kopfschmerzphasen von Migräneanfällen mit und ohne Aura.
Zolmitriptan N02CC03 AscoTop®	Akutbehandlung von Migränekopfschmerzen mit oder ohne Aura.
Rizatriptan N02CC04 Maxalt®	Akute Behandlung der Kopfschmerzphase von Migräneanfällen mit oder ohne Aura bei Erwachsenen.
Almotriptan N02CC05 Almogran®	Akute Behandlung der Kopfschmerzphase von Migräneanfällen mit oder ohne Aura.
Eletriptan N02CC06 Relpax®	Relpax wird angewendet bei Erwachsenen zur Akutbehandlung der Kopfschmerzphase bei Migräneanfällen mit oder ohne Aura.
Frovatriptan N02CC07 Allegro®	Akutbehandlung der Kopfschmerzphase von Migräneanfällen mit oder ohne Aura. Allegro ist zur Anwendung bei Erwachsenen bestimmt.
Weitere	

II. Zugelassene Arzneimittel im Anwendungsgebiet	
Ergotamin N02AC02 Ergo-Kranit® Migräne	Behandlung von Migräne-Anfällen (insbesondere sehr lange Anfälle), wenn andere Therapien nicht wirksam oder nicht indiziert sind.
Rimegepant N02CD06 Vydura® *[in Deutschland nicht marktverfügbar]*	VYDURA wird angewendet zur • Akuttherapie der Migräne mit oder ohne Aura bei Erwachsenen. • […]

Quellen: AMIce-Datenbank, Fachinformationen

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2022-B-305 (Lasmiditan)

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	20. Dezember 2022

Inhaltsverzeichnis

Abkürzungsverzeichnis

APC	Asperin, paracetamol, caffeine
AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
G-BA	Gemeinsamer Bundesausschuss
GIN	Guidelines International Network
GoR	Grade of Recommendations
HR	Hazard Ratio
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
KI	Konfidenzintervall
LoE	Level of Evidence
NICE	National Institute for Health and Care Excellence
NSAID	Nonsteroidal anti-inflammatory drug
OR	Odds Ratio
OTC	Over the counter
RR	Relatives Risiko
SIGN	Scottish Intercollegiate Guidelines Network
TRIP	Turn Research into Practice Database
WHO	World Health Organization

1 Indikation

Akutbehandlung der Kopfschmerzphase von Migräne-Attacken mit oder ohne Aura bei Erwachsenen.

Hinweis zur Synopse: Informationen hinsichtlich nicht zugelassener Therapieoptionen sind über die vollumfängliche Darstellung der Leitlinienempfehlungen dargestellt.

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen und evidenzbasierten systematischen Leitlinien zur Indikation *Migräne* durchgeführt und nach PRISMA-S dokumentiert [A]. Die Recherchestrategie wurde vor der Ausführung anhand der PRESS-Checkliste begutachtet [B]. Es erfolgte eine Datenbankrecherche ohne Sprachrestriktion in: The Cochrane Library (Cochrane Database of Systematic Reviews), PubMed. Die Recherche nach grauer Literatur umfasste eine gezielte, iterative Handsuche auf den Internetseiten von Leitlinienorganisationen. Ergänzend wurde eine freie Internetsuche (*https://www.google.com/*) unter Verwendung des privaten Modus, nach aktuellen deutsch- und englischsprachigen Leitlinien durchgeführt.

Die Erstrecherche wurde am 18.08.2020 abgeschlossen, die folgenden am 07.01.2022 und 25.11.2022. Die Recherchestrategie der Erstrecherche wurde unverändert übernommen und der Suchzeitraum jeweils auf die letzten fünf Jahre eingeschränkt. Die letzte Suchstrategie inkl. Angabe zu verwendeter Suchfilter ist am Ende der Synopse detailliert dargestellt. Die Recherchen ergaben insgesamt 1.760 Referenzen.

In einem zweistufigen Screening wurden die Ergebnisse der Literaturrecherche bewertet. Im ersten Screening wurden auf Basis von Titel und Abstract nach Population, Intervention, Komparator und Publikationstyp nicht relevante Publikationen ausgeschlossen. Zudem wurde eine Sprachrestriktion auf deutsche und englische Referenzen vorgenommen. Im zweiten Screening wurden die im ersten Screening eingeschlossenen Publikationen als Volltexte gesichtet und auf ihre Relevanz und methodische Qualität geprüft. Dafür wurden dieselben Kriterien wie im ersten Screening sowie Kriterien zur methodischen Qualität der Evidenzquellen verwendet. Basierend darauf, wurden insgesamt 5 Referenzen eingeschlossen. Es erfolgte eine synoptische Darstellung wesentlicher Inhalte der identifizierten Referenzen.

3 Ergebnisse

3.1 Cochrane Reviews

Es wurden keine CR im AWG identifiziert.

3.2 Systematische Reviews

Diener HC et al., 2022 [2].

Aspirin, paracetamol (acetaminophen) and caffeine for the treatment of acute migraine attacks: A systemic review and meta-analysis of randomized placebo-controlled trials

Fragestellung

We performed a meta-analysis for the comparison of APC versus placebo, which has not been done to date.

Methodik

Population:

- Patients experiencing episodic migraines with at least moderate headache intensity

Intervention:

- APC

Komparator:

- Placebo

Endpunkte:

- Main outcomes:
  - pain-free response at 2 h and pain relief (from severe or moderate to mild or no pain) at 2 h
- Additional outcomes:
  - responses at other time points (0.5–6 h), reduction of nausea, photophobia, phonophobia, restoration of usual activities, and adverse events (AEs).

Recherche/Suchzeitraum:

- Embase up to 25 August 2020

Qualitätsbewertung der Studien:

- Cochrane risk of bias tool

Ergebnisse

Anzahl eingeschlossener Studien:

- 7 studies with a total of 3,306 patients

Charakteristika der Population:

- Keine detaillierten Angaben zu Baselinecharakteristika vorhanden

- The studies investigated two tablets of usual APC combinations, corresponding to 500/400/100 mg aspirin/paracetamol/caffeine, or 500/500/130 mg. In all studies, medications were taken when the pain of the treated migraine attack was moderate or severe.

Qualität der Studien:

- We judged the 'risk of bias' assessments unanimously as low
- All studies provided information concerning the randomization process and the method used for blinding investigators and patients. Deviations from the intended treatments were not possible due to the masked treatment: rescue medication use was more often reported in the placebo groups and a potential bias could only be an underestimation of the true APC effect. The percentage of missing data was negligible, probably because of the short duration of the observation intervals. Assessment of outcomes was carried out in blinded conditions. Not all investigated variables were included in all individual studies and therefore not all studies could be integrated in all meta-analyses; but all studies reported their specific primary endpoints, which were generally measuring very similar effects to our efficacy endpoints, so that we can exclude a reporting bias.

Studienergebnisse:

Summary of findings for the main outcomes for the comparison of aspirin, paracetamol, caffeine with placebo

Outcomes	Patients (Studies)	Events/Patients		Relative effect	Anticipated absolute rates %			
		Placebo	APC	RR (95% CI)	Placebo[a]	APC (95% CI)	RD (95% CI)	Evidence (GRADE)
Pain-free at								
30 min	2565 (5)	11/934	26/1631	1.04 (0.43–2.52)	1.05	1.09 (0.5–2.7)	0.04 (−0.6–1.6)	moderate[b]
1 h	2565 (5)	36/934	159/1631	1.80 (1.25–2.58)	4.1	7.4 (5.1–10.6)	3.3 (1.0–6.5)	high
2 h	2934 (6)	141/1055	567/1879	2.18 (1.43–3.32)	9.0	19.6 (12.9–29.9)	10.6 (3.9–20.9)	high
3 h	2565 (5)	166/934	731/1631	2.43 (1.67–3.55)	15.2	36.9 (25.4–54.0)	21.7 (10.2–39.8)	high
4 h	2565 (5)	235/934	863/1631	1.99 (1.48–2.67)	22.0	43.8 (32.6–58.7)	21.8 (10.6–36.7)	high
6 h	1220 (3)	142/618	305/602	2.20 (1.87–2.60)	20.8	45.8 (38.9–54.1)	25.0 (18.1–33.3)	high
Pain relief at								
30 min	1771 (5)	61/746	141/1025	1.46 (0.97–2.20)	7.8	11.4 (7.6–17.2)	3.6 (−0.2–9.4)	moderate[b]
1 h	1771 (5)	142/746	420/1025	2.04 (1.72–2.42)	17.8	36.3 (30.6–43.1)	18.5 (12.8–25.3)	high
2 h	1771 (5)	265/746	679/1025	1.74 (1.56–1.93)	31.2	54.3 (48.7–60.2)	23.1 (17.5–29.0)	high
3 h	1771 (5)	322/746	776/1025	1.67 (1.52–1.82)	38.0	63.5 (57.8–69.2)	25.5 (19.8–31.2)	high
4 h	1771 (5)	371/746	828/1025	1.56 (1.44–1.69)	49.0	76.4 (70.6–82.8)	27.4 (21.6–33.8)	high
6 h	1220 (3)	320/618	473/602	1.51 (1.39–1.65)	52.9	79.9 (73.5–87.3)	27.0 (20.6–34.4)	high
No photophobia								
2 h	1587 (4)	153/738	328/849	1.77 (1.21–2.60)	17.0	30.1 (20.6–44.2)	13.1 (3.6–27.2)	high
6 h	1220 (3)	195/618	353/602	1.85 (1.62–2.12)	33.0	61.1 (53.5–70.0)	28.1 (20.5–37.0)	high
No phonophobia								
2 h	1586 (4)	173/737	351/849	1.66 (1.20–2.30)	19.9	33.0 (23.9–45.8)	13.1 (4.0–25.9)	high
6 h	1220 (3)	206/618	353/602	1.76 (1.55–2.00)	34.0	59.8 (52.7–68.0)	25.8 (18.7–34.0)	high
No nausea at								
2 h	1587 (4)	426/737	552/850	1.10 (1.00–1.20)				high
6 h	1220 (3)	371/618	448/602	1.23 (1.14–1.33)	57.0	70.1 (65.0–75.8)	13.1 (8.0–18.8)	high
No/little funct. dis.								
2 h	1220 (3)	210/618	356/602	1.74 (1.53–1.98)	34.0	59.2 (52.0–67.3)	25.2 (18.0–33.3)	high
6 h	1220 (3)	250/618	414/602	1.70 (1.52–1.90)	38.0	64.6 (57.8–72.2)	26.6 (19.8–34.2)	high
AE	3202 (6)	88/1124	226/2078	1.71 (1.34–2.17)	10.8	18.5 (14.5–23.4)	7.7 (3.7–12.6)	high
Serious AE	3306 (7)	0/1159	0/2147	./.	0.0	0.0	0.0	high

Note: The rate in the APC group and the RD (and their 95% CIs) are calculated from the assumed rate in the placebo group and the relative effect (RR) of ACP (and its 95% CI).
Abbreviations: AE, adverse event; APC, aspirin, paracetamol, caffeine; CI, confidence interval; RD, rate difference; RR, rate ratio.
[a]Median placebo rate across studies.
[b]Downgrading due to imprecision.

Anmerkung/Fazit der Autoren

In conclusion, the present meta-analysis demonstrates good efficacy for APC versus placebo in terms of both the International Headache Society-recommended primary outcome, "rate of pain-free patients at 2 h" and the secondary outcome, "rate of pain relief at 2 h". The tolerability was good and indicates that APC is an effective and well-tolerated OTC treatment for acute migraine attacks.

VanderPluym JH et al., 2021 [5].

Acute Treatments for Episodic Migraine in Adults: A Systematic Review and Meta-analysis

Siehe auch: Singh RBH et al., 2020 [4]. Acute Treatments for Episodic Migraine.

Fragestellung

In this systematic review, the benefits and harms associated with acute treatments for episodic migraine were assessed, including pharmacologic and nonpharmacologic therapies.

Methodik

Population:

- adult patients (≥18 years) with episodic migraine

Intervention:

- abortive pharmacologic therapy or noninvasive nonpharmacologic abortive therapy

Komparator:

- placebo, usual care, another pharmacologic therapy, noninvasive nonpharmacologic therapy, wait list, no treatment, or attention control

Endpunkte:

- Primary outcomes:
  - pain freedom, pain relief, sustained pain freedom, sustained pain relief, and adverse events
- Additional outcomes:
  - improved function, restored function, pain as reported with a pain scale, function as reported with a function scale, opioid overdose, and medication overuse headache

Recherche/Suchzeitraum:

- EMBASE, Epub Ahead of Print, In-Process & Other Non-Indexed Citations, MEDLINE Daily, MEDLINE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, PsycINFO, and Scopus from database inception to February 24, 2021, were searched

Qualitätsbewertung der Studien:

- Cochrane Collaboration's Risk of Bias 2 tool for RCTs
- Items from AMSTAR for systematic reviews (of triptans and NSAIDs)
- The strength of evidence (SOE) was graded following the Agency for Healthcare Research and Quality Methods Guide for Effectiveness and Comparative Effectiveness Reviews and categorized as "high," "moderate," "low," or "insufficient evidence"

Ergebnisse

Anzahl eingeschlossener Studien:

- Evidence on triptans and NSAIDs was summarized from15 systematic reviews. For other interventions, 115 RCTs from 121 articles with 28,803 patients were included in the analyses

Charakteristika der Population:

- Keine aggregierten Charakteristika je Wirkstoffklasse verfügbar

Qualität der Studien:

- Numerous systematic reviews have been published evaluating triptans and NSAIDs. Most of the systematic reviews were judged to have high credibility.
- The overall risk of bias for RCTs on Ergot Alkaloids was high (2 RCTs with low risk; 2 moderate risk; and 11 high risk)
- 1 RCT on acetaminophen had a low risk of bias, 1 had a moderate risk of bias

Studienergebnisse

Triptans und NSAIDs

According to 7 systematic reviews, triptans (various administration routes, including oral, subcutaneous, and intranasal) compared with placebo were significantly associated with increased pain freedom and pain relief at 2 hours and 1 day (high SOE), and increased risk of mild and transient adverse events (eg, malaise, nausea, chest pain, flushing sensation, palpitation, paresthesia).

According to 3 systematic reviews, NSAIDs (various administration routes, including oral, intravenous, and intramuscular) compared with placebo were significantly associated with increased pain freedom and pain relief at 2 hours and 1 day (moderate SOE), and increased risk of mild and transient adverse events (eg, dyspepsia, nausea, somnolence, dizziness).

According to 1 systematic review, the combination of sumatriptan (oral) and naproxen (oral) compared with placebo was significantly associated with improved pain freedom (high SOE) and pain relief (high SOE) at 2 hours, sustained pain freedom (high SOE) and sustained pain relief (high SOE) at 1 day, and improved function (high SOE) at 2 hours.

Comparison	Outcome	Time	Findings, RR (95% CI)*	Study design and sample size
Triptans				
Naratriptan, 2.5 mg (oral) vs placebo[11]	Pain free	2 h	2.52 (1.78-3.57)	6 RCTs; 2358 patients
		1 d	2.58 (1.99-3.35)	
	Pain relief	2 h	1.81 (1.55-2.11)	
		1 d	2.11 (1.75-2.54)	
	Sustained pain relief	1 d	2.43 (2.11-2.80)	
Zolmitriptan, 2.5 mg (oral and nasal spray) vs placebo[12]	Pain relief	2 h	2.06 (1.91-2.22)	11 RCTs; 4904 patients
	Sustained pain free	1 d	3.51 (2.12-5.79)	2 RCTs; 984 patients
	Sustained pain relief	1 d	2.92 (2.37-3.61)	4 RCTs; 2059 patients
Rizatriptan, 10 mg (oral) vs placebo[13]	Pain relief	2 h	71% vs 38%; $P < .001$	7 RCTs; 3328 patients
	Pain free	2 h	41% vs 10%; $P < .001$	
	Sustained pain relief	1 d	37% vs 18%; $P < .001$	
	Sustained pain free	1 d	25% vs 7%; $P < .001$	
Frovatriptan, 2.5 mg (oral) vs placebo[14]	Pain free	2 h	3.70 (2.59-5.29)	5 RCTs; 2866 patients
			RD, 0.09 (0.07-0.10)	
		1 d	2.67 (2.21-3.22)	
			RD, 0.18 (0.15-0.21)	
	Pain relief	2 h	1.66 (1.47-1.88)	
		1 d	1.83 (1.66-2.00)	
Almotriptan, 12.5 mg (oral) vs placebo[15]	Pain relief	2 h	1.68 (1.42-1.98); $I^2 = 41.90\%$	5 RCTs; 1429 patients
			RD, 0.25 (0.19-0.31)	
	Pain free	2 h	2.15 (1.64-2.80); $I^2 = 39.60\%$	5 RCTs; 1590 patients
			RD, 0.19 (0.14-0.25)	
	Sustained pain free	1 d	2.12 (1.64-2.75)	5 RCTs
			RD, 0.14 (0.11-0.18)	
Sumatriptan, 100 mg (oral) vs placebo[16]	Pain free	2 h	3.20 (2.84-3.62); $I^2 = 37.00\%$	15 RCTs and comparative observational studies; 6571 patients
	Pain relief	2 h	1.93 (1.82-2.04); $I^2 = 67.00\%$	20 RCTs and comparative observational studies; 7811 patients
	Sustained pain free	1 d	2.81 (2.30-3.44); $I^2 = 31.00\%$	5 RCTs and comparative observational studies, 2891 patients
	Sustained pain relief	1 d	2.12 (1.87-2.39); $I^2 = 0.00\%$	5 RCTs and comparative observational studies; 4116 patients
	Improved function	2 h	1.87 (1.65-2.11); $I^2 = 0.00\%$	6 RCTs and comparative observational studies; 1827 patients
Sumatriptan, 6 mg (subcutaneous) vs placebo[17]	Pain free	2 h	3.85 (3.32-4.46); $I^2 = 62.00\%$	11 RCTs and comparative observational studies; 2522 patients
	Pain relief	2 h	2.50 (2.29-2.73); $I^2 = 75.00\%$	12 RCTs and comparative observational studies; 2738 patients
	Sustained pain free	1 d	2.18 (1.61-2.95)	2 RCTs and comparative observational studies; 752 patients
	Restored function	2 h	3.40 (2.66-4.35)	2 RCTs and comparative observational studies; 750 patients
	Improved function	2 h	3.21 (2.68-3.84)	3 RCTs and comparative observational studies; 1328 patients
NSAIDs				
Diclofenac, 50 mg (oral) vs placebo[18]	Pain free	2 h	2.02 (1.57-2.61); $I^2 = 63.00\%$	2 RCTs; 1477 patients
	Pain relief	2 h	1.47 (1.31-1.65); $I^2 = 0.00\%$	2 RCTs; 1477 patients
	Sustained pain free	1 d	2.25 (1.68-3.01); $I^2 = 45.00\%$	2 RCTs; 1578 patients
	Restored function	2 h	2.36 (1.80-3.08); $I^2 = 0.00\%$	2 RCTs; 873 patients
Ibuprofen, 400 mg (oral) vs placebo[19]	Pain free	2 h	1.91 (1.60-2.28); $I^2 = 81.00\%$	6 RCTs; 2575 patients
	Pain relief	2 h	2.17 (1.92-2.45); $I^2 = 92.00\%$	7 RCTs; 1815 patients
	Sustained pain relief	1 d	2.17 (1.76-2.69); $I^2 = 75.00\%$	4 RCTs; 879 patients
	Improved function	2 h	1.61 (1.38-1.89); $I^2 = 78.00\%$	3 RCTs; 1114 patients
Aspirin (oral) vs placebo[20]	Pain free	2 h	2.08 (1.70-2.55); $I^2 = 0.00\%$	6 RCTs; 2027 patients
	Pain relief	2 h	1.64 (1.48-1.83); $I^2 = 0.00\%$	6 RCTs; 2027 patients
	Sustained pain relief	1 d	1.63 (1.37-1.95); $I^2 = 0.00\%$	3 RCTs; 1142 patients
Triptans plus NSAIDs				
Sumatriptan (oral) plus naproxen (oral) vs placebo[21]	Pain free	2 h	3.65 (2.97-4.49); $I^2 = 38.00\%$	4 RCTs; 2596 patients
	Pain relief	2 h	2.16 (1.95-2.39); $I^2 = 0.00\%$	4 RCTs; 2596 patients
	Sustained pain free	1 d	3.43 (2.69-4.36); $I^2 = 0.00\%$	4 RCTs; 2596 patients
	Sustained pain relief	1 d	2.61 (2.27-2.99); $I^2 = 0.00\%$	4 RCTs; 2596 patients
	Improved function	2 h	3.36 (2.63-4.29); $I^2 = 0.00\%$	3 RCTs; 1984 patients

Abbreviations: NSAID, nonsteroidal anti-inflammatory drug; RCT, randomized clinical trial; RD, risk difference; RR, relative risk.

* Results extracted from existing systematic reviews with various details. Data are RR (95% CI) unless otherwise noted.

Ergot Alkaloids

Fifteen RCTs with 2535patients were included in the analyses of ergot alkaloid medications. The overall risk of bias was high (2 RCTs with low risk; 2, moderate risk; and 11, high risk). No notable differences in findings between studies with low and moderate/high risk of bias were found.

Compared with placebo, dihydroergotamine (3 RCTs; intranasal) was associated with significantly more pain freedom and pain relief at 2 hours, 1 day, and 1week (moderate to high SOE), sustained pain freedom and pain relief at 1 day and 1 week (high SOE), and gastrointestinal adverse events.

Compared with placebo, ergotamine plus caffeine (1 RCT; oral) was associated with significantly more pain relief at 2 hours (moderate SOE).

Acetaminophen

Compared with placebo, acetaminophen was associated with significantly improved pain freedom at 2 hours (RR 1.89 [95% CI, 1.24-2.86]; I^2 = 0.00%; RD 0.07 [95%CI 0.03-0.12]; 2 RCTs; 729 patients; moderate SOE) and 1 day (RR 1.78 [95%CI 1.38-2.30]; I^2 = 0.00%; RD 0.15 [95%CI 0.09-0.21]; 2 RCTs; 729 patients; moderate SOE) and pain relief at 2 hours (RR, 1.61 [95%CI, 1.33-1.95]; I^2 = 0.00%; RD 0.18 [95%CI,0.11-0.25]; 2 RCTs; 729 patients; moderate SOE) and 1 day (RR 1.71 [95%CI, 1.43-2.04]; I^2 = 0.00%; RD 0.22 [95%CI 0.15-0.29]; 2 RCTs; 729 patients; moderate SOE). There was no significant difference on adverse events.

Anmerkung/Fazit der Autoren

There are several acute treatments for migraine with varying degrees of supporting evidence. Use of triptans, NSAIDs, acetaminophen, dihydroergotamine, calcitonin gene-related peptide antagonists, lasmiditan, and some nonpharmacologic treatments was associated with improved pain and function. The evidence for many other interventions, including opioids, was limited.

3.3 Leitlinien

Department of Veterans Affairs Department of Defense (VA/DoD), 2020 [1].

Clinical practice guideline for the primary care management of headache

Zielsetzung/Fragestellung

This CPG is intended to provide primary care providers (PCPs) with a framework by which to evaluate, treat, and manage the individual needs and preferences of patients with headache, thereby leading to improved clinical outcomes.

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium;
- Interessenkonflikte dargelegt; finanzielle Unabhängigkeit unklar;
- Systematische Suche, Auswahl und Bewertung der Evidenz;
- Formale Konsensusprozesse unklar; externes Begutachtungsverfahren dargelegt;

- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt;
- Regelmäßige Überprüfung der Aktualität unklar.

Recherche/Suchzeitraum:

- Embase, Medline, PsychInfo, Agency for Healthcare Research and Quality, Cochrane Database of Systematic Reviews from January 1, 2009, to March 6, 2019

LoE / GoR

- This CPG uses the GRADE methodology to assess the quality of the evidence base and assign a strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation:
  - Balance of desirable and undesirable outcomes
  - Confidence in the quality of the evidence
  - Values and preferences
  - Other implications, as appropriate, e.g.:
    - Resource use
    - Equity
    - Acceptability
    - Feasibility
    - Subgroup considerations
- The GRADE of a recommendation is based on the following elements:
  - Four decision domains used to determine the strength and direction (described above)
  - Relative strength (Strong or Weak)
  - Direction (For or Against)
- Using these elements, the grade of each recommendation is presented as part of a continuum:
  - Strong For (or “We recommend offering this option …”)
  - Weak For (or “We suggest offering this option …”)
  - No recommendation for or against (or “There is insufficient evidence …”)
  - Weak Against (or “We suggest not offering this option …”)
  - Strong Against (or “We recommend against offering this option …”)

Sonstige methodische Hinweise

- Laut Publikation basiert die Einschätzung der „quality of evidence“ auf einer Bewertung mittels GRADE. In diese Einschätzung fließt regelhaft eine Einschätzung des Biasrisikos ein. Ergebnisse der Biasrisikobewertung sind der Publikation nicht zu entnehmen.

Empfehlungen

Pharmacotherapy: Migraine – Abortive

26. We recommend sumatriptan (oral or subcutaneous), the combination of sumatriptan/naproxen, or zolmitriptan (oral or intranasal) for the acute treatment of migraine.	[155-158]	Strong for	Reviewed, New-added
27. We suggest frovatriptan or rizatriptan for the acute treatment of migraine.	[159,160]	Weak for	Reviewed, New-added
28. We suggest triptans instead of opioids or non-opioid analgesics to lower the risk of medication overuse headache for the acute treatment of migraine.	[51,161]	Weak for	Reviewed, New-added
29. We suggest ibuprofen, naproxen, aspirin, or acetaminophen for the acute treatment of migraine.	[162-166]	Weak for	Reviewed, New-added
30. We suggest greater occipital nerve block for the acute treatment of migraine.	[167-169] **Additional references:** [170,171]	Weak for	Reviewed, New-added
31. We suggest intravenous magnesium for the acute treatment of migraine.	[128,172] **Additional references:** [173-176]	Weak for	Reviewed, New-added

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Scottish Intercollegiate Guidelines Network (SIGN), 2018 [3].
Healthcare Improvement Scotland (HIS)
Pharmacological management of migraine - A national clinical guideline

Zielsetzung

This guideline provides recommendations based on current evidence for best practice in the acute and prophylactic management of adults with migraine using pharmacological therapies or devices. The focus is on adults with acute migraine and preventative treatment in patients with episodic or chronic migraine and medication-overuse headache. Studies of children with migraine were not included, however the recommendations could be considered for treating adolescents with migraine.

The guideline excludes complementary, physical and psychological therapies, and specialist surgical interventions.

Methodik

Grundlage der Leitlinie

- Update: This guideline updates and replaces section 6 of SIGN 107: Diagnosis and management of headache in adults.
- Repräsentatives Gremium.
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt.
- Systematische Suche, Auswahl und Bewertung der Evidenz.
- Konsensusprozesse und externes Begutachtungsverfahren dargelegt.
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt.
- Regelmäßige Überprüfung der Aktualität gesichert.

Recherche/Suchzeitraum:

- Systematic literature review: Databases searched include Medline, Embase, Cinahl, PsycINFO and the Cochrane Library. The year range covered was 2011–2016. Internet searches were carried out on various websites including the US National Guidelines Clearinghouse.
- Literature search for patient issues: Databases searched include Medline, Embase, Cinahl and PsycINFO, and the results were summarised by the SIGN Patient Involvement Officer and presented to the guideline development group.

LoE & GoR

KEY TO EVIDENCE STATEMENTS AND RECOMMENDATIONS	
LEVELS OF EVIDENCE	
1++	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, eg case reports, case series
4	Expert opinion
RECOMMENDATIONS	
Some recommendations can be made with more certainty than others. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the 'strength' of the recommendation). The 'strength' of a recommendation takes into account the quality (level) of the evidence. Although higher-quality evidence is more likely to be associated with strong recommendations than lower-quality evidence, a particular level of quality does not automatically lead to a particular strength of recommendation. Other factors that are taken into account when forming recommendations include: relevance to the NHS in Scotland; applicability of published evidence to the target population; consistency of the body of evidence, and the balance of benefits and harms of the options.	
R	For '**strong**' recommendations on interventions that '**should**' be used, the guideline development group is confident that, for the vast **majority** of people, the intervention (or interventions) will do more good than harm. For '**strong**' recommendations on interventions that '**should not**' be used, the guideline development group is confident that, for the vast **majority** of people, the intervention (or interventions) will do more harm than good.
R	For '**conditional**' recommendations on interventions that should be '**considered**', the guideline development group is confident that the intervention will do more good than harm for **most** patients. The choice of intervention is therefore more likely to vary depending on a person's values and preferences, and so the healthcare professional should spend more time discussing the options with the patient.
GOOD-PRACTICE POINTS	
✓	Recommended best practice based on the clinical experience of the guideline development group.

Treatment for patients with acute migraine

ASPIRIN

Empfehlung: Aspirin (900 mg) is recommended as first-line treatment for patients with acute migraine.

Aspirin, in doses for migraine, is not an analgesic of choice during pregnancy and should not be used in the third trimester of pregnancy.[17]

A Cochrane review of 13 studies (4,222 participants) reported that aspirin 900 mg and aspirin 1,000 mg were effective in achieving pain free at two hours compared to placebo (NNT=8.1). For sustained pain relief at 24 hours aspirin 1,000 mg had an NNT of 6.6 compared to placebo.[21] (LoE: 1++)

Aspirin alone had similar efficacy to sumatriptan 50 mg, and sumatriptan 100 mg was superior to aspirin and metoclopramide combined.[21] (LoE: 1++)

Associated symptoms of nausea, vomiting, photophobia (NNT=7.7) and phonophobia (NNT=6.6) were reduced by aspirin when compared to placebo. The addition of metoclopramide further reduced nausea (NNT=2.6) and vomiting.[21] (LoE: 1++)

Aspirin is a potential gastrointestinal irritant and may cause ulcers or gastrointestinal bleeding, however adverse effects from short-term use are mostly mild and transient.[21] Aspirin should not be used in patients under 16 years

of age due to the risk of Reye's syndrome.[17] The use of aspirin during pregnancy, especially of intermittent high doses, should be avoided.[22] Aspirin is contraindicated during the third trimester of pregnancy.[17] (LoE: 1++)

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

Ibuprofen (400 mg) is recommended as first-line treatment for patients with acute migraine. If ineffective, the dose should be increased to 600 mg.

A Cochrane review found ibuprofen to be superior to placebo in all doses between 200 mg and 600 mg for pain free at two hours and sustained pain relief at 24 hours for patients with acute migraine with moderate to severe baseline pain. The NNT for achieving the outcome of pain free at two hours was 9.7 for 200 mg and 7.2 for 400 mg.[23] (LoE: 1++)

Naproxen has also been found to be effective for two hour pain relief compared to placebo for patients with acute migraine. The NNT for pain free at two hours was 11. Results did not vary for doses of 500 mg and 825 mg.[24] (LoE: 1++)

Diclofenac potassium 50 mg is reported to have a relative benefit over placebo, relative risk (RR) 2.0 (95% confidence interval (CI) 1.6 to 2.6), NNT=8.9, for pain free at two hours in patients with acute migraine.[25] (LoE: 1++)

Naproxen and ibuprofen were also effective in relieving migraine-associated symptoms of nausea, photophobia, phonophobia and functional disability compared to placebo.[23,24] (LoE: 1++)

No serious adverse events were reported in the trials.[23-25] NSAIDs can cause gastrointestinal problems with long-term use.17 They should also be used with caution in patients with asthma as NSAIDs may worsen the condition.[17] (LoE: 1++)

In pregnancy, ibuprofen is the anti-inflammatory agent of first choice until gestational week 28. After 28 weeks of gestation, repeated use of ibuprofen should be avoided.[26] (LoE: 4)

Ibuprofen is the only NSAID which is licensed for patients with acute migraine.

PARACETAMOL

Empfehlung: Paracetamol (1,000 mg) can be considered for treatment of patients with acute migraine who are unable to take other acute therapies.

Due to its safety profile, paracetamol is first choice for the short-term relief of mild to moderate headache during any trimester of pregnancy.[22,26]

A Cochrane review identified three studies (717 participants) and reported a relative benefit of paracetamol 1,000 mg in achieving pain free at two hours as 1.8 (95% CI, 1.2 to 2.6), NNT=12, compared to placebo in patients with moderate or severe acute migraine.[27] (LoE: 1++)

In two studies including 1,140 patients with acute migraine, a combination of paracetamol 1,000 mg plus metoclopramide 10 mg had similar efficacy to sumatriptan 100 mg for headache relief at two hours (39% of participants reported relief using paracetamol and metoclopramide versus 42% for sumatriptan).[27] (LoE: 1++)

For pain free and sustained headache relief at 24 hours, paracetamol was more effective than placebo, but not compared to rizatriptan.[27] (LoE: 1++)

No serious adverse events were reported in the trials. Paracetamol is better tolerated than NSAIDs or triptans.[27] (LoE: 1++)

Paracetamol is commonly used in all trimesters of pregnancy although routine use should be avoided.

ANTIEMETICS

Empfehlung: Metoclopramide (10 mg) or prochlorperazine (10 mg) can be considered in the treatment of headache in patients with acute migraine. They can be used either as an oral or parenteral formulation depending on presentation and setting.

Empfehlung: Metoclopramide (10 mg) or prochlorperazine (10 mg) should be considered for patients presenting with migraine-associated symptoms of nausea or vomiting. They can be used either as an oral or parenteral formulation depending on presentation and setting.

Metoclopramide should not be used regularly due to the risk of extrapyramidal side effects.

Metoclopramide 10 mg (oral) in combination with aspirin 900 mg had similar efficacy to 100 mg sumatriptan in achieving the outcome of pain free at two hours.[21] Similar results were found for paracetamol 1,000 mg combined

with metoclopramide 10 mg versus sumatriptan.[27] However, aspirin and metoclopramide provided significantly better relief of associated symptoms, with an NNT of 2.6 (95% CI 2.1 to 3.1). It was particularly beneficial in reducing vomiting, NNT=2.1 (95% CI 1.5 to 3.7).[21] (LoE: 1++)

A randomised controlled trial (RCT) comparing different doses of metoclopramide found that all doses provided an improvement in pain response, measured using an 11-point numerical rating score for pain (NRS). Most patients improved by more than 50%. Individual improvement with metoclopramide was 4.7 NRS units for 10 mg, 4.9 for 20 mg and 5.3 for 40 mg.[28] (LoE: 1+)

A meta-analysis found that phenothiazines are superior to placebo for complete headache relief up to one hour after treatment (odds ratio (OR) 15.02, 95% CI 7.57 to 29.82). There was no significant difference in efficacy for complete headache relief when compared to metoclopramide.[29] (LoE: 1+)

Both prochlorperazine 10 mg and metoclopramide 20 mg (both coadministered with diphenhydramine and given intravenously) were found to be effective for pain relief at one hour for patients with acute migraine, as recorded on the NRS scale. At two hours the NRS for pain after treatment with prochlorperazine was 6.4 from a baseline NRS of 8.4, and for metoclopramide 5.9 from a baseline NRS of 8.8. The overall difference was 0.6 (95% CI -0.6 to 1.8), with an NNT of 17 for pain free at two hours.[30] (LoE: 1+)

Reporting of side effects was inconsistent amongst trials.[21,29] Most side effects were minor.[21] Akathisia was reported in trials of metoclopramide and prochlorperazine in 5–9% of participants.[28,30] Drowsiness and dizziness was also noted. More dropouts were noted as the dose of metoclopramide increased.[28] (LoE: 1+)

TRIPTANS

Empfehlung: Triptans are recommended as first-line treatment for patients with acute migraine. The first choice is sumatriptan (50–100 mg), but others should be offered if sumatriptan fails.

Empfehlung: In patients with severe acute migraine or early vomiting, nasal zolmitriptan or subcutaneous sumatriptan should be considered.

Empfehlung: Triptans are recommended for the treatment of patients with acute migraine associated with menstruation.

Empfehlung: Sumatriptan can be considered for treatment of acute migraine in pregnant women in all stages of pregnancy. The risks associated with use should be discussed before commencing treatment.

For patients experiencing acute migraine, triptans are superior to placebo, for pain relief, pain free within two hours and sustained pain relief at 24 hours.[31-35] (LoE: 1++)

An overview of Cochrane reviews reported that sumatriptan is an effective abortive treatment for acute migraine episodes.[33] The subcutaneous route is the most effective in terms of pain relief at two hours from moderate to severe baseline pain, with an NNT of 2.5 for 4 mg and 2.3 for a 6 mg dose. Efficacy was significantly improved if treatment was taken early, while pain was mild. For oral sumatriptan 50 mg the NNT for pain free at two hours was 6.1 for moderate to severe baseline pain and 4.4 for mild baseline pain. For 100 mg sumatriptan the NNT was 4.7 for pain free at two hours for moderate to severe pain and 2.4 for mild pain. Intranasal sumatriptan is also effective for pain free at two hours (NNT=3.1).[33] (LoE: 1++)

In studies comparing sumatriptan to other triptans, zolmitriptan and almotriptan showed similar efficacy.[33] Rizatriptan 10 mg was superior to all doses of sumatriptan for achieving pain free at two hours. Rizatriptan 5 mg had similar efficacy to sumatriptan 50 mg. Eletriptan 40 mg and 80 mg was superior to both doses of sumatriptan for the outcome of pain free at two hours and was associated with reduced need for rescue medication.[33] (LoE: 1++)

Compared to other therapies, sumatriptan 100 mg was superior for achieving pain free at two hours than aspirin 900 mg with metoclopramide 10 mg, or paracetamol 1,000 mg and metoclopramide 10 mg.[3]3 Sumatriptan was superior to effervescent aspirin 1,000 mg for headache relief at two hours.[33] (LoE: 1++)

For patients with menstrually-related migraine (MRM), sumatriptan resulted in a therapeutic gain with 25% of patients pain free at two hours with 50 mg and 34% with 100 mg compared to placebo.[35] Rizatriptan, frovatriptan and zolmitriptan were also reported to provide benefit for acute treatment of patients with MRM.[34,35] (LoE: 1++)

Adverse events reported in the trials were described as mild to moderate. Serious adverse events were rare.[33 31] (LoE: 1++)

Patients using rizatriptan and propranolol should be given a maximum dose of 5 mg rizatriptan due to the risk of interactions and rizatriptan should not be taken within two hours of taking propranolol.[17]

One study of cardiovascular outcomes with triptan use reported an OR of 0.86 (95% CI 0.52 to 1.43), for a serious cardiovascular event.[36] Triptans are contraindicated in patients with uncontrolled hypertension and in symptomatic

cardiovascular and cerebrovascular disease.[17] Trials of triptans have focused on a population aged 18–65 years. There is therefore no information on triptan use in the over 65s. Hypertension, cardiovascular disease and cerebrovascular disease are all more common in older people. Age is not a contraindication to use of triptans but age and vascular risk factors should be taken into account before prescribing triptans in the over 65s.[17] (LoE: 2++)

The United States Food and Drug Administration (FDA) issued a warning following a small number of case reports of serotonin syndrome in patients whilst taking triptans and selective serotonin reuptake inhibitors (SSRIs). This has been reviewed and a consensus statement produced by the American Headache Society. Clinical information in the FDA report was lacking and it was concluded that there is insufficient information to determine whether there is an increased risk of serotonin syndrome in patients taking triptans and SSRIs together compared with patients taking SSRIs alone. Given the frequency of coprescribing any risk is very small. It is therefore reasonable to prescribe triptans in patients on SSRIs.[37] (LoE: 4)

Registry data has given increasing confidence in the use of triptans in pregnancy. A meta-analysis on the use of triptans, in particular sumatriptan, at all stages of pregnancy compared with women with migraine who did not use triptans showed that the use of triptans in pregnancy is not associated with an increased risk of major congenital malformation or prematurity.[38] This is supported by an additional cohort study.[39] The risk of spontaneous abortion rates was reported to be higher (OR 1.41, 95% CI 1.11 to 1.80) in the meta-analysis, but this was not assessed in all of the studies and was based on a small number of patients.38 A more recent, larger cohort study (432 women) reported there was no increased risk of spontaneous abortion with triptan use.[39] (LoE: 2++)

A further cohort study, where women completed validated questionnaires about their child at 18 and 36 months, suggested that prenatal triptan use (primarily in the first trimester) may be associated with externalising behaviour problems (1.36-fold risk).[40] The evidence is subject to possible confounders and should be interpreted with caution. (LoE: 2+)

Sumatriptran is the preferred triptan based on efficacy, safety profile and cost. For patients with early vomiting, a nasal or subcutaneous triptan may be more effective. Nasal zolmitriptan 5 mg and sumatriptan 6 mg subcutaneous are effective (see Table 1, section 3.9). Where treatment with paracetamol (all trimesters) or ibuprofen (first and second trimester only) fail, the use of triptans, in particular sumatriptan, in all stages of pregnancy can be considered. None of the triptans are classed as non-teratogenic.

COMBINED THERAPIES

Empfehlung: Combination therapy using sumatriptan (50–85 mg) and naproxen (500 mg) should be considered for the treatment of patients with acute migraine.

A combination of sumatriptan 50–85 mg and naproxen 500 mg is better than placebo or monotherapy with active comparators in patients with acute migraine.[41] Fifty percent of patients with mild pain were pain free at two hours with combination therapy compared to 18% in the placebo group (NNT=3.1, 95% CI 2.9 to 3.5). When baseline pain was moderate to severe the NNT was 4.9 (95% CI 4.3 to 5.7) compared to placebo.41 The associated features of nausea, photophobia, phonophobia and functional disability were also better managed when combination therapy was used compared to placebo or monotherapy.[41] (LoE: 1++)

The relative benefit of combination therapy when compared to sumatriptan alone was 1.4 with a NNT of 10. However, compared to naproxen alone combination therapy was clearly superior, with a relative benefit of 2.0, NNT=6.1.[41] (LoE: 1++)

Adverse effects were more common with combination therapy than placebo or naproxen alone, but were reported to be mild.[41] (LoE: 1++)

STEROIDS

Two meta-analyses reported that use of steroids (prednisolone or dexamethasone) in addition to other acute treatments provided a small benefit in reducing the rate of moderate or severe headache at 24–72 hours (NNT=10).[42,43] The studies included in the meta-analyses were small and some reported no statistical difference to placebo. There was also heterogeneity in the additional acute therapies used. Pooled data from six studies reporting a secondary outcome of totally resolved migraine showed no significant benefit from steroids compared to placebo.[43] (LoE: 1+)

Adverse events were mild and transient.[42,43] In all but one study steroids were delivered intravenously to patients presenting to the emergency department. Intravenous steroids are not a viable option in routine practice. (LoE: 1+)

No evidence was identified on the use of prednisolone as a tapered treatment in patients with prolonged migraine (>3 days).

Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 11 of 12, November 2022) am 24.11.2022

#	Suchfrage
1	MeSH descriptor: [Migraine Disorders] explode all trees
2	(migrain*):ti,ab,kw
3	(hemicrania*):ti,ab,kw
4	#1 OR #2 OR #3
5	#4 with Cochrane Library publication date from Nov 2017 to present, in Cochrane Reviews

Systematic Reviews in PubMed am 24.11.2022

verwendete Suchfilter:
Konsentierter Standardfilter für Systematische Reviews (SR), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 02.01.2020.

#	Suchfrage
1	"migraine disorders"[mh]
2	migrain*[tiab]
3	hemicrania*[tiab]
4	#1 OR #2 OR #3
5	(#4) AND (((Meta-Analysis[ptyp] OR systematic[sb] OR ((systematic review [ti] OR meta-analysis[pt] OR meta-analysis[ti] OR systematic literature review[ti] OR this systematic review[tw] OR pooling project[tw] OR (systematic review[tiab] AND review[pt]) OR meta synthesis[ti] OR meta-analy*[ti] OR integrative review[tw] OR integrative research review[tw] OR rapid review[tw] OR umbrella review[tw] OR consensus development conference[pt] OR practice guideline[pt] OR drug class reviews[ti] OR cochrane database syst rev[ta] OR acp journal club[ta] OR health technol assess[ta] OR evid rep technol assess summ[ta] OR jbi database system rev implement rep[ta]) OR (clinical guideline[tw] AND management[tw]) OR ((evidence based[ti] OR evidence-based medicine[mh] OR best practice*[ti] OR evidence synthesis[tiab]) AND (review[pt] OR diseases category[mh] OR behavior and behavior mechanisms[mh] OR therapeutics[mh] OR evaluation study[pt] OR validation study[pt] OR guideline[pt] OR pmcbook)) OR ((systematic[tw] OR systematically[tw] OR critical[tiab] OR (study selection[tw]) OR (predetermined[tw] OR inclusion[tw] AND criteri* [tw]) OR exclusion criteri*[tw] OR main outcome measures[tw] OR standard of care[tw] OR standards of care[tw]) AND (survey[tiab] OR surveys[tiab] OR overview*[tw] OR review[tiab] OR reviews[tiab] OR search*[tw] OR handsearch[tw] OR analysis[ti] OR critique[tiab] OR appraisal[tw] OR (reduction[tw] AND (risk[mh] OR risk[tw]) AND (death OR recurrence))) AND (literature[tiab] OR articles[tiab] OR publications[tiab] OR publication [tiab] OR bibliography[tiab] OR bibliographies[tiab] OR published[tiab] OR pooled data[tw] OR unpublished[tw] OR citation[tw] OR citations[tw] OR database[tiab] OR internet[tiab] OR textbooks[tiab] OR references[tw] OR scales[tw] OR papers[tw] OR datasets[tw]

#	Suchfrage
	OR trials[tiab] OR meta-analy*[tw] OR (clinical[tiab] AND studies[tiab]) OR treatment outcome[mh] OR treatment outcome[tw] OR pmcbook)) NOT (letter[pt] OR newspaper article[pt])) OR Technical Report[ptyp]) OR (((((trials[tiab] OR studies[tiab] OR database*[tiab] OR literature[tiab] OR publication*[tiab] OR Medline[tiab] OR Embase[tiab] OR Cochrane[tiab] OR Pubmed[tiab])) AND systematic*[tiab] AND (search*[tiab] OR research*[tiab]))) OR ((((((((((HTA[tiab]) OR technology assessment*[tiab]) OR technology report*[tiab]) OR (systematic*[tiab] AND review*[tiab])) OR (systematic*[tiab] AND overview*[tiab])) OR meta-analy*[tiab]) OR (meta[tiab] AND analyz*[tiab])) OR (meta[tiab] AND analys*[tiab])) OR (meta[tiab] AND analyt*[tiab]))) OR (((review*[tiab]) OR overview*[tiab]) AND ((evidence[tiab]) AND based[tiab]))))))
6	(#5) AND ("2017/11/01"[PDAT] : "3000"[PDAT])
7	(#6) NOT "The Cochrane database of systematic reviews"[Journal]
8	(#7) NOT (retracted publication [pt] OR retraction of publication [pt])

Leitlinien in PubMed am 24.11.2022

verwendete Suchfilter:
Konsentierter Standardfilter für Leitlinien (LL), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 21.06.2017.

#	Suchfrage
1	"migraine disorders"[mh]
2	"migrain*"[ti]
3	"hemicrania*"[ti]
4	"headache disorders, primary"[mh:noexp]
5	"Headache Disorders"[mh:noexp]
6	"headache"[majr]
7	"headache*"[ti]
8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
9	(#8) AND (Guideline[ptyp] OR Practice Guideline[ptyp] OR guideline*[Title] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] OR recommendation*[ti])
10	(#9) AND ("2017/11/01"[PDAT] : "3000"[PDAT])
11	(#10) NOT (retracted publication [pt] OR retraction of publication [pt])

Iterative Handsuche nach grauer Literatur, abgeschlossen am 25.11.2022

- Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)
- Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF)

- National Institute for Health and Care Excellence (NICE)
- Scottish Intercollegiate Guideline Network (SIGN)
- World Health Organization (WHO)

- Dynamed / EBSCO
- Guidelines International Network (GIN)
- Trip Medical Database

Referenzen

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2. **Diener HC, Gaul C, Lehmacher W, Weiser T.** Aspirin, paracetamol (acetaminophen) and caffeine for the treatment of acute migraine attacks: a systemic review and meta-analysis of randomized placebo-controlled trials. Eur J Neurol 2022;29(1):350-357.
3. **Scottish Intercollegiate Guidelines N.** Pharmacological management of migraine [online]. Edinburgh (GBR): SIGN; 2018. [Zugriff: 21.11.2022]. (SIGN Publication; Band 155). URL: https://www.sign.ac.uk/media/1091/sign155.pdf.
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5. **VanderPluym JH, Halker Singh RB, Urtecho M, Morrow AS, Nayfeh T, Torres Roldan VD, et al.** Acute treatments for episodic migraine in adults: a systematic review and meta-analysis. JAMA 2021;325(23):2357-2369.

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[B] **McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C.** PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. J Clin Epidemiol 2016;75:40-46. https://doi.org/10.1016/j.jclinepi.2016.01.0

Gemeinsamer Bundesausschuss

Schriftliche Beteiligung der wissenschaftlich-medizinischen Fachgesellschaften und der Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

- keine eingegangenen schriftlichen Rückmeldungen gem. § 7 Absatz 6 VerfO