Supplementary Online Content

Locher C, Kossowsky J, Koechlin H, et al. Efficacy, safety and acceptability of pharmacologic treatments for pediatric migraine prophylaxis: a systematic review and network meta-analysis. *JAMA Pediatr.* Published online February 10, 2020. doi:10.1001/jamapediatrics.2019.5856

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eAppendix 1. Search Terms

Medline Search Strategy (Adapted for other databases)

#	Searches
1	randomi* controlled trial.pt.
2	placebo.ab.
3	drug therapy.fs.
4	random*.ab.
5	trial.ab.
6	groups.ab.
7	1 or 2 or 3 or 4 or 5 or 6
8	exp animals/ not humans.sh.
9	7 not 8
10	exp migraine disorders/dh, dt, pc, su, th
11	migrain*.mp.
12	vascular headaches/dt, pc, su, th
13	(vascular adj3 headache*).mp.
14	10 or 11 or 12 or 13
15	exp adolescent/ or exp child/ or exp infant/
16	(child* or adolescen* or infant* or juvenile* or pediatric* or paediatric* or
	developmental age).mp.
17	15 or 16
18	9 and 14 and 17

eAppendix 2. GRADE Ratings for each network

Using the Grading of Recommendations Assessment, Development, and Evaluation ratings (GRADE)³ as well as the recently developed web application to apply this framework⁴, we estimated the certainty of evidence for each network estimate according to the following criteria:

Study limitations (Within study bias): We categorized the overall risk of bias of each study. According to the Cochrane Risk of Bias tool⁵, we rated five risk of bias items (i.e., allocation sequence concealment, adequate blinding, incomplete outcome data, selective outcome reporting, and other potential threats to validity). We calculated the average risk of bias by building the mean of all risk of bias items. For example: a study would be judged as *medium* risk of bias [some concerns] when the individual items would be once *high risk* [major concerns], three times *low risk* [no concerns], and twice *medium OR unclear risk* [some concerns]. We then used the contribution matrix to calculate the percentage of contribution from each study, and finally assessed the study limitation for each network estimate based on the weighted average risk of bias of the contributing studies. We selected the rule "Average Risk of Bias" in order to calculate the within study bias.

Publication bias (Across studies bias): Since there is so far a lack of a concrete methodology of assessing across-studies bias (publication bias) in NMA, a comparison-adjusted funnel plot with accompanying Egger test for asymmetry was conducted.

Indirectness: We judged that there was no concern in this domain as the included studies matched our inclusion criteria and study questions.

Imprecision: In line with previous analyses⁶, we considered a clinically meaningful threshold for standardized mean difference (SMD) to be 0.20.

Heterogeneity: We evaluated the degree of concerns through comparing the clinical inference based on the 95% confidence intervals (CI) and that based on the 95% prediction interval (PI), the latter reflecting the degree of heterogeneity. Appling the same clinical inference framework as for imprecision, we saw no concerns in heterogeneity when the two judgements matched (e.g. no concern based on 95% CI and no concern based on 95% PI), some concerns when they differed by one degree (e.g. no concern based on 95% CI but some concerns based on 95% PI), and major concerns when they differed by two degrees (e.g. no concern based on 95% CI but major concerns based on 95% PI).

Incoherence (Inconsistency): For inconsistency, we looked at the results of side splitting and we saw major concerns when p<0.05 but no concern otherwise.

Efficacy

We found some concerns for *within-study bias* (i.e., study limitations) for several pair-wise comparisons. In terms of the *across-study bias* (i.e., publication bias), the Egger test for funnel plot asymmetry was non-significant (p=0.93) indicating that selection bias is not a big threat to the network meta-analysis. There was no concern for *indirectness*, since the included studies all matched our study questions. Evaluating *imprecision*, we found that the two statistically significant comparisons (i.e., propranolol vs placebo; topiramate vs. placebo) revealed a clinically significant effect size. Furthermore, we examine *heterogeneity*, which is represented by the 95% prediction interval for each individual comparison. For both, propranolol vs. placebo and topiramate vs. placebo, the 95% prediction interval was non-significant. Furthermore, we found evidence for substantial and statistically significant heterogeneity in the network (within design Q=26.13, p<.001, tau²=0.18; I²=75.1%). Finally, there was no evidence of *inconsistency* between the direct and indirect evidence, i.e., all p-values were above 5%. Also, we identified no evidence of inconsistency in the NMA when calculating the global design-by-treatment interaction test (between designs Q=2.08, p=.556).

Comparison	Number of Studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
		Mixe	d evidence					
Butterbur root extract vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low 🔹
Cinnarizine vs Placebo	1	No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate -
Cinnarizine vs Propranolol	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
CoEnzyme Q10 vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Flunarizine vs Placebo	1	Some concerns		No concerns	Some concerns	Some concerns	No concerns	Low -
L-5-Hydroxytryptophan (L-5HTP) vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Nimodipine vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Placebo vs Propranolol	1	Some concerns		No concerns	No concerns	Major concerns	No concerns	Low
Placebo vs Riboflavin	3	No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate 🔻
Placebo vs Sodium Valproate	1	No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate -
Placebo vs Topiramate	2	Some concerns		No concerns	No concerns	Major concerns	No concerns	Low -
Pregabalin vs Propranolol	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low 🔹
Propranolol vs Sodium Valproate	2	Some concerns		No concerns	Some concerns	Some concerns	No concerns	Low -
Propranolol vs Topiramate	2	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •

	Indire	ct evidence					
Butterbur root extract vs Cinnarizine	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Butterbur root extract vs CoEnzyme Q10	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Butterbur root extract vs Flunarizine	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Butterbur root extract vs L-5-Hydroxytryptophan (L-5HTP)	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Butterbur root extract vs Nimodipine	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Butterbur root extract vs Pregabalin	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Butterbur root extract vs Propranolol	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Butterbur root extract vs Riboflavin	 No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate •
Butterbur root extract vs Sodium Valproate	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Butterbur root extract vs Topiramate	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Cinnarizine vs CoEnzyme Q10	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Cinnarizine vs Flunarizine	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Cinnarizine vs L-5-Hydroxytryptophan (L-5HTP)	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Cinnarizine vs Nimodipine	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Cinnarizine vs Pregabalin	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Cinnarizine vs Riboflavin	 No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate •
Cinnarizine vs Sodium Valproate	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Cinnarizine vs Topiramate	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
CoEnzyme Q10 vs Flunarizine	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
CoEnzyme Q10 vs L-5-Hydroxytryptophan (L-5HTP)	 Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •

CoEnzyme Q10 vs Nimodipine	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
CoEnzyme Q10 vs Pregabalin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
CoEnzyme Q10 vs Propranolol	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
CoEnzyme Q10 vs Riboflavin	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate •
CoEnzyme Q10 vs Sodium Valproate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
CoEnzyme Q10 vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Flunarizine vs L-5-Hydroxytryptophan (L-5HTP)	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Flunarizine vs Nimodipine	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Flunarizine vs Pregabalin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Flunarizine vs Propranolol	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Flunarizine vs Riboflavin	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate •
Flunarizine vs Sodium Valproate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Flunarizine vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
L-5-Hydroxytryptophan (L-5HTP) vs Nimodipine	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
L-5-Hydroxytryptophan (L-5HTP) vs Pregabalin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
L-5-Hydroxytryptophan (L-5HTP) vs Propranolol	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
L-5-Hydroxytryptophan (L-5HTP) vs Riboflavin	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate •
L-5-Hydroxytryptophan (L-5HTP) vs Sodium Valproate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
L-5-Hydroxytryptophan (L-5HTP) vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Nimodipine vs Pregabalin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Nimodipine vs Propranolol	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •

Nimodipine vs Riboflavin	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate •
Nimodipine vs Sodium Valproate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Nimodipine vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Placebo vs Pregabalin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Pregabalin vs Riboflavin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Pregabalin vs Sodium Valproate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Pregabalin vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Propranolol vs Riboflavin	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate -
Riboflavin vs Sodium Valproate	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate -
Riboflavin vs Topiramate	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate -
Sodium Valproate vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •

Acceptability

We did not find evidence for heterogeneity (within design Q=1.99, p=.851, tau²=0.00; I²=0%). There was no evidence of inconsistency between the direct and indirect evidence, i.e., all p-values were above 5%. Also, we found no evidence of inconsistency in the NMA when calculating the global design-by-treatment interaction test (between designs Q=3.14, p=.208).

Comparison	Number of Studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
			Mixed evidence					
Amitriptylin vs Melatonin	1	No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate 🔽
Butterbur root extract vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Cinnarizine vs Placebo	1	No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate 🔽
Cinnarizine vs Propranolol	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low
CoEnzyme Q10 vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Flunarizine vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Melatonin vs Placebo	1	No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate 🝷
Nimodipine vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low
Placebo vs Riboflavin	3	No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate -
Placebo vs Sodium Valproate	1	No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate 🝷
Placebo vs Topiramate	2	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Pregabalin vs Propranolol	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Propranolol vs Sodium Valproate	2	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Propranolol vs Topiramate	2	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -

		Indirect evidence			
Amitriptylin vs Butterbur root extract	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate •
Amitriptylin vs Cinnarizine	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate -
Amitriptylin vs CoEnzyme Q10	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate -
Amitriptylin vs Flunarizine	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate -
Amitriptylin vs Nimodipine	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate -
Amitriptylin vs Placebo	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate -
Amitriptylin vs Pregabalin	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate -
Amitriptylin vs Propranolol	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate -
Amitriptylin vs Riboflavin	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate -
Amitriptylin vs Sodium Valproate	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate -
Amitriptylin vs Topiramate	 No concerns		No concerns Major concerns	No concerns No concerns	Moderate -
Butterbur root extract vs Cinnarizine	 Some concerns		No concerns Major concerns	No concerns No concerns	Low -
Butterbur root extract vs CoEnzyme Q10	 Some concerns		No concerns Major concerns	No concerns No concerns	Low -
Butterbur root extract vs Flunarizine	 Some concerns		No concerns Major concerns	No concerns No concerns	Low -
Butterbur root extract vs Melatonin	 Some concerns		No concerns Major concerns	No concerns No concerns	Low -
Butterbur root extract vs Nimodipine	 Some concerns		No concerns Major concerns	No concerns No concerns	Low -
Butterbur root extract vs Pregabalin	 Some concerns		No concerns Major concerns	No concerns No concerns	Low -
Butterbur root extract vs Propranolol	 Some concerns		No concerns Major concerns	No concerns No concerns	Low -
Butterbur root extract vs Riboflavin	 Some concerns		No concerns Major concerns	No concerns No concerns	Low -
Butterbur root extract vs Sodium Valproate	 Some concerns		No concerns Major concerns	No concerns No concerns	Low -

Butterbur root extract vs Topiramate	 Some concerns	 No concerns		No concerns No concerns	Low -
Cinnarizine vs CoEnzyme Q10	 Some concerns	 No concerns	Major concerns	No concerns No concerns	Low
Cinnarizine vs Flunarizine	 Some concerns	 No concerns		No concerns No concerns	Low -
Cinnarizine vs Melatonin	 No concerns	 No concerns	Major concerns	No concerns No concerns	Moderate -
Cinnarizine vs Nimodipine	 Some concerns	 No concerns	Major concerns	No concerns No concerns	Low -
Cinnarizine vs Pregabalin	 Some concerns	 No concerns	Major concerns	No concerns No concerns	Low -
Cinnarizine vs Riboflavin	 No concerns	 No concerns	Major concerns	No concerns No concerns	Moderate -
Cinnarizine vs Sodium Valproate	 No concerns	 No concerns	Major concerns	No concerns No concerns	Moderate -
Cinnarizine vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns No concerns	Low -
CoEnzyme Q10 vs Flunarizine	 Some concerns	 No concerns	Major concerns	No concerns No concerns	Low
CoEnzyme Q10 vs Melatonin	 Some concerns	 No concerns	Major concerns	No concerns No concerns	Low -
CoEnzyme Q10 vs Nimodipine	 Some concerns	 No concerns	Major concerns	No concerns No concerns	Low
CoEnzyme Q10 vs Pregabalin	 Some concerns	 No concerns	Major concerns	No concerns No concerns	Low
CoEnzyme Q10 vs Propranolol	 Some concerns	 No concerns	Major concerns	No concerns No concerns	Low
CoEnzyme Q10 vs Riboflavin	 Some concerns	 No concerns	Major concerns	No concerns No concerns	Low -
CoEnzyme Q10 vs Sodium Valproate	 Some concerns	 No concerns		No concerns No concerns	Low -
CoEnzyme Q10 vs Topiramate	 Some concerns	 No concerns		No concerns No concerns	Low -
Flunarizine vs Melatonin	 Some concerns	 No concerns		No concerns No concerns	Low -
Flunarizine vs Nimodipine	 Some concerns	 No concerns		No concerns No concerns	Low -
Flunarizine vs Pregabalin	 Some concerns	 No concerns		No concerns No concerns	Low -

Flunarizine vs Propranolol	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Flunarizine vs Riboflavin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Flunarizine vs Sodium Valproate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Flunarizine vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Melatonin vs Nimodipine	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Melatonin vs Pregabalin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Melatonin vs Propranolol	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate -
Melatonin vs Riboflavin	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate -
Melatonin vs Sodium Valproate	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate -
Melatonin vs Topiramate	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate -
Nimodipine vs Pregabalin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Nimodipine vs Propranolol	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Nimodipine vs Riboflavin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Nimodipine vs Sodium Valproate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Nimodipine vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Placebo vs Pregabalin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Placebo vs Propranolol	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Pregabalin vs Riboflavin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Pregabalin vs Sodium Valproate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Pregabalin vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low -

Propranolol vs Riboflavin	 No concerns	 No concerns		No concerns	No concerns	Moderate -
Riboflavin vs Sodium Valproate	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate -
Riboflavin vs Topiramate	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate -
Sodium Valproate vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low -

Safety

Studies showed no significant heterogeneity (within design Q=0.21, p=.900, tau2=0.00; $I^2=0\%$). In terms of inconsistency, we found no differences between the direct and indirect evidence. Finally, there was no evidence of inconsistency in the NMA according to the global design-by-treatment interaction test (between designs Q=0.12, p=.732).

Comparison	Number of Studies	Within-study bias	Across-studies bias	Indirectness	Imprecision	Heterogeneity	Incoherence	Confidence rating
			Mixed evidence					
Butterbur root extract vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low •
Cinnarizine vs Propranolol	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Flunarizine vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Nimodipine vs Placebo	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Placebo vs Riboflavin	1	No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate -
Placebo vs Sodium Valproate	1	No concerns		No concerns	Major concerns	No concerns	No concerns	Moderate -
Placebo vs Topiramate	1	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Propranolol vs Sodium Valproate	2	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -
Propranolol vs Topiramate	2	Some concerns		No concerns	Major concerns	No concerns	No concerns	Low -

		Indirect evidence				
Butterbur root extract vs Cinnarizine	 Some concerns		No concerns	Major concerns	No concerns No concerns	Low -
Butterbur root extract vs Flunarizine	 Some concerns		No concerns		No concerns No concerns	Low -
Butterbur root extract vs Nimodipine	 Some concerns		No concerns		No concerns No concerns	Low -
Butterbur root extract vs Propranolol	 Some concerns		No concerns		No concerns No concerns	Low -
Butterbur root extract vs Riboflavin	 Some concerns		No concerns		No concerns No concerns	Low -
Butterbur root extract vs Sodium Valproate	 Some concerns		No concerns		No concerns No concerns	Low -
Butterbur root extract vs Topiramate	 Some concerns		No concerns	Major concerns	No concerns No concerns	Low -
Cinnarizine vs Flunarizine	 Some concerns		No concerns	Major concerns	No concerns No concerns	Low -
Cinnarizine vs Nimodipine	 Some concerns		No concerns	Major concerns	No concerns No concerns	Low -
Cinnarizine vs Placebo	 Some concerns		No concerns	Major concerns	No concerns No concerns	Low -
Cinnarizine vs Riboflavin	 Some concerns		No concerns		No concerns No concerns	Low -
Cinnarizine vs Sodium Valproate	 Some concerns		No concerns	Major concerns	No concerns No concerns	Low -
Cinnarizine vs Topiramate	 Some concerns		No concerns	Major concerns	No concerns No concerns	Low -
Flunarizine vs Nimodipine	 Some concerns		No concerns	Major concerns	No concerns No concerns	Low -
Flunarizine vs Propranolol	 Some concerns		No concerns		No concerns No concerns	Low -
Flunarizine vs Riboflavin	 Some concerns		No concerns		No concerns No concerns	Low -
Flunarizine vs Sodium Valproate	 Some concerns		No concerns	Major concerns	No concerns No concerns	Low -
Flunarizine vs Topiramate	 Some concerns		No concerns	Major concerns	No concerns No concerns	Low -

Nimodipine vs Propranolol	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Nimodipine vs Riboflavin	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Nimodipine vs Sodium Valproate	 Some concerns	 No concerns		No concerns	No concerns	Low -
Nimodipine vs Topiramate	 Some concerns	 No concerns		No concerns	No concerns	Low -
Placebo vs Propranolol	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •
Propranolol vs Riboflavin	 No concerns	 No concerns		No concerns	No concerns	Moderate -
Riboflavin vs Sodium Valproate	 No concerns	 No concerns		No concerns	No concerns	Moderate -
Riboflavin vs Topiramate	 No concerns	 No concerns	Major concerns	No concerns	No concerns	Moderate -
Sodium Valproate vs Topiramate	 Some concerns	 No concerns	Major concerns	No concerns	No concerns	Low •

eAppendix 3. Details on Inconsistency

Efficacy – Local approach

Back-calculation method to split direct and indirect evidence

Random effects model:

comparison k prop mm direct iniff z p-value Butterbur root extract:(Grayme QU 0 0										
Butterbur root extract:(Ginorizine 0 0 -0.238 -0.238 -0.239 Butterbur root extract:(Funorizine 0 0 -0.239 -0.239 -0.239 Butterbur root extract:(Finorizine 0 0 -0.268 -0.268 -0.268 Butterbur root extract:Finorizine 0 0 -0.268 -0.2680 -0.2680 Butterbur root extract:Finorizine 0 0 -0.613 -0.613 -0.613 Butterbur root extract:Finorizine 0 0 -0.238 -0.613 -0.613 Butterbur root extract:Finorizine 0 0 -0.238 -0.238 -0.238 Butterbur root extract:Finorizine 0 0 -0.238 -0.238 -0.338 Cinnarizine:Finorizine 0 0 -0.235 -0.238 -0.238 -0.238 Cinnarizine:Finorizine 0 0 -0.235 -0.233 -0.608 -0.808 -0.333 Cinnarizine:Finorizine 0 0 -0.235 -0.235 -0.235 -0.235 -0.235 -0.235 -0.235 -0.235 -0.235 -0.235 -0.235 -0.235	comparison	k	prop	nma	direct	indir.	Diff	z	p-value	
Butterbur root extract:(Danyme Q10 0 0 -0.934	•								P	
Butterbur root extract:Flumerizine 0 0 0.303 0.3039 0.3039 Butterbur root extract:Rimodipine 0 0 0.0000 0.0000 0.3039 Butterbur root extract:Propanolal 0 0 0.0000 0.0000 0.0000 Butterbur root extract:Propanolal 0 0 0.0000 0.0000 0.0000 Butterbur root extract:RiboTlavin 0 0 0.1947 0.01947 0.01947 Butterbur root extract:Topiranate 0 0 0.0235 0.02200 0.0220 Cinnarizine:Charge 010 0 0.0233 0.1233 0.0233 Cinnarizine:Charge 010 0 0 0.2335 0.2335 0.6000 0.85 0.3788 Cinnarizine:Charge 010 0 0 0.0233 0.1688 0.3788 Cinnarizine:Solum Valproxte 0 0 0.0333 0.6639 0.878 0.3788 Cinnarizine:Solum Valproxte 0 0 0.3334 0.6600 0.88 0.3788 Cinnarizine:Solum Valproxte 0 0 0.8335 0.6333 0.6335 0.6335							•	•	•	
Butterbur root extract:l-5-Hydroxytrpytophan (L-STP) 0 0 0.2688 0.2088 0.2088 0.2088 0.00000 0.0000 0.0000 0.0000 0.0000 0.00000 0.00000 0.0000 0.000	Butterbur root extract:CoEnzyme Q10	0	0	-0.2984		-0.2984				
Butterbur root extract:l-5-Hydroxytrpytophan (L-STP) 0 0 0.2688 0.2088 0.2088 0.2088 0.00000 0.0000 0.0000 0.0000 0.0000 0.00000 0.00000 0.0000 0.000	Butterbur root extract Elunarizine	Ø	Ø	-0 9319		-0 9319				
Butterbur root extract:Nimodipine 0 0 0.0000			_				•	•	•	
Butterbur root extract:Progenoli 0 0 -0.8139 . 0.8080 Butterbur root extract:Progenoli 0 0 -0.8139 . 0.8139 Butterbur root extract:Sodiawi Valprozet 0 0 -0.2175 . 0.2175 Butterbur root extract:Topiranate 0 0 -0.2080 . 0.2080 Cinnarizine:Conzyme Q10 0 0 -0.2381 . 0.2280 . 0.2280 Cinnarizine:Conzyme Q10 0 0 -0.2381 . 0.2383 . 0.2280 Cinnarizine:Conzyme Q10 0 0 -0.2381 . 0.2383 . 0.2383 Cinnarizine:Placebo 1 0.57 0 .0135 0 .01385 0 .01385 . 0.3185 Cinnarizine:Placebo 1 0.57 0 .0135 0 .0138 0 .0188 -0.6660 -0.8 80 0 .0788 Cinnarizine:Placebo 1 0 .57 0 .0135 0 .0138 0 .0188 -0.6660 -0.8 80 0 .0188 Cinnarizine:Placebo 1 0 .57 0 .0135 0 .0138 0 .0188 -0.6660 -0.8 80 0 .0188 Cinnarizine:Placebo 1 0 .0 .0135 0 .0138 0 .0188 0 .0188 0 .0188 0 .0188 Cinnarizine:Placebo 1 0 .0 .0135 0 .0138 0 .0188	Butterbur root extract:L-5-Hydroxytryptophan (L-5HIP)	0	0	0.2068			•	•	•	
Butterbur root extract:Progenoli 0 0 -0.8139 . 0.8080 Butterbur root extract:Progenoli 0 0 -0.8139 . 0.8139 Butterbur root extract:Sodiawi Valprozet 0 0 -0.2175 . 0.2175 Butterbur root extract:Topiranate 0 0 -0.2080 . 0.2080 Cinnarizine:Conzyme Q10 0 0 -0.2381 . 0.2280 . 0.2280 Cinnarizine:Conzyme Q10 0 0 -0.2381 . 0.2383 . 0.2280 Cinnarizine:Conzyme Q10 0 0 -0.2381 . 0.2383 . 0.2383 Cinnarizine:Placebo 1 0.57 0 .0135 0 .01385 0 .01385 . 0.3185 Cinnarizine:Placebo 1 0.57 0 .0135 0 .0138 0 .0188 -0.6660 -0.8 80 0 .0788 Cinnarizine:Placebo 1 0 .57 0 .0135 0 .0138 0 .0188 -0.6660 -0.8 80 0 .0188 Cinnarizine:Placebo 1 0 .57 0 .0135 0 .0138 0 .0188 -0.6660 -0.8 80 0 .0188 Cinnarizine:Placebo 1 0 .0 .0135 0 .0138 0 .0188 0 .0188 0 .0188 0 .0188 Cinnarizine:Placebo 1 0 .0 .0135 0 .0138 0 .0188	Butterbur root extract:Nimodipine	0	0	-0.0000		-0.0000				
Butterbur root extract:Pregabolin 0 0 0.8.033										
Butterbur root extract:Programolal 0 0 0.6018 - 0.6018 - 0.6018 - 0.018 Butterbur root extract:RiboToxin 0 0 0.61947 - 0.175 - 0.2175 - 0.2175 Butterbur root extract:Topiramte 0 0 0.6196 - 0.99676 - 0.9956 - 0.9956 - 0.9966 - 0.9966 - 0.99676 - 0.9956 - 0							•	•	•	
Butterbur root extract:Sidolfavin 0 0.1947 -0.1947 Butterbur root extract:Topiramate 0 0.2906 Butterbur root extract:Topiramate 0 0.4134 Cinnarizine:Fluanzizine 0 0.4134 Cinnarizine:Ture:Placebin 0 0.2535 .0.7253 Cinnarizine:Fluanzine:Proporabolin 0 0.2334 .0.6188 0.4118 Cinnarizine:Fluanzine:Topiramate 0 0.4234 Cinnarizine:Statin Valproate 0 0.4335 Cinnarizine:Statin Valproate 0 0.4335 Cofanzyme Q10:Fluanzine 0 0.4335 Cofanzyme Q10:Fluanzine 0 0.4335 Cofanzyme Q10:Fluanzine 0 0.4334	Butterbur root extract:Pregabalin	0	0	-0.8139		-0.8139				
Butterbur root extract:Sidolfavin 0 0.1947 -0.1947 Butterbur root extract:Topiramate 0 0.2906 Butterbur root extract:Topiramate 0 0.4134 Cinnarizine:Fluanzizine 0 0.4134 Cinnarizine:Ture:Placebin 0 0.2535 .0.7253 Cinnarizine:Fluanzine:Proporabolin 0 0.2334 .0.6188 0.4118 Cinnarizine:Fluanzine:Topiramate 0 0.4234 Cinnarizine:Statin Valproate 0 0.4335 Cinnarizine:Statin Valproate 0 0.4335 Cofanzyme Q10:Fluanzine 0 0.4335 Cofanzyme Q10:Fluanzine 0 0.4335 Cofanzyme Q10:Fluanzine 0 0.4334	Butterbur root extract:Propranolol	0	0	-0.6018		-0.6018				
Butterbur not extract:Softum Valproate 0 0 -0.275							•	•	•	
Butterbur root extract:Topiranate 0 0 -0.5986	Butterbur root extract:Riboflavin	0	0	-0.1947	•	-0.1947	•	•	•	
Cinnarizine:Fluanzizine (10 0 0 0.2200	Butterbur root extract:Sodium Valproate	0	0	-0.2175		-0.2175				
Cinnarizine:Fluanzizine (10 0 0 0.2200	•									
Cinnarizine:I-G-Hydroxytryptophan (L-SHTP) 0 0.7253	•		-				•	•	•	
Cinnarizine:L-5-Hydroxytryptophan (L-5HTP) 0 0 0.7253 0.7253 0.7253 Cinnarizine:Nanodjino 0 0.7253 0.5185 0.7318 0.8318 0.6600 0.88 0.3798 Cinnarizine:Propabali 0 0 0.2554 0.0255 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0	Cinnarizine:CoEnzyme Q10	0	0	0.2200		0.2200				
Cinnarizine:L-5-Hydroxytryptophan (L-5HTP) 0 0 0.7253 0.7253 0.7253 Cinnarizine:Nanodjino 0 0.7253 0.5185 0.7318 0.8318 0.6600 0.88 0.3798 Cinnarizine:Propabali 0 0 0.2554 0.0255 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0.02555 0	Cinnarizine: Flunarizine	0	0	-0.4134		-0.4134				
Cinnarizine:Hisolipine 0 0.5185 0.5335 0.5335 0.5335 0.5335 0.5355 0.5355 0.5355 0.5355 0.5155 0.5155 0.5155 0.5155 0.5137 0.1337 0.1337 0.1337 0.1337 0.1337 0.1337 0.1337 0.1337 0.1337 0.5135 0.5155 0.5155 0.5155 0.5155 0.5135					•		•	•	•	
Cinnarizine:Placebo 1 0.57 0.518 0.238 0.8318 0.8018 0.860 0.88 0.3798 Cinnarizine:Placebo 1 0.56 0.033 0.1688 0.4911 0.6600 0.88 0.3798 Cinnarizine:Riboflavin 0 0 0.333 0.333 0.333 0.333 Cinnarizine:Stodium Valproate 0 0 0.0319 0.3318 0.333 Cinnarizine:Toginame 0 0 0.0721 0.0721 0.533 Conzyme Q10:Flamparizine 0 0 0.0535 0.553 0.5 CoEnzyme Q10:Flamparizine 0 0 0.555 0.553 0.5 CoEnzyme Q10:Placebo 1 1.00 0.2984 0.2984 0.5 CoEnzyme Q10:Stodium Valproate 0 0 0.810 0.0810 0.5 CoEnzyme Q10:Stodium Valproate 0 0.0810 0.0810 0.5 CoEnzyme Q10:Stodium Valproate 0 0 0.0319 0.9319 0.5 Flunarizine:Hendpine 0 0 0.1337 0.1387 0.5 Flunarizine:Propranolol 0 0 0.3391 0.9319 0.5 Flunarizine:Propranolol 0 0 0.7372 0.7372 0.7724 0.7724 0.724 Flunarizine:Flucebo 1 1.00 0.2088 0.2068 0.5 L-5-Hydroxytryptophan (L-SHTP):Propranolol 0 0 0.4263 0.4243 0.5 Proppadolin:Placebo 1 1.00 0 0.4263 0.4243 0.5 Proppadolin:Placebo 1 0.00 0.4268 0.5033 0.4263 0.7 Proppadolin:Placebo 1 0.00 0.4268			0	0.7253	•	0.7253	•	•	•	
Cinnarizine:Placebo 1 0.57 0.518 0.238 0.8318 0.8018 0.860 0.88 0.3798 Cinnarizine:Placebo 1 0.56 0.033 0.1688 0.4911 0.6600 0.88 0.3798 Cinnarizine:Riboflavin 0 0 0.333 0.333 0.333 0.333 Cinnarizine:Stodium Valproate 0 0 0.0319 0.3318 0.333 Cinnarizine:Toginame 0 0 0.0721 0.0721 0.533 Conzyme Q10:Flamparizine 0 0 0.0535 0.553 0.5 CoEnzyme Q10:Flamparizine 0 0 0.555 0.553 0.5 CoEnzyme Q10:Placebo 1 1.00 0.2984 0.2984 0.5 CoEnzyme Q10:Stodium Valproate 0 0 0.810 0.0810 0.5 CoEnzyme Q10:Stodium Valproate 0 0.0810 0.0810 0.5 CoEnzyme Q10:Stodium Valproate 0 0 0.0319 0.9319 0.5 Flunarizine:Hendpine 0 0 0.1337 0.1387 0.5 Flunarizine:Propranolol 0 0 0.3391 0.9319 0.5 Flunarizine:Propranolol 0 0 0.7372 0.7372 0.7724 0.7724 0.724 Flunarizine:Flucebo 1 1.00 0.2088 0.2068 0.5 L-5-Hydroxytryptophan (L-SHTP):Propranolol 0 0 0.4263 0.4243 0.5 Proppadolin:Placebo 1 1.00 0 0.4263 0.4243 0.5 Proppadolin:Placebo 1 0.00 0.4268 0.5033 0.4263 0.7 Proppadolin:Placebo 1 0.00 0.4268	Cinnarizine:Nimodipine	0	0	0.5185		0.5185				
Cinnarizine:Prognobalin 0 0 0.0330 0.1682 0.4311 0.6600 0.88 0.3798 Cinnarizine:Tiopiramate 0 0.3213 0.3213 0.3798 Cinnarizine:Topiramate 0 0.8310 0.3213 0.3798 Cinnarizine:Topiramate 0 0.8023 0.8335 0.3234 CoEnzyme Q10:Li-S-Hydroxytryptohan (1-SHP) 0 0.5853 0.6353 0.3934 CoEnzyme Q10:Filesobalin 0 0.2384 0.2384 0.2384 0.2384 CoEnzyme Q10:Firegabalin 0 0.6337 0.6334 0.3934 0.3934 0.3934 CoEnzyme Q10:Firegabalin 0 0.6139 0.6319 0.3934 0.3934 0.3934 CoEnzyme Q10:Firegabalin 0 0.810 0.1387 1.387 0.5673 Flunarizine:Fropramolol 0 0.9319 0.9319 0.9319 0.9319 Flunarizine:Fropramolol 0 0.3301 0.3301 0.5331 0.572 Flunarizine:Fropromolol 0 0.3301	Cinnarizine·Placebo	1	0 57	0 5185	0 2318	0 8918	-0 6600	-0 88	0 3798	
Cinnarizine:Rofum Valproate 0 0.833 0.1688 -0.4911 0.6600 0.88 0.3798 Cinnarizine:Sofium Valproate 0 0.3236 0.3238 Cinnarizine:Sofium Valproate 0 0.3326 0.3238 CoEnzyme Q10:Flumarizine 0 0.6.635 0.6353 0.553 CoEnzyme Q10:Flumarizine 0 0.6.635 0.5653 0.5653 CoEnzyme Q10:Placebo 11.00 0.2884 0.2984 0.2984 CoEnzyme Q10:Propranolol 0 0.6355 0.6515 CoEnzyme Q10:Propranolol 0 0.6375 0.6155 CoEnzyme Q10:Propranolol 0 0.0397 0.6137 CoEnzyme Q10:Sodium Valproate 0 0.0819 0.9319 Flunarizine:KoFlumarizine 10 0.9319 0.9319 Flunarizine:Riboflum 0 0.9319 0.9319 Flunarizine:Riboflum 0 0.0372 0.7372 . Flunarizine:Riboflum 0 0.0313 0.9319 . Flunarizine:Riboflum 0 0.0313 0.9311 .							-0.0000	-0.00	0.5750	
Cinnarizine:Kiboflavin 0 0 0.3238 0.3238 Cinnarizine:Topiramate 0 0.8010 0.8010 Cinnarizine:Topiramate 0 0.8021 0.8021 CoEnzyme Q10:Flumarizine 0 0.8033 0.8033 CoEnzyme Q10:Flumarizine 0 0.8033 0.8033 CoEnzyme Q10:Flumarizine 0 0.2844 0.2844 CoEnzyme Q10:Froganoll 0 0.8034 0.8034 CoEnzyme Q10:Froganoll 0 0.8104 0.8034 CoEnzyme Q10:Froganoll 0 0.8104 0.80310 CoEnzyme Q10:Froganoll 0 0.8104 0.80310 CoEnzyme Q10:Froganoll 0 0.8104 0.80310 CoEnzyme Q10:Froganoll 0 0.8104 0.8104 Flunarizine:Frogabalin 0 0.3301 0.3301 0.5319	Cinnarizine:Pregabalin	0	0	-0.2954		-0.2954		•	•	
Cinnarizine:Kiboflavin 0 0 0.3238 0.3238 Cinnarizine:Topiramate 0 0.8010 0.8010 Cinnarizine:Topiramate 0 0.8021 0.8021 CoEnzyme Q10:Flumarizine 0 0.8033 0.8033 CoEnzyme Q10:Flumarizine 0 0.8033 0.8033 CoEnzyme Q10:Flumarizine 0 0.2844 0.2844 CoEnzyme Q10:Froganoll 0 0.8034 0.8034 CoEnzyme Q10:Froganoll 0 0.8104 0.8034 CoEnzyme Q10:Froganoll 0 0.8104 0.80310 CoEnzyme Q10:Froganoll 0 0.8104 0.80310 CoEnzyme Q10:Froganoll 0 0.8104 0.80310 CoEnzyme Q10:Froganoll 0 0.8104 0.8104 Flunarizine:Frogabalin 0 0.3301 0.3301 0.5319	Cinnarizine: Propranolol	1	0.62	-0.0833	0.1688	-0.4911	0.6600	0.88	0.3798	
Cinnarizine:Sodium Volproate 0 0.3010							0.0000	0.00	0.5150	
Cinnorizine:Topiramate 0 0 -0.0721 -0.6335 -0.6335 CoEnzyme Q10:Fluanzizine 0 0 -6.6335 -0.6335 -0.6335 CoEnzyme Q10:Fluanzizine 0 0 -2884 .0.2844 -0.3034 CoEnzyme Q10:Floreabel 11.00 0 -2884 .0.2844 -0.3034 CoEnzyme Q10:Floreabel 11.00 0 -0.3834 -0.3034 -0.3034 CoEnzyme Q10:Floreabel 0 0 -0.3837 -0.1037 -0.1037 CoEnzyme Q10:Floreabel 0 0 -0.2922 -0.2922 -0.2922 Flunarizine:Floreabel 11.00 0 9.319 0.3319 -0.1107 Flunarizine:Floreabel 11.00 0 0.3301 0.3301 -0.1202 Flunarizine:Siboflavin 0 0 0.7372 0.7372 -7372 Flunarizine:Siboflavin 0 0 0.3413 0.3413 -0.1108 L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.2668 -0.2668 -0.2668 L-5-Hydroxytryptophan (L-SHTP):Regabalin 0 0 -0.2668 -0.2668 -0.2668 L-5-Hydroxytryptophan (L-SHTP):Regabalin 0 0 -0.4268 -0.4243 -0.4243 L-5-Hydroxytryptophan (L-SHTP):Re			0	0.3238	•	0.3238	•	•	•	
Cinnorizine:Topiramate 0 0 -0.0721 -0.6335 -0.6335 CoEnzyme Q10:Fluanzizine 0 0 -6.6335 -0.6335 -0.6335 CoEnzyme Q10:Fluanzizine 0 0 -2884 .0.2844 -0.3034 CoEnzyme Q10:Floreabel 11.00 0 -2884 .0.2844 -0.3034 CoEnzyme Q10:Floreabel 11.00 0 -0.3834 -0.3034 -0.3034 CoEnzyme Q10:Floreabel 0 0 -0.3837 -0.1037 -0.1037 CoEnzyme Q10:Floreabel 0 0 -0.2922 -0.2922 -0.2922 Flunarizine:Floreabel 11.00 0 9.319 0.3319 -0.1107 Flunarizine:Floreabel 11.00 0 0.3301 0.3301 -0.1202 Flunarizine:Siboflavin 0 0 0.7372 0.7372 -7372 Flunarizine:Siboflavin 0 0 0.3413 0.3413 -0.1108 L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.2668 -0.2668 -0.2668 L-5-Hydroxytryptophan (L-SHTP):Regabalin 0 0 -0.2668 -0.2668 -0.2668 L-5-Hydroxytryptophan (L-SHTP):Regabalin 0 0 -0.4268 -0.4243 -0.4243 L-5-Hydroxytryptophan (L-SHTP):Re	Cinnarizine:Sodium Valproate	0	0	0.3010		0.3010				
CoEnzyme Q10:LFunarizine 0 0 0.5953 0.5353 0.5353 CoEnzyme Q10:Nimodipine 0 0 0.2984 0.2984 0.2984 CoEnzyme Q10:Placebo 11.00 0.2984 0.2984 0.2984 0.2984 CoEnzyme Q10:Placebo 11.00 0 0.2984 0.2984 0.2984 CoEnzyme Q10:Propranoloi 0 0.4334 -0.3034 0.0337 CoEnzyme Q10:Sodium Valproate 0 0 0.810 0.8810 0.8810 CoEnzyme Q10:Sodium Valproate 0 0 0.9319 0.9319 0.9319 0.9319 Flunarizine:Nimodipine 0 0 0.1337 1.1387 1.1387 1.1387 Flunarizine:Propranolol 0 0 0.3319 0.3319 Flunarizine:Propranolol 0 0 0.3301 0.3301 Flunarizine:Propranolol 0 0 0.3311 0.3313 Flunarizine:Propranolol 0 0 0.3413 0.3413 Flunarizine:Propranolol 1.00									-	
CoEnzyme Q10:L-5-Hydroxytryptophan (L-5HTP) 0 0 0.593 0.2984 0.2984 CoEnzyme Q10:Pregabalin 0 0 0.2984 0.2984 0.2984 CoEnzyme Q10:Pregabalin 0 0 0.3934 - 0.3934 CoEnzyme Q10:Pregabalin 0 0 0.3934 - 0.3934 CoEnzyme Q10:Stodium Valprotet 0 0 0.810 0.810 - CoEnzyme Q10:Stodium Valprotet 0 0 0.8110 0.8137 - CoEnzyme Q10:Stodium Valprotet 0 0 0.9319 0.9319 - - Flunarizine:Fluoratine:Pregabalin 0 0 0.3341 0.3391 - - Flunarizine:Riboflavin 0 0 0.7372 0.7372 - - Flunarizine:Sodium Valprote 0 0 0.7372 0.7372 - - Flunarizine:Sodium Valproteb 1 0 0.7372 0.7372 - - Fluoratizine:Sodium Valproteb 1 0 0.7372 0.7372 - - Fluoratizine:Sodium Valproteb 1 0							•	•	•	
CoEnzyme Q10:Ntmodipine 0 0 0.2984 0.2984 CoEnzyme Q10:Pregabalin 0 0 0.2984 0.2984 CoEnzyme Q10:Pregabalin 0 0 0.9394 0.5155 CoEnzyme Q10:Sofium Valproate 0 0 0.8139 0.1037 CoEnzyme Q10:Sofium Valproate 0 0 0.8130 0.1037 CoEnzyme Q10:Sofium Valproate 0 0 0.8130 0.1037 CoEnzyme Q10:Topiramet 0 0 0.9319 0.9319 0.9319 Flunarizine:Nemorizine:Nimodipine 0 0 0.9319 0.9319 0.9319 Flunarizine:Progranolol 0 0 0.3301 0.1180 0.1180 Flunarizine:Progranolol 0 0 0.3301 0.3301 0.1180 Flunarizine:Sofium Valproate 0 0 0.7372 0.7372 0.7372 Flunarizine:Sofium Valproate 0 0 0.744 0.7144 0.7144 L-5-Hydroxytryptophan (L-SHTP):Picpabalin 0 0 0.2068 0.2068 0.2068 L-5-Hydroxytryptophan (L-SHTP):Picparanolol 0 0 0.4016 0.7774	CoEnzyme Q10:Flunarizine	0	0	-0.6335		-0.6335				
CoEnzyme Q10:Ntmodipine 0 0 0.2984 0.2984 CoEnzyme Q10:Pregabalin 0 0 0.2984 0.2984 CoEnzyme Q10:Pregabalin 0 0 0.9394 0.5155 CoEnzyme Q10:Sofium Valproate 0 0 0.8139 0.1037 CoEnzyme Q10:Sofium Valproate 0 0 0.8130 0.1037 CoEnzyme Q10:Sofium Valproate 0 0 0.8130 0.1037 CoEnzyme Q10:Topiramet 0 0 0.9319 0.9319 0.9319 Flunarizine:Nemorizine:Nimodipine 0 0 0.9319 0.9319 0.9319 Flunarizine:Progranolol 0 0 0.3301 0.1180 0.1180 Flunarizine:Progranolol 0 0 0.3301 0.3301 0.1180 Flunarizine:Sofium Valproate 0 0 0.7372 0.7372 0.7372 Flunarizine:Sofium Valproate 0 0 0.744 0.7144 0.7144 L-5-Hydroxytryptophan (L-SHTP):Picpabalin 0 0 0.2068 0.2068 0.2068 L-5-Hydroxytryptophan (L-SHTP):Picparanolol 0 0 0.4016 0.7774			-							
Cofrayme Q10:Placebo 1 1.00 0.2984 0.2984 0.2984 0.2984 0.2984 0.51555 0.51555<							•	•	•	
CoEnzyme Q10:Pregabalin 0 0 -0.3155 CoEnzyme Q10:Stobflavin 0 0 -0.3034 CoEnzyme Q10:Stobflavin 0 0 0.01037 CoEnzyme Q10:Stobflavin 0 0 0.0237 CoEnzyme Q10:Stobflavin 0 0 0.0212 CoEnzyme Q10:Stobflavin 0 0 0.9319 0.9319 Flunarizine:L-5-Hydroxytrybtophon (L-SHTP) 0 0.1138 0.1180 Flunarizine:Propranolol 0 0 0.9319 0.9319 Flunarizine:Propranolol 0 0 0.1180 0.1180 Flunarizine:Sodium Valproate 0 0 0.3301 0.3301 Flunarizine:Sodium Valproate 0 0 0.7372 Flunarizine:Sodium Valproate 0 0 0.4313 0.3413 Flunarizine:Sodium Valproate 0 0 0.4206 <	CoEnzyme Q10:Nimodipine	0	0	0.2984	•	0.2984	•	•	•	
CoEnzyme Q10:Pregabalin 0 0 -0.3155 CoEnzyme Q10:Stobflavin 0 0 -0.3034 CoEnzyme Q10:Stobflavin 0 0 0.01037 CoEnzyme Q10:Stobflavin 0 0 0.0237 CoEnzyme Q10:Stobflavin 0 0 0.0212 CoEnzyme Q10:Stobflavin 0 0 0.9319 0.9319 Flunarizine:L-5-Hydroxytrybtophon (L-SHTP) 0 0.1138 0.1180 Flunarizine:Propranolol 0 0 0.9319 0.9319 Flunarizine:Propranolol 0 0 0.1180 0.1180 Flunarizine:Sodium Valproate 0 0 0.3301 0.3301 Flunarizine:Sodium Valproate 0 0 0.7372 Flunarizine:Sodium Valproate 0 0 0.4313 0.3413 Flunarizine:Sodium Valproate 0 0 0.4206 <	CoEnzyme 010:Placebo	1	1.00	0.2984	0.2984	-	-			
CoEnzyme Q10:RiboTavin 0 0 -0.934 -0.934 CoEnzyme Q10:RiboTavin 0 0 0.1037 CoEnzyme Q10:Sodium Valproate 0 0 0.0817 CoEnzyme Q10:Topiramate 0 0 0.9317 Flunarizine:LS-Hydroxytryptophan (L-SHTP) 0 0 0.9319 Flunarizine:Pregabalin 0 0 0.9319 0.9319 Flunarizine:Pregabalin 0 0 0.7372 0.7372 Flunarizine:Pregabalin 0 0 0.7314 0.7372 Flunarizine:Pregabalin 0 0 0.7372 0.7372 Flunarizine:Riboflavin 0 0 0.7343 0.3413 Flunarizine:Riboflavin 0 0 0.3413 0.3413 L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 0.8087 L-5-Hydroxytryptophan (L-SHTP):Sodium Valproate 0 0 0.4243 L-5-Hydroxytryptophan (L-SHTP):Sodium Valproate 0 0 0.4243							•	•	•	
CoEnzyme Q10:Riboflowin 0 0 0.1037 0.1037 CoEnzyme Q10:Sodium Valproate 0 0.0810 0.0810 0.0810 CoEnzyme Q10:Sodium Valproate 0 0.0810 0.0810 0.0810 Flunarizine:Nimodpine 0 0 0.9319 0.9319 0.9319 Flunarizine:Pregabalin 0 0 0.1180 0.1180 0.1180 Flunarizine:Pregabalin 0 0 0.3301 0.3301 0.3301 Flunarizine:Sodium Valproate 0 0 0.7174 0.7174 0.7144 Flunarizine:Sodium Valproate 0 0 0.3413 0.3413 0.4144 L-5-Hydroxytryptophan (L-SHTP):Proproanolol 0 0 0.3413 0.4144 0.7144 L-5-Hydroxytryptophan (L-SHTP):Proproanolol 0 0 0.3413 0.412 0.4416 L-5-Hydroxytryptophan (L-SHTP):Proproanolol 0 0 0.4016 0.40268 0.2068 0.2068 0.2068 0.2068 0.2068 0.2068 0.2068 0.2068 0.2068 0.2068 0.2068 0.2068 0.2068 0.2068 <							•	•	•	
CoEnzyme Q10:Sodium Valproate 0 0 0.0810 0.0810 0.0810 CoEnzyme Q10:Topiramate 0 0 0.02322 0.02322 0.02322 0.02322 Flunarizine:L-5-Hydroxytryptophan (L-SHTP) 0 0 1.1387 1.1387 0.02313 Flunarizine:Propranolol 0 0 0.0330 0.03301 0.03301 0.03301 Flunarizine:Propranolol 0 0 0.3301 0.3301 0.03301 0.03301 Flunarizine:Sodium Valproate 0 0 0.7372 0.7372 0.7372 0.7372 Flunarizine:Sodium Valproate 0 0 0.7344 0.0744 0.7144 0.7144 L-5-Hydroxytryptophan (L-SHTP):Programolo 1 0 0.2068 -0.2068 -0.2068 L-5-Hydroxytryptophan (L-SHTP):Programolo 1 0 0.4243 -0.4208 -1.0208 L-5-Hydroxytryptophan (L-SHTP):Programolo 0 0 -0.8087 -0.8087 -0.8087 L-5-Hydroxytryptophan (L-SHTP):Programolo 0 0 -0.4203 -0.7974 -0.7974 L-5-Hydroxytryptophan (L-SHTP):Forgabalin 0 0 -0.8087	CoEnzyme Q10:Propranolol	0	0	-0.3034		-0.3034				
CoEnzyme Q10:Sodium Valproate 0 0 0.0810 0.0810 0.0810 CoEnzyme Q10:Topiramate 0 0 0.02322 0.02322 0.02322 0.02322 Flunarizine:L-5-Hydroxytryptophan (L-SHTP) 0 0 1.1387 1.1387 0.02313 Flunarizine:Propranolol 0 0 0.0330 0.03301 0.03301 0.03301 Flunarizine:Propranolol 0 0 0.3301 0.3301 0.03301 0.03301 Flunarizine:Sodium Valproate 0 0 0.7372 0.7372 0.7372 0.7372 Flunarizine:Sodium Valproate 0 0 0.7344 0.0744 0.7144 0.7144 L-5-Hydroxytryptophan (L-SHTP):Programolo 1 0 0.2068 -0.2068 -0.2068 L-5-Hydroxytryptophan (L-SHTP):Programolo 1 0 0.4243 -0.4208 -1.0208 L-5-Hydroxytryptophan (L-SHTP):Programolo 0 0 -0.8087 -0.8087 -0.8087 L-5-Hydroxytryptophan (L-SHTP):Programolo 0 0 -0.4203 -0.7974 -0.7974 L-5-Hydroxytryptophan (L-SHTP):Forgabalin 0 0 -0.8087	CoEnzyme 010.Riboflavin	Ø	0	0 1037		0 1037				
CoEnzyme Q10:Topiramete 0 0 -0.2322 -0.2322 Flunarizine:L-5-Hydroxytryptophan (L-5HTP) 0 0 1.1387 Flunarizine:L-5-Hydroxytryptophan (L-5HTP) 0 0 0.9319 Flunarizine:Placebo 11.000 0.9319 0.9319 Flunarizine:Propranoll 0 0 0.3301 0.3301 Flunarizine:Floorlavin 0 0 0.3301 0.3301 Flunarizine:Floorlavin 0 0 0.3772 0.7372 Flunarizine:Floorlavin 0 0 0.7144 0.7144 L-5-Hydroxytryptophan (L-SHTP):Placebo 1 0 0.2668 L-5-Hydroxytryptophan (L-SHTP):Progranoll 0 0 0 0.8087 L-5-Hydroxytryptophan (L-SHTP):Propranoll 0 0 0 0.8087 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 0.4243 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 0.8139			-		•		•	•	•	
Flunarizine:L-5-Hydroxytrytophan (L-5HPP) 0 0 1.1387 1.1387 Flunarizine:Nimodipine 0 0.9319 0.9319 Flunarizine:Placebo 11.00 0.9319 0.9319 Flunarizine:Pregabalin 0 0 0.1180 0.1180 Flunarizine:Propranolol 0 0.3301 0.3301 . Flunarizine:Propranolol 0 0.7372 0.7372 . Flunarizine:Sodium Valproate 0 0.7144 0.7144 . Flunarizine:Topiranate 0 0.3413 0.3413 . L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 -0.2068 - . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 -1.0208 - . L-5-Hydroxytryptophan (L-SHTP):Stooltavin 0 -0.4243 - . L-5-Hydroxytryptophan (L-SHTP):Stooltavin 0 -0.4243 - . . L-5-Hydroxytryptophan (L-SHTP):Stooltavin 0 -0.4243 - . . L-5-Hydroxytryptophan (L-SHTP):Stooltavin 0 -0.6018 - . . Nimod	CoEnzyme Q10:Sodium Valproate	0	0	0.0810		0.0810		•		
Flunarizine:L-5-Hydroxytrytophan (L-5HPP) 0 0 1.1387 1.1387 Flunarizine:Nimodipine 0 0.9319 0.9319 Flunarizine:Placebo 11.00 0.9319 0.9319 Flunarizine:Pregabalin 0 0 0.1180 0.1180 Flunarizine:Propranolol 0 0.3301 0.3301 . Flunarizine:Propranolol 0 0.7372 0.7372 . Flunarizine:Sodium Valproate 0 0.7144 0.7144 . Flunarizine:Topiranate 0 0.3413 0.3413 . L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 -0.2068 - . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 -1.0208 - . L-5-Hydroxytryptophan (L-SHTP):Stooltavin 0 -0.4243 - . L-5-Hydroxytryptophan (L-SHTP):Stooltavin 0 -0.4243 - . . L-5-Hydroxytryptophan (L-SHTP):Stooltavin 0 -0.4243 - . . L-5-Hydroxytryptophan (L-SHTP):Stooltavin 0 -0.6018 - . . Nimod	CoEnzyme 010:Topiramate	0	0	-0.2922		-0.2922				
Flunarizine:Nimodipine 0 0.9319 0.9319 Flunarizine:Placebo 1 1.00 0.9319 0.9319 Flunarizine:Progranolol 0 0.1180 0.1180 Flunarizine:Flooplavin 0 0.3301 0.3301 . Flunarizine:Flooplavin 0 0.7372 0.7372 . Flunarizine:Flooplavin 0 0.7144 0.7144 . Flunarizine:Fopiranate 0 0.3413 . . L-5-Hydroxytryptophan (L-SHTP):Piropranolol 0 02068 . . L-5-Hydroxytryptophan (L-SHTP):Progranolol 0 -0.4016 . . L-5-Hydroxytryptophan (L-SHTP):Proparanolol 0 -0.4208 . . L-5-Hydroxytryptophan (L-SHTP):Proparanolol 0 -0.4243 . . L-5-Hydroxytryptophan (L-SHTP):Piropranate 0 0 -0.4243 . . L-5-Hydroxytryptophan (L-SHTP):Piropranate 0 0 -0.4243 . . L-5-Hydroxytryptophan (L-SHTP):Piropranate 0 0 -0.4243 . . Nimodipine:Placebo 1 1.00 -										
Flunarizine:Placebo 1 1.00 0.9319 0.9319 0.1180 0.1180 Flunarizine:Pregabalin 0 0 0.1180 0.1180 0.1180 Flunarizine:Pregabalin 0 0 0.3301 0.3301 . Flunarizine:Riboflavin 0 0 0.7372 0.7372 . Flunarizine:Topiramate 0 0 0.7144 . . Flunarizine:Topiramate 0 0 0.3413 .0.3413 . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 0 -0.2068 . . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 0 -1.0208 . . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 0 -0.4063 . . L-5-Hydroxytryptophan (L-SHTP):Siboflavin 0 0 -0.4243 . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.8087 . . . L-5-Hydroxytryptophan (L-SHTP):Soldium Valproate 0 0 -0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Soldium Valproate 0					•		•	•	•	
Flunarizine:Pregabalin 0 0 0.1180 0.1180 Flunarizine:Propranolol 0 0 0.3301 0.3301 . Flunarizine:Riboflavin 0 0 0.7372 0.7372 . Flunarizine:Sodium Valproate 0 0 0.7144 0.7144 . Flunarizine:Sodium Valproate 0 0 0.4313 0.3413 . L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.2068 . . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 0 -1.0208 . . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 0 -0.4016 . . L-5-Hydroxytryptophan (L-SHTP):Riboflavin 0 0 -0.4243 . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.4243 . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.8139 . . Mimodipine:Pregabalin 0 0 -0.8139 . . . Nimodipine:Progranolol 0 0 -0.613 . . . Nimodipine:Progranolol 0 0 -0.8139 . . .	Flunarizine:Nimodipine	0	0	0.9319		0.9319				
Flunarizine:Pregabalin 0 0 0.1180 0.1180 Flunarizine:Propranolol 0 0 0.3301 0.3301 . Flunarizine:Riboflavin 0 0 0.7372 0.7372 . Flunarizine:Sodium Valproate 0 0 0.7144 0.7144 . Flunarizine:Sodium Valproate 0 0 0.4313 0.3413 . L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.2068 . . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 0 -1.0208 . . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 0 -0.4016 . . L-5-Hydroxytryptophan (L-SHTP):Riboflavin 0 0 -0.4243 . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.4243 . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.8139 . . Mimodipine:Pregabalin 0 0 -0.8139 . . . Nimodipine:Progranolol 0 0 -0.613 . . . Nimodipine:Progranolol 0 0 -0.8139 . . .	Elunarizine: Placebo	1	1.00	0.9319	0.9319					
Flunarizine:Propranolol 0 0 0.3301 0.3301 . . Flunarizine:Riboflavin 0 0 0.7372 0.7372 . . Flunarizine:Sodium Valproate 0 0 0.7144 0.7144 . . Flunarizine:Topiramate 0 0 0.3413 0.3413 . . L-5-Hydroxytryptophan (L-SHTP):Placebo 1 0 0.2668 . . . L-5-Hydroxytryptophan (L-SHTP):Progranolol 0 0 0.4016 . . . L-5-Hydroxytryptophan (L-SHTP):Soldium Valproate 0 0 0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Soldium Valproate 0 0 0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 0.8087 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 0.4243 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 0.1087 <						0 1100	•	•	•	
Flunarizine:Riboflavin 0 0.7372 0.7372 . . Flunarizine:Sodium Valproate 0 0.7144 0.7144 . . Flunarizine:Topiramate 0 0 0.3413 . . . L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.2068 . . . L-5-Hydroxytryptophan (L-SHTP):Progabalin 0 0 -1.0208 . . . L-5-Hydroxytryptophan (L-SHTP):Propranolol 0 -0.48087 L-5-Hydroxytryptophan (L-SHTP):StoofLavin 0 -0.4243 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 -0.4243 .	Flunarizine:Predabalin		0							
Flunarizine:Riboflavin 0 0.7372 0.7372 . . Flunarizine:Sodium Valproate 0 0.7144 0.7144 . . Flunarizine:Topiramate 0 0.3413 . . . L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.2068 . . L-5-Hydroxytryptophan (L-SHTP):Progabalin 0 -1.0208 . . . L-5-Hydroxytryptophan (L-SHTP):Propranolol 0 -0.4887 . . . L-5-Hydroxytryptophan (L-SHTP):StoofLavin 0 -0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 -0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 -0.8139 Nimodipine:Progranol 0 0 -0.8139 Nimodipine:Riboflavin 0 -0.1947 Nimodipine:Sodium Valproate 0 0 0.1947 .		•	•	0.1100	•	0.1100	•	•	•	
Flunarizine:Riboflavin 0 0.7372 0.7372 . . Flunarizine:Sodium Valproate 0 0.7144 0.7144 . . Flunarizine:Topiramate 0 0.3413 . . . L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.2068 . . L-5-Hydroxytryptophan (L-SHTP):Progabalin 0 -1.0208 . . . L-5-Hydroxytryptophan (L-SHTP):Propranolol 0 -0.4887 . . . L-5-Hydroxytryptophan (L-SHTP):StoofLavin 0 -0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 -0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 -0.8139 Nimodipine:Progranol 0 0 -0.8139 Nimodipine:Riboflavin 0 -0.1947 Nimodipine:Sodium Valproate 0 0 0.1947 .		v		0.1100	•	0.1100	•	•		
Flunarizine:Sodium Valproate 0 0.7144 0.7144 . Flunarizine:Topiramate 0 0.3413 .0.3413 . L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.2068 . . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 0 -0.2068 . . . L-5-Hydroxytryptophan (L-SHTP):Progranolol 0 0 -0.8087 . . . L-5-Hydroxytryptophan (L-SHTP):Riboflavin 0 0 0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Slobinu Valproate 0 0 -0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Slobinu Valproate 0 0 -0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Sodium Valproate 0 0 0.4243 .										
Flunarizine:Sodium Valproate 0 0.7144 0.7144 . Flunarizine:Topiramate 0 0.3413 .0.3413 . L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.2068 . . L-5-Hydroxytryptophan (L-SHTP):Pregabalin 0 0 -0.2068 . . . L-5-Hydroxytryptophan (L-SHTP):Progranolol 0 0 -0.8087 . . . L-5-Hydroxytryptophan (L-SHTP):Riboflavin 0 0 0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Slobinu Valproate 0 0 -0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Slobinu Valproate 0 0 -0.4243 . . . L-5-Hydroxytryptophan (L-SHTP):Sodium Valproate 0 0 0.4243 .										
Flunarizine:Topiramate 0 0 0.3413 0.3413 0.3413 L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.2068 -0.2068 0.3413 L-5-Hydroxytryptophan (L-SHTP):Placebo 1 0 0 -2.068 0.2068 0.2068 L-5-Hydroxytryptophan (L-SHTP):Propranolol 0 0 -0.2087 -0.2087 0.3087 L-5-Hydroxytryptophan (L-SHTP):Robrlavin 0 0 -0.4016 0.4243 0.4243 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.7974 0.7974 0.7974 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.8139 0.8139 0.8139 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.6018 0.7974 0.7974 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 0.8139 0.8139 0.8139 Nimodipine:Propranolol 0 0 0.8139 0.8139 0.8139 0.8139 Nimodipine:Propranolol 0 0 0.2175 0.2175 0.2175 0.2175 0.2175 0.2175 0.2175 0.2175 0	Flunarizine:Propranolol	0	0	0.3301		0.3301				
L-5-Hydroxytryptophan (L-SHTP):Nimodipine 0 0 -0.20680.2068	Flunarizine:Propranolol Flunarizine:Riboflavin	0 0	0	0.3301 0.7372		0.3301 0.7372			:	
L-5-Hydroxytryptophan (L-SHTP):Placebo 1 1.00 -0.2068 -0.2068	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate	0 0 0	0	0.3301 0.7372 0.7144		0.3301 0.7372 0.7144	:		:	
L-5-Hydroxytryptophan (L-SHTP):Placebo 1 1.00 -0.2068 -0.2068	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate	0 0 0	0 0 0	0.3301 0.7372 0.7144	:	0.3301 0.7372 0.7144			:	
L-5-Hydroxytryptophan (L-5HTP):Pregabalin 0 0 -1.02081.0208 L-5-Hydroxytryptophan (L-5HTP):Propranolol 0 0 -0.80870.8087 L-5-Hydroxytryptophan (L-5HTP):Riboflavin 0 0 0.40160.4016 L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate 0 0 -0.42430.4243 L-5-Hydroxytryptophan (L-5HTP):Topiramate 0 0 -0.7974	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Topiramate	0 0 0	0 0 0	0.3301 0.7372 0.7144 0.3413	:	0.3301 0.7372 0.7144 0.3413				
L-5-Hydroxytryptophan (L-SHTP):Propranolol 0 0 -0.80870.8087 L-5-Hydroxytryptophan (L-SHTP):Riboflavin 0 0 -0.404160.4016 L-5-Hydroxytryptophan (L-SHTP):Riboflavin 0 0 -0.42430.4243 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.7974 Nimodipine:Placebo 1 1.00 -0.0000 0.0000	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine	0 0 0 0	0 0 0 0	0.3301 0.7372 0.7144 0.3413 -0.2068	:	0.3301 0.7372 0.7144 0.3413				
L-5-Hydroxytryptophan (L-SHTP):Propranolol 0 0 -0.80870.8087 L-5-Hydroxytryptophan (L-SHTP):Riboflavin 0 0 -0.404160.4016 L-5-Hydroxytryptophan (L-SHTP):Riboflavin 0 0 -0.42430.4243 L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.7974 Nimodipine:Placebo 1 1.00 -0.0000 0.0000	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine	0 0 0 0	0 0 0 0	0.3301 0.7372 0.7144 0.3413 -0.2068	:	0.3301 0.7372 0.7144 0.3413				
L-5-Hydroxytryptophan (L-5HTP):Riboflavin 0 0 -0.40160.4016 L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate 0 0 -0.79740.7974 Nimodipine:Progabalin 0 0 -0.81390.8139 Nimodipine:Progabalin 0 0 -0.81390.8139 Nimodipine:Progabalin 0 0 -0.81390.8139 Nimodipine:Propranolol 0 0 -0.60180.6018 Nimodipine:Riboflavin 0 0 -0.19470.1947 Nimodipine:Sodium Valproate 0 0 -0.2175 Nimodipine:Topiramate 0 0 -0.8139	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-SHTP):Placebo	0 0 0 0 1	0 0 0 0 1.00	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068	-0.2068	0.3301 0.7372 0.7144 0.3413 -0.2068				
L-5-Hydroxytryptophan (L-SHTP): Sodium Valproate 0 0 -0.42430.4243	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Pregabalin	0 0 0 0 1 0	0 0 0 1.00 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -1.0208	-0.2068	0.3301 0.7372 0.7144 0.3413 -0.2068 -1.0208				
L-5-Hydroxytryptophan (L-SHTP): Sodium Valproate 0 0 -0.42430.4243	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Propranolol	0 0 0 0 1 0	0 0 0 1.00 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -1.0208	-0.2068	0.3301 0.7372 0.7144 0.3413 -0.2068 -1.0208				
L-5-Hydroxytryptophan (L-SHTP):Topiramate 0 0 -0.79740.7974 Nimodipine:Placebo 1 1.00 -0.0000 0.0000	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Propranolol	0 0 0 0 1 0	0 0 0 1.00 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -1.0208 -0.8087	-0.2068	0.3301 0.7372 0.7144 0.3413 -0.2068 -1.0208 -0.8087				
Nimodipine:Placebo 1 1.00 -0.0000 0.0000 .	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Propranolol L-5-Hydroxytryptophan (L-5HTP):Riboflavin	0 0 0 0 1 0 0	0 0 0 0 1.00 0 0 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -1.0208 -0.8087 -0.4016	-0.2068	0.3301 0.7372 0.7144 0.3413 -0.2068 -1.0208 -0.8087 -0.4016				
Nimodipine:Pregabalin 0 -0.8139 -0.8139 . . Nimodipine:Propranolol 0 0 -0.6018 -0.6018 . . Nimodipine:Riboflavin 0 0 -0.1947 -0.1947 . . Nimodipine:Sodium Valproate 0 0 -0.2175 . . . Nimodipine:Topiramate 0 -0.5906 Pregabalin:Placebo 0 0 .8139 . . . Propranolol:Placebo 1 0.19 0.6018 1.5075 0.3876 1.1199 1.51 0.1300 Riboflavin:Placebo 3 1.00 0.1947 0.1947 Sodium Valproate:Placebo 1 0.54 0.2175 0.1019 0.3522 -0.2504 -0.38 0.7027 Topiramate:Placebo 2 0.66 0.5966 0.5533 0.6629 -0.1095 -0.18 0.8569 Pregabalin:Riboflavin 0 0 0.2121 0.2121 . . .	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Propranolol L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate	0 0 0 0 1 0 0 0	0 0 0 0 1.00 0 0 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -1.0208 -0.8087 -0.4016 -0.4243		0.3301 0.7372 0.7144 0.3413 -0.2068 -1.0208 -0.8087 -0.4016 -0.4243				
Nimodipine:Pregabalin 0 -0.8139 -0.8139 . . Nimodipine:Propranolol 0 0 -0.6018 -0.6018 . . Nimodipine:Riboflavin 0 0 -0.1947 -0.1947 . . Nimodipine:Sodium Valproate 0 0 -0.2175 . . . Nimodipine:Topiramate 0 -0.5906 Pregabalin:Placebo 0 0 .8139 . . . Propranolol:Placebo 1 0.19 0.6018 1.5075 0.3876 1.1199 1.51 0.1300 Riboflavin:Placebo 3 1.00 0.1947 0.1947 Sodium Valproate:Placebo 1 0.54 0.2175 0.1019 0.3522 -0.2504 -0.38 0.7027 Topiramate:Placebo 2 0.66 0.5966 0.5533 0.6629 -0.1095 -0.18 0.8569 Pregabalin:Riboflavin 0 0 0.2121 0.2121 . . .	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Sodium Valproate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Progabalin L-5-Hydroxytryptophan (L-5HTP):Progranolol L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate L-5-Hydroxytryptophan (L-5HTP):Topiramate	0 0 0 0 1 0 0 0 0 0	0 0 0 1.00 0 0 0 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -1.0208 -0.8087 -0.4016 -0.4243 -0.7974		0.3301 0.7372 0.7144 0.3413 -0.2068 -1.0208 -0.8087 -0.4016 -0.4243				
Nimodipine:Propranolol 0 -0.6018 -0.6018 . . Nimodipine:Riboflavin 0 -0.1947 -0.1947 . . Nimodipine:Sodium Valproate 0 -0.2175 . . . Nimodipine:Sodium Valproate 0 -0.5906 . . . Nimodipine:Topiramate 0 -0.5906 . . . Pregabalin:Placebo 0 0.8139 . . . Propranolol:Placebo 1 0.1947 0.1947 . . . Sodium Valproate:Placebo 1 0.1947 0.1947 Sodium Valproate:Placebo 1 0.54 0.2175 0.1019 0.3522 -0.2504 -0.38 0.7027 Topiramate:Placebo 2 0.66 0.5906 0.533 0.6629 -0.1095 -0.18 0.8569 Pregabalin:Riboflavin 0 0 0.2121 0.2121 . . . Pregabalin:Riboflavin 0 0 0.5964 . . <	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Sodium Valproate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Progabalin L-5-Hydroxytryptophan (L-5HTP):Progranolol L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate L-5-Hydroxytryptophan (L-5HTP):Topiramate	0 0 0 0 1 0 0 0 0 0	0 0 0 1.00 0 0 0 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -1.0208 -0.8087 -0.4016 -0.4243 -0.7974	-0.2068	0.3301 0.7372 0.7144 0.3413 -0.2068 -1.0208 -0.8087 -0.4016 -0.4243				
Nimodipine:Riboflavin 0 -0.1947 -0.1947 . Nimodipine:Sodium Valproate 0 -0.2175 . . Nimodipine:Sodium Valproate 0 -0.2175 . . Nimodipine:Topiramate 0 -0.5906 . . Pregabalin:Placebo 0 0.8139 . . Propranolol:Placebo 1 0.6018 1.5075 0.3876 1.1199 1.51 0.1300 Riboflavin:Placebo 1 0.54 0.2127 0.1019 0.3522 -0.2504 -0.38 0.7027 Topiramate:Placebo 2 0.54 0.2121 0.2121 . . . Pregabalin:Riboflavin 0 0 0.5192 0.6192 . . . Pregabalin:Riboflavin 0 0 0.5964 0.5964 . . . Pregabalin:Topiramate 0 0 0.4071 0.4071 . . . Pregabalin:Riboflavin 0 0 0.4071 Pregabal	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Propranolol L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Rojramate L-5-Hydroxytryptophan (L-5HTP):Topiramate L-5-Hydroxytryptophan (L-5HTP):Topiramate	0 0 0 0 1 0 0 0 0 0 1	0 0 0 0 1.00 0 0 0 0 0 1.00	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -0.2068 -0.8087 -0.4016 -0.4243 -0.7974 -0.0000	-0.2068	0.3301 0.7372 0.7144 0.3413 -0.2068 -1.0208 -0.8087 -0.4016 -0.4243 -0.7974				
Nimodipine:Sodium Valproate 0 -0.2175 . . . Nimodipine:Topiramate 0 -0.5906 . . . Pregabalin:Placebo 0 0.8139 . . . Propranolol:Placebo 1 0.919 0.6018 1.5075 0.3876 1.1199 1.51 0.1300 Riboflavin:Placebo 1 0.54 0.2175 0.1019 0.3522 -0.2504 -0.38 0.7027 Sodium Valproate:Placebo 1 0.54 0.2125 0.1019 0.3522 -0.2504 -0.38 0.7027 Topiramate:Placebo 2 0.66 0.5966 0.5533 0.6629 -0.1095 -0.18 0.8569 Pregabalin:Propranolol 1 1.00 0.2121 0.2121 . . . Pregabalin:Sodium Valproate 0 0.6192 . 0.6192 . . . Pregabalin:Topiramate 0 0.2233 Pregabalin:Sodium Valproate 0 0.4071 . . .<	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Godium Valproate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate L-5-Hydroxytryptophan (L-5HTP):Topiramate L-5-Hydroxytryptophan (L-5HTP):Topiramate Nimodipine:Pregabalin	0 0 0 0 1 0 0 0 0 0 1 0	0 0 0 0 1.00 0 0 0 0 1.00 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -1.0208 -0.8028 -0.8028 -0.4016 -0.4243 -0.7974 -0.0000 -0.8139	-0.2068 0.0000	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.808 -0.808 -0.4016 -0.4243 -0.7974 -0.8139				
Nimodipine:Sodium Valproate 0 -0.2175 . . . Nimodipine:Topiramate 0 -0.5906 . . . Pregabalin:Placebo 0 0.8139 . . . Propranolol:Placebo 1 0.919 0.6018 1.5075 0.3876 1.1199 1.51 0.1300 Riboflavin:Placebo 1 0.54 0.2175 0.1019 0.3522 -0.2504 -0.38 0.7027 Sodium Valproate:Placebo 1 0.54 0.2125 0.1019 0.3522 -0.2504 -0.38 0.7027 Topiramate:Placebo 2 0.66 0.5966 0.5533 0.6629 -0.1095 -0.18 0.8569 Pregabalin:Propranolol 1 1.00 0.2121 0.2121 . . . Pregabalin:Sodium Valproate 0 0.6192 . 0.6192 . . . Pregabalin:Topiramate 0 0.2233 Pregabalin:Sodium Valproate 0 0.4071 . . .<	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Godium Valproate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate L-5-Hydroxytryptophan (L-5HTP):Topiramate L-5-Hydroxytryptophan (L-5HTP):Topiramate Nimodipine:Pregabalin	0 0 0 0 1 0 0 0 0 0 1 0	0 0 0 0 1.00 0 0 0 0 1.00 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -1.0208 -0.8028 -0.8028 -0.4016 -0.4243 -0.7974 -0.0000 -0.8139	-0.2068 0.0000	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.808 -0.808 -0.4016 -0.4243 -0.7974 -0.8139				
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Sodium Valproate:Topiramate 0 0 -0.37310.3731	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Pregabalin L-5-Hydroxytryptophan (L-5HTP):Prepranolol L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate L-5-Hydroxytryptophan (L-5HTP):Topiramate L-5-Hydroxytryptophan (L-5HTP):Topiramate Nimodipine:Pregabalin Nimodipine:Pregabalin Nimodipine:Riboflavin Nimodipine:Sodium Valproate Nimodipine:Topiramate Pregabalin:Placebo Riboflavin:Placebo Propranolol:Placebo Progranolol:Placebo Sodium Valproate:Placebo Pregabalin:Propranolol Pregabalin:Riboflavin Pregabalin:Riboflavin Pregabalin:Topiramate Propranolol:Sodium Valproate Progranolol:Sodium Valproate Progranolol:Sodium Valproate Progranolol:Sodium Valproate Propranolol:Sodium Valproate Propranolol:Sodium Valproate	00000100001000000131210000220	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -0.4016 -0.4243 -0.7974 -0.07974 -0.6018 -0.1947 -0.2175 -0.5906 0.8139 0.6018 0.1947 0.2175 0.5906 0.21211 0.6192 0.2121 0.6192 0.233 0.4071 0.3844 0.0112 -0.0227	-0.2068 	0.3301 0.7372 0.7144 0.3413 -0.2008 -0.2008 -0.4016 -0.4243 -0.797- -0.4016 -0.4243 -0.6018 -0.1947 -0.2175 -0.5906 0.8139 0.3876 0.3522 0.6629 0.5964 0.2233 0.4071 0.5964 0.2233 0.4071	-0.2504 -0.1095	-0.38 -0.18	0.1300 0.7027 0.8569	
	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Progradol L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate L-5-Hydroxytryptophan (L-5HTP):Topiramate Nimodipine:Pregabalin Nimodipine:Propranolol Nimodipine:Propranolol Nimodipine:Riboflavin Nimodipine:Rogabalin Nimodipine:Topiramate Pregabalin:Placebo Riboflavin:Placebo Sodium Valproate:Placebo Propranolol:Placebo Progranolol:Placebo Pregabalin:Placebo Sodium Valproate:Placebo Pregabalin:Placebo Pregabalin:Placebo Sodium Valproate:Placebo Pregabalin:Placebo Pregabalin:Propranolol Pregabalin:Sodium Valproate Pregabalin:Topiramate Propranolol:Riboflavin Propranolol:Riboflavin Propranolol:Sodium Valproate Riboflavin:Sodium Valproate Riboflavin:Sodium Valproate Riboflavin:Topiramate Riboflavin:Sodium Valproate	00000100001000001312100002200	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -0.4028 -0.40243 -0.7974 -0.4018 -0.6018 -0.1947 -0.2175 -0.5906 0.1947 0.2175 0.5906 0.2121 0.6018 0.2121 0.5964 0.2233 0.4071 0.3844 0.0112 -0.0227 -0.3959	-0.2068	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -0.8087 -0.40243 -0.7974 -0.4243 -0.7974 -0.6018 -0.1947 -0.2175 -0.5906 0.8139 0.3876 0.3876 0.3872 0.6629 0.6192 0.5964 0.2233 0.4071 0.5673 0.4071 0.5673 0.4071	-0.2504 -0.1095	-0.38 -0.18	0.1300 0.7027 0.8569	
	Flunarizine:Propranolol Flunarizine:Riboflavin Flunarizine:Sodium Valproate Flunarizine:Sodium Valproate Flunarizine:Topiramate L-5-Hydroxytryptophan (L-5HTP):Nimodipine L-5-Hydroxytryptophan (L-5HTP):Progradol L-5-Hydroxytryptophan (L-5HTP):Riboflavin L-5-Hydroxytryptophan (L-5HTP):Sodium Valproate L-5-Hydroxytryptophan (L-5HTP):Topiramate Nimodipine:Pregabalin Nimodipine:Propranolol Nimodipine:Propranolol Nimodipine:Riboflavin Nimodipine:Rogabalin Nimodipine:Topiramate Pregabalin:Placebo Riboflavin:Placebo Sodium Valproate:Placebo Propranolol:Placebo Progranolol:Placebo Pregabalin:Placebo Sodium Valproate:Placebo Pregabalin:Placebo Pregabalin:Placebo Sodium Valproate:Placebo Pregabalin:Placebo Pregabalin:Propranolol Pregabalin:Sodium Valproate Pregabalin:Topiramate Propranolol:Riboflavin Propranolol:Riboflavin Propranolol:Sodium Valproate Riboflavin:Sodium Valproate Riboflavin:Sodium Valproate Riboflavin:Topiramate Riboflavin:Sodium Valproate	00000100001000001312100002200	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -0.4028 -0.40243 -0.7974 -0.4018 -0.6018 -0.1947 -0.2175 -0.5906 0.1947 0.2175 0.5906 0.2121 0.6018 0.2121 0.5964 0.2233 0.4071 0.3844 0.0112 -0.0227 -0.3959	-0.2068	0.3301 0.7372 0.7144 0.3413 -0.2068 -0.2068 -0.8087 -0.40243 -0.7974 -0.4243 -0.7974 -0.6018 -0.1947 -0.2175 -0.5906 0.8139 0.3876 0.3876 0.3872 0.6629 0.6192 0.5964 0.2233 0.4071 0.5673 0.4071 0.5673 0.4071	-0.2504 -0.1095	-0.38 -0.18	0.1300 0.7027 0.8569 0.7027	

Legend:	
comparison	- Treatment comparison
k	- Number of studies providing direct evidence
prop	- Direct evidence proportion
nma	- Estimated treatment effect (SMD) in network meta-analysis
direct	- Estimated treatment effect (SMD) derived from direct evidence
indir.	- Estimated treatment effect (SMD) derived from indirect evidence
Diff	- Difference between direct and indirect treatment estimates
z	- z-value of test for disagreement (direct versus indirect)
p-value	 p-value of test for disagreement (direct versus indirect)

Efficacy – Global approach

Q statistics to assess homogeneity / consistency

 Q df
 p-value

 Total
 32.13
 8 < 0.0001</td>

 Within designs
 26.13
 5 < 0.0001</td>

 Between designs
 6.01
 3
 0.1113

Design-specific decomposition of within-designs Q statistic

DesignQ df p-valuePlacebo:Riboflavin15.9820.0003Placebo:Topiramate0.8310.3626Propranolol:Sodium Valproate4.4710.0345Propranolol:Topiramate4.8510.0276

Between-designs Q statistic after detaching of single designs

Detached design Q df p-value Cinnarizine:Propranolol 4.58 2 0.1010 Placebo:Cinnarizine 4.58 2 0.1010 Placebo:Propranolol 1.04 2 0.5932 Placebo:Sodium Valproate 5.75 2 0.0563 Placebo:Topiramate 5.91 2 0.0520 Propranolol:Sodium Valproate 5.75 2 0.0563 Propranolol:Topiramate 5.91 2 0.0520 Q statistic to assess consistency under the assumption of a full design-by-treatment interaction random effects model Q df p-value tau.within tau2.within

Between designs 2.08 3 0.5561 0.5172 0.2675

Acceptability – Local approach

Back-calculation method to split direct and indirect evidence

Random effects model:

comparison	k	prop	nma	direct	indir.	RoR	z	p-value
Amitriptylin:Butterbur root extract	0	0	0.6178		0.6178			
Amitriptylin:Cinnarizine	0	0	0.5162		0.5162			
Amitriptylin:CoEnzyme Q10	0	0	0.6957		0.6957			
Amitriptylin:Flunarizine	0	0	0.5870		0.5870			•
Amitriptylin:Melatonin	1	1.00	1.1739	1.1739				
Amitriptylin:Nimodipine	0	0	0.7414		0.7414			
Amitriptylin:Placebo	0	0	0.5870		0.5870			
Amitriptylin:Pregabalin	0	0	0.6204		0.6204			
Amitriptylin:Propranolol	0	0	0.6069		0.6069			
Amitriptylin:Riboflavin	0	0	1.1922		1.1922			
Amitriptylin:Sodium Valproate	0	0	0.3917		0.3917			
Amitriptylin:Topiramate	0	0	0.5833		0.5833			
Butterbur root extract:Cinnarizine	0	0	0.8356		0.8356		•	
Butterbur root extract:CoEnzyme Q10	0	0	1.1259		1.1259			
Butterbur root extract:Flunarizine	0	0	0.9500		0.9500			
Butterbur root extract:Melatonin	0	0	1.9000		1.9000		•	
Butterbur root extract:Nimodipine	0	0	1.2000		1.2000		•	•
Butterbur root extract:Placebo	1	1.00	0.9500	0.9500			•	•
Butterbur root extract:Pregabalin	0	0	1.0041		1.0041			
Butterbur root extract:Propranolol	0	0	0.9822		0.9822		•	
Butterbur root extract:Riboflavin	0	0	1.9297		1.9297		•	
Butterbur root extract:Sodium Valproate	0	0	0.6341		0.6341			
Butterbur root extract:Topiramate	0	0	0.9440		0.9440			
Cinnarizine:CoEnzyme Q10	0	0	1.3475		1.3475			
Cinnarizine:Flunarizine	0	0	1.1370		1.1370		•	•
Cinnarizine:Melatonin	0	0	2.2739		2.2739		•	•
Cinnarizine:Nimodipine		-	1.4362		1.4362	•	•	•
Cinnarizine:Placebo	1	0.57	1.1370	2.0000	0.5449	3.6707	1.03	0.3026
Cinnarizine:Pregabalin			1.2017		1.2017		•	•
Cinnarizine:Propranolol						0.2724	-1.03	0.3026
Cinnarizine:Riboflavin			2.3095		2.3095	•	•	•
Cinnarizine:Sodium Valproate			0.7588		0.7588	•	•	•
Cinnarizine:Topiramate	0	0	1.1298	•	1.1298	•	•	•

CoEnzyme Q10:Flunarizine			0.8438			0.8438			
CoEnzyme Q10:Melatonin			1.6875			1.6875	•	•	•
CoEnzyme Q10:Nimodipine			1.0658			1.0658	•		
CoEnzyme Q10:Placebo		1.00	0.8438	0.8	438	•	•		•
CoEnzyme Q10:Pregabalin	0	0	0.8918			0.8918			
CoEnzyme Q10:Propranolol		0	0.8724			0.8724			
CoEnzyme Q10:Riboflavin		0	1.7139			1.7139			
CoEnzyme Q10:Sodium Valproate		0	0.5631			0.5631			
CoEnzyme Q10:Topiramate	0	0	0.8384			0.8384			
Flunarizine:Melatonin	0	0	2.0000			2.0000			
Flunarizine:Nimodipine	0	0	1.2632			1.2632			
Flunarizine:Placebo	1	1.00	1.0000	1.0	000				
Flunarizine:Pregabalin	0	0	1.0569			1.0569			
Flunarizine:Propranolol	0	0	1.0339			1.0339			
Flunarizine:Riboflavin	0	0	2.0312			2.0312			
Flunarizine:Sodium Valproate	0	0	0.6674			0.6674			
Flunarizine:Topiramate	0	0	0.9937			0.9937			
Melatonin:Nimodipine	0	0	0.6316			0.6316			
Melatonin:Placebo	1	1.00	0.5000	0.5	000				
Melatonin:Pregabalin	0	0	0.5285			0.5285			
Melatonin:Propranolol		0	0.5170			0.5170			
Melatonin:Riboflavin	0	0	1.0156			1.0156			
Melatonin:Sodium Valproate		0	0.3337			0.3337			
Melatonin:Topiramate	0	0	0.4968			0.4968			
Nimodipine:Placebo	1	1.00	0.7917	0.7	917				
Nimodipine:Pregabalin			0.8367			0.8367			
Nimodipine:Propranolol	0	0	0.8185			0.8185			
Nimodipine:Riboflavin		0	1.6081			1.6081			
Nimodipine:Sodium Valproate		0	0.5284			0.5284			
Nimodipine:Topiramate		0	0.7867			0.7867			
Pregabalin:Placebo			0.9462			0.9462			
Propranolol:Placebo			0.9672			0.9672			
Riboflavin:Placebo									
Sodium Valproate:Placebo						0.6889	2.5123	0.86	0.3890
Topiramate:Placebo									0.0815
Pregabalin:Propranolol									
Pregabalin:Riboflavin			1.9219			1.9219			
Pregabalin:Sodium Valproate			0.6315			0.6315			
· · · · · · · · · · · · · · · · · · ·	-	•			•				
Pregabalin:Topiram	ate	0	0 0.94	02		. 0.9402	2.		
Propranolol:Ribofla	vin	0	0 1.96	46		. 1.9646	5.		
Propranolol:Sodium Valpro	ate	20.	55 0.64	55 0	.976	4 0.3887	2.5123	0.86	0.3890
Propranolol:Topiram			53 0.96	11 0	.402	7 2.6143	8 0.1540	-1.74	0.0815
Riboflavin:Sodium Valpro			0 0.32	86		. 0.3286	5.		
Riboflavin:Topiram			0 0.48			. 0.4892		•	•
Sodium Valproate:Topiram	ate	0	0 1.48	89		. 1.4889).	•	•
end:									
mparison - Treatment comparison - Number of studies provi	din	a di -	act and	dana	~				
	uru	y utr	ect evi	uenc					

Lege com

k	- Number of studies providing direct evidence
prop	- Direct evidence proportion
nma	- Estimated treatment effect (RR) in network meta-analysis
direct	- Estimated treatment effect (RR) derived from direct evidence
indir.	- Estimated treatment effect (RR) derived from indirect evidence
RoR	- Ratio of Ratios (direct versus indirect)
z	 z-value of test for disagreement (direct versus indirect)
p-value	- p-value of test for disagreement (direct versus indirect)

Acceptability - Global approach

Q statistics to assess homogeneity / consistency Q df p-value 5.13 7 0.6439 Total Within designs 1.99 5 0.8507 Between designs 3.14 2 0.2077 Design-specific decomposition of within-designs Q statistic Design Q df p-value Placebo:Riboflavin 1.20 2 0.5500 Placebo:Topiramate 0.04 1 0.8359 Propranolol:Sodium Valproate 0.51 1 0.4756 Propranolol:Topiramate 0.24 1 0.6230 Between-designs Q statistic after detaching of single designs Detached design Q df p-value Cinnarizine: Propranolol 2.08 1 0.1492 Placebo:Cinnarizine 2.08 1 0.1492 Placebo:Sodium Valproate 2.40 1 0.1213 Placebo:Topiramate 0.11 1 0.7429 Propranolol:Sodium Valproate 2.40 1 0.1213 Propranolol:Topiramate 0.11 1 0.7429 Q statistic to assess consistency under the assumption of a full design-by-treatment interaction random effects model 0 df n value tau within tau? withi

		Q	at	p-value	tau.within	tauz.witnin	
Between	designs	3.14	2	0.2077	0	0	

Safety – Local approach

Back-calculation method to split direct and indirect evidence

Random effects model:

comparison	k	prop	nma	direct	indir.	RoR	z	p-value
Butterbur root extract:Cinnarizine	0	0	0.5424		0.5424			•
Butterbur root extract:Flunarizine	0	0	0.1359		0.1359			
Butterbur root extract:Nimodipine	0	0	0.9024		0.9024			
Butterbur root extract:Placebo	1	1.00	0.9512	0.9512				
Butterbur root extract:Propranolol	0	0	0.5424		0.5424			
Butterbur root extract:Riboflavin	0	0	1.2167		1.2167			
Butterbur root extract:Sodium Valproate	0	0	0.3962		0.3962			
Butterbur root extract:Topiramate	0	0	0.2839		0.2839			
Cinnarizine:Flunarizine	0	0	0.2505		0.2505			
Cinnarizine:Nimodipine	0	0	1.6639		1.6639			
Cinnarizine:Placebo	0	0	1.7538		1.7538			
Cinnarizine:Propranolol								
Cinnarizine:Riboflavin			2.2433		2.2433	•		•
Cinnarizine:Sodium Valproate		-	0.7305		0.7305	•	•	•
Cinnarizine:Topiramate					0.5234	•		•
Flunarizine:Nimodipine		-	6.6410	-	6.6410	•	•	•
Flunarizine:Placebo	_			7.0000	•	•	•	•
Flunarizine:Propranolol			3.9913	•	3.9913	•	•	•
Flunarizine:Riboflavin			8.9535		8.9535	•		•
Flunarizine:Sodium Valproate			2.9155	•	2.9155	•	•	•
Flunarizine:Topiramate			2.0890	•	2.0890	•	•	•
Nimodipine:Placebo					•	•	•	•
Nimodipine:Propranolol			0.6010		0.6010	•	•	•
Nimodipine:Riboflavin			1.3482		1.3482	•	•	•
Nimodipine:Sodium Valproate			0.4390		0.4390	•	•	•
Nimodipine:Topiramate			0.3146	•	0.3146	•	•	•
Propranolol:Placebo			1.7538	•	1.7538	•	•	•
Riboflavin:Placebo					•	•		•
Sodium Valproate:Placebo								
Topiramate:Placebo				2.8286		0.4586	-0.34	0.7315
Propranolol:Riboflavin			2.2433		2.2433			·
Propranolol:Sodium Valproate							0.34	0.7315
Propranolol:Topiramate						0.4586	-0.34	0.7315
Riboflavin:Sodium Valproate			0.3256		0.3256	•	•	•
Riboflavin:Topiramate			0.2333		0.2333	•	•	•
Sodium Valproate:Topiramate	0	0	0.7165	•	0.7165	•	·	•

Legend:

comparison	- Treatment comparison
k	- Number of studies providing direct evidence
prop	- Direct evidence proportion
nma	- Estimated treatment effect (RR) in network meta-analysis
direct	- Estimated treatment effect (RR) derived from direct evidence
indir.	- Estimated treatment effect (RR) derived from indirect evidence
RoR	- Ratio of Ratios (direct versus indirect)
z	 z-value of test for disagreement (direct versus indirect)
p-value	- p-value of test for disagreement (direct versus indirect)

Safety – Global approach

Q statistics to assess homogeneity / consistency Q df p-value
 Q at p-value

 Total
 0.33
 3
 0.9545

 Within designs
 0.21
 2
 0.8998

 Between designs
 0.12
 1
 0.7315
 Design-specific decomposition of within-designs Q statistic Design Q df p-value Propranolol:Sodium Valproate 0.00 1 0.9911 Propranolol:Topiramate 0.21 1 0.6460 Between-designs Q statistic after detaching of single designs Detached design Q df p-value Placebo:Sodium Valproate 0.00 0 --Placebo:Topiramate 0.00 0 --Propranolol:Sodium Valproate 0.00 0 --Propranolol:Topiramate 0.00 0 --Q statistic to assess consistency under the assumption of a full design-by-treatment interaction random effects model Q df p-value tau.within tau2.within Between designs 0.12 1 0.7315 0 0

eAppendix 4. Details on Publication Bias

Currently, there is a lack of a concrete methodology of assessing across-studies bias (publication bias) for a network meta-analytic approach. Therefore, a comparison-adjusted funnel plot with accompanying Egger test for asymmetry was conducted². See eFigures 2, 3, and 4 for results.

eAppendix 5. Details on Prediction Intervals

Prediction intervals help in the clinical interpretation of the *heterogeneity* by providing a region within which a given percentage of true treatment effects are expected, were calculated.¹ For example, a 95% prediction interval estimates where the true effects are to be expected for 95% of similar (exchangeable) studies that might be conducted in the future. Reporting a prediction interval in addition to the standardized mean differences and confidence intervals can help estimate the range of true effects that can be expected in future settings.

70% Prediction Interval

```
Number of studies: k = 19
Number of treatments: n = 12
Number of pairwise comparisons: m = 19
Number of designs: d = 14
```

Random effects model

<pre>Treatment estimate (sm = 'SMD'</pre>	, comparison: othe	er treatments vs 'Placebo'):
	SMD	95%-CI 70%-PI
Butterbur root extract	-0.0000 [-1.1517;	1.1517] [-0.8113; 0.8113]
Cinnarizine	0.5185 [-0.2116;	1.2486] [-0.1136; 1.1506]
CoEnzyme Q10	0.2984 [-0.6082;	1.2051] [-0.4042; 1.0011]
Flunarizine	0.9319 [-0.1179;	1.9817] [0.1670; 1.6968]
L-5-Hydroxytryptophan (L-5HTP)	-0.2068 [-1.4029;	0.9893] [-1.0388; 0.6252]
Nimodipine	-0.0000 [-1.0526;	1.0526] [-0.7662; 0.7662]
Placebo		
Pregabalin	0.8139 [-0.2757;	1.9036] [0.0310; 1.5968]
Propranolol	0.6018 [0.0317;	1.1720] [0.0259; 1.1778]
Riboflavin	0.1947 [-0.3883;	0.7778] [-0.3855; 0.7749]
Sodium Valproate	0.2175 [-0.4235;	0.8585] [-0.3823; 0.8173]
Topiramate	0.5906 [0.0266;	1.1547] [0.0166; 1.1646]

Quantifying heterogeneity / inconsistency: tau^2 = 0.1803; I^2 = 75.1%

Tests of heterogeneity (within designs) and inconsistency (between designs): Q d.f. $p\mbox{-value}$

	Ų	а.т.	p-value
Total	32.13	8	< 0.0001
Within designs	26.13	5	< 0.0001
Between designs	6.01	3	0.1113

75% Prediction Interval

Number of studies: k = 19 Number of treatments: n = 12 Number of pairwise comparisons: m = 19 Number of designs: d = 14

Random effects model

Treatment estimate (sm = 'SMD'	, compari	son: othe	r treatme	ents vs 'P	lacebo'):
	SMD		95%-CI		75%-PI
Butterbur root extract	-0.0000	[-1.1517;	1.1517]	[-0.9093;	0.9093]
Cinnarizine	0.5185	[-0.2116;	1.2486]	[-0.1899;	1.2269]
CoEnzyme Q10	0.2984	[-0.6082;	1.2051]	[-0.4891;	1.0860]
Flunarizine	0.9319	[-0.1179;	1.9817]	[0.0746;	1.7892]
L-5-Hydroxytryptophan (L-5HTP)	-0.2068	[-1.4029;	0.9893]	[-1.1393;	0.7256]
Nimodipine	-0.0000	[-1.0526;	1.0526]	[-0.8587;	0.8587]
Placebo					•
Pregabalin	0.8139	[-0.2757;	1.9036]	[-0.0635;	1.6913]
Propranolol	0.6018	[0.0317;	1.1720]	[-0.0437;	1.2474]
Riboflavin	0.1947	[-0.3883;	0.7778]	[-0.4555;	0.8450]
Sodium Valproate	0.2175	[-0.4235;	0.8585]	[-0.4547;	0.8897]
Topiramate	0.5906	[0.0266;	1.1547]	[-0.0527;	1.2339]

Quantifying heterogeneity / inconsistency: tau^2 = 0.1803; I^2 = 75.1%

Tests of heterogeneity (within designs) and inconsistency (between designs): Q d.f. p-value Total 32.13 8 < 0.0001 Within designs 26.13 5 < 0.0001 Between designs 6.01 3 0.1113

95% Prediction Interval

Number of studies: k = 19 Number of treatments: n = 12 Number of pairwise comparisons: m = 19 Number of designs: d = 14

Random effects model

Treatment estimate (sm = 'SMD'	, compart	ison: othe	r treatme	ents vs 'Placebo'):
	SMD		95%-CI	95%-PI
Butterbur root extract	-0.0000	[-1.1517;	1.1517]	[-1.7142; 1.7142]
Cinnarizine	0.5185	[-0.2116;	1.2486]	[-0.8171; 1.8540]
CoEnzyme Q10	0.2984	[-0.6082;	1.2051]	[-1.1862; 1.7831]
Flunarizine	0.9319	[-0.1179;	1.9817]	[-0.6843; 2.5481]
L-5-Hydroxytryptophan (L-5HTP)	-0.2068	[-1.4029;	0.9893]	[-1.9647; 1.5511]
Nimodipine	-0.0000	[-1.0526;	1.0526]	[-1.6189; 1.6189]
Placebo				
Pregabalin	0.8139	[-0.2757;	1.9036]	[-0.8402; 2.4681]
Propranolol	0.6018	[0.0317;	1.1720]	[-0.6151; 1.8188]
Riboflavin	0.1947	[-0.3883;	0.7778]	[-1.0311; 1.4206]
Sodium Valproate	0.2175	[-0.4235;	0.8585]	[-1.0498; 1.4847]
Topiramate	0.5906	[0.0266;	1.1547]	[-0.6222; 1.8034]

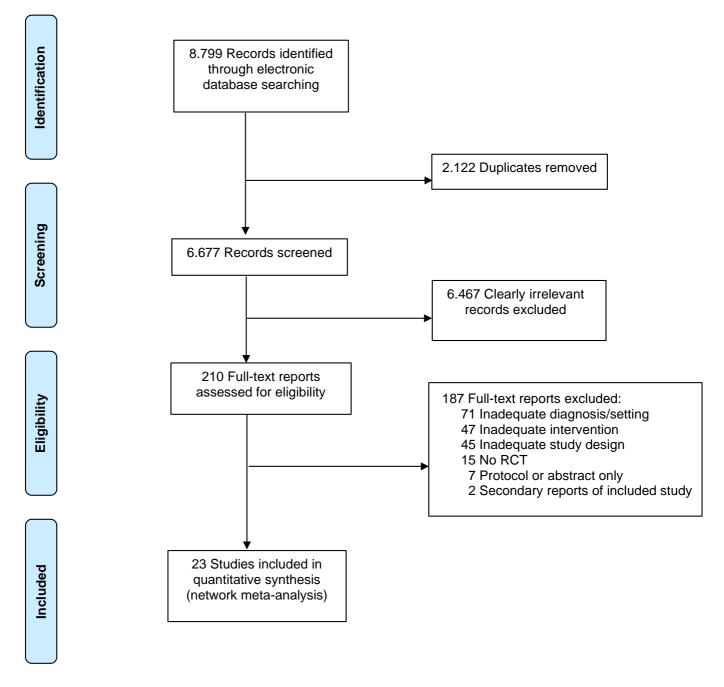
Quantifying heterogeneity / inconsistency: tau^2 = 0.1803; I^2 = 75.1%

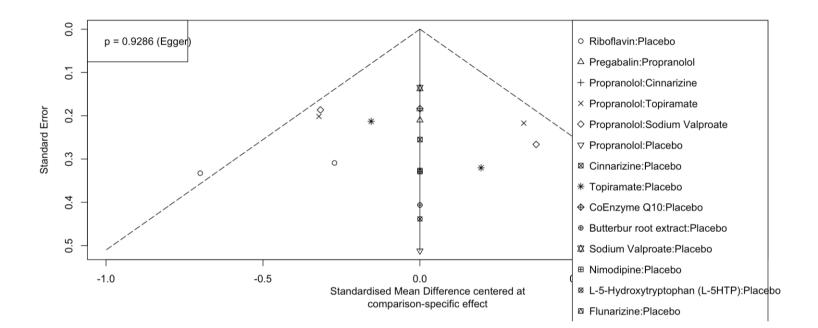
Tests of heterogeneity (within designs) and inconsistency (between designs): Q d.f. p-value Total 32.13 8 < 0.0001 Within designs 26.13 5 < 0.0001 Between designs 6.01 3 0.1113

eAppendix 6. Results of Long-term Analysis

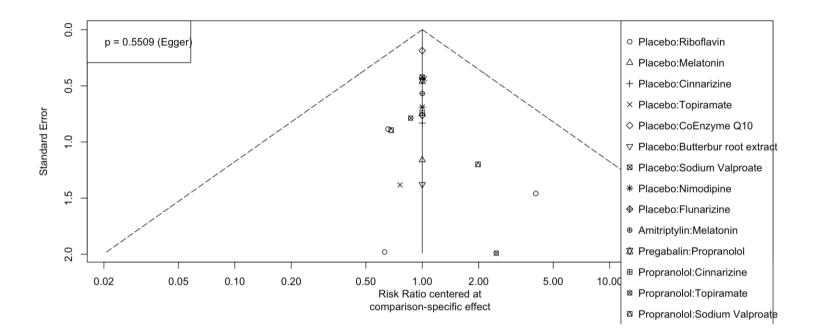
For the analysis of long-term effects, we added the measurements with 5-6 months as well as more than 6 months to the data-set. We preferably considered the data with the longest time window after randomization. Two additional studies were considered in the long-term analysis which were not included in the main analysis^{7,8}. See eFigures 5, 6, and 7 and eTables 3a, 3b, and 3c for results.

eFigure 1. Flow Chart

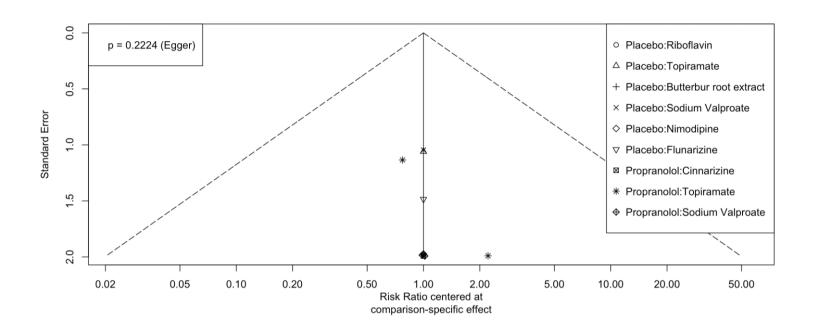




eFigure 2. Funnel plot with accompanying Egger test: Efficacy



eFigure 3. Funnel plot with accompanying Egger test: Acceptability



eFigure 4. Funnel plot with accompanying Egger test: Safety

eFigure 5. Long-Term Efficacy – Forest Plot

	Comparison: Active Drug vs Placebo)		
Treatment	(Random Effects Model)	SMD	95%-CI	P-score
Flunarizine (1 / 21)		0.93	[-0.10; 1.96]	0.84
Pregabalin (1 / 46)		0.65	[-0.39; 1.69]	0.72
Propranolol (7 / 297)		0.44	[-0.08; 0.96]	0.64
Cinnarizine (2 / 87)		0.43	[-0.27; 1.14]	0.61
Nimodipine (1 / 18)		0.46	[-0.58; 1.50]	0.60
Topiramate (7 / 423)		0.29	[-0.12; 0.70]	0.52
CoEnzyme Q10 (1 / 60)		0.30	[-0.58; 1.18]	0.51
Amitriptylin (2 / 132)		0.22	[-0.54; 0.98]	0.45
Riboflavin (3 / 107)		0.20	[-0.37; 0.77]	0.44
Sodium Valproate (3 / 315)		0.11	[-0.50; 0.73]	0.36
Butterbur root ex (1 / 19)		0.00	[-1.13; 1.13]	0.34
Placebo (16 / 491)		0.00		0.24
L-5-Hydroxytrypto (1 / 10)		-0.21	[-1.38; 0.97]	0.24
	-1 0 1			
	Favours 'Placebo' Favours 'Active Dr	ug'		

eFigure 6. Long-Term Acceptability – Forest Plot

Treatment	Comparison: Active Drug vs Placebo (Random Effects Model)	RR	95%-CI	P-score
Riboflavin (3 / 107)		0.49	[0.12; 1.97]	0.80
CoEnzyme Q10 (1 / 60)		0.84	[0.58; 1.22]	0.67
Nimodipine (1 / 18)		0.79	[0.21; 3.06]	0.62
Melatonin (2 / 58)		0.90	[0.31; 2.63]	0.57
Placebo (15 / 492)		1.00		0.54
Butterbur root ex (1 / 20)		0.95	[0.06; 14.13]	0.52
Flunarizine (1 / 24)		1.00	[0.22; 4.47]	0.51
Pregabalin (1 / 46)		1.08	[0.29; 4.05]	0.48
Propranolol (6 / 289)		1.10	[0.41; 2.94]	0.47
Cinnarizine (2 / 94)		1.22	[0.36; 4.12]	0.41
Amitriptylin (3 / 190)		1.22	[0.78; 1.93]	0.38
Topiramate (7 / 443)		1.34	[0.92; 1.95]	0.29
Sodium Valproate (3 / 323)		1.55	[0.73; 3.30]	0.25
	0.1 0.5 1 2 10			
F	avours 'Active Drug' Favours 'Placebo'			

eFigure 7. Long-Term Safety – Forest Plot

	Comparison: Active Drug vs Place	ebo		
Treatment	(Random Effects Model)	RR	95%-CI	P-score
Placebo (9 / 311)		1.00		0.69
Riboflavin (1 / 27)		0.78	[0.02; 37.83]	0.63
Butterbur root ex (1 / 20)		0.95	[0.02; 45.63]	0.60
Nimodipine (1 / 18)		1.05	[0.02; 50.43]	0.58
Propranolol (5 / 244)		1.40	[0.22; 8.94]	0.56
Cinnarizine (1 / 60)	*	— 1.40 [0.02; 105.46]	0.53
Sodium Valproate (3 / 323)		2.22	[0.38; 13.03]	0.42
Amitriptylin (2 / 144)		2.31	[0.61; 8.70]	0.40
Topiramate (6 / 421)	· · ·	2.49	[0.90; 6.93]	0.36
Flunarizine (1 / 24)		— 7.00 [0.38; 128.47]	0.21
	0.01 0.1 1 10	100		
Fa	vours 'Active Drug' Favours 'Placet	00'		

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Bias ^a
Apostol 2008	Efficacy Acceptability Safety	250 mg/day Divalproex sodium extended release	500 mg/day Divalproex sodium extended release	1000 mg/day Divalproex sodium extended release	Placebo Identical tablets	migraine	ICHD second edition	250 mg: 14.2 (1.69) 500 mg: 14.1 (1.56) 1000 mg: 14.3 (1.66) Placebo: 14.2 (1.50)	250 mg: 64.2 500 mg: 54 1000 mg: 46.6 Placebo: 52	USA	Low
Ashrafi 2005	Efficacy Acceptability Safety	Sodium Valproate (up to 40 mg/kg/day in 2 doses)	Propranolol (1–3 mg/kg/day in two doses)	-	-	migraine without aura	ICHD first edition	Sodium Valporate: 10.0 (2.30) Propranolol: 10.0 (2.70)	Sodium Valporate: 36.8 Propranolol: 31	not reported	Moderate
Ashrafi 2014	Efficacy Acceptability	Cinnarizine (1.5 mg/kg/day for <30kg, if >30kg: 50mg)		-	Placebo Pill	migraine with and without aura	ICHD second edition	Cinnarizine: 16.7 (2.4) Placebo: 8.9 (1.9)	Cinnarizine: 46.6 Placebo: 65.6	Iran	Low
Bakhshand eh Bali 2015	Efficacy Acceptability	Pregabalin (50-75 mg/day)	Propanolol (10-20 mg/day, in 2 doses)	-	-	migraine with and without aura	ICHD second edition	Pregabalin: 9.95 (n.r.) Propranolol:9. 81 (n.r.)	Pregabalin: 26 Propranolol: 31.1	Iran	Moderate
Battistella 1990	Efficacy Acceptability Safety	Nimodipine (10-20 mg/day in 3 doses)	-	-	Placebo Drops	migraine with and without aura	ICHD first edition	Nimodipine: 12.0 (3.4) Placebo:12.4 (3.3)	Nimodipine: 50 Placebo 52.6	Italy	Moderate

eTable 1a. Demographics and Study Characteristics

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Bias ^a
Bidabadi 2010	Efficacy Acceptability Safety	Propranolol (3 mg/kg/day in 2 doses; after one month: 2 mg/kg/day)	Sodium Valproate (30 mg/kg/day in 2 doses; after one month: 15 mg/kg/day)	-	-	migraine without aura	ICHD second edition	Propranolol: 9.8 (2.8) Sodium Valproate: 9.9 (2.57)	Propranolol: 37 Sodium Valproate 30	Iran	Moderate
Bruijn 2010	Efficacy Acceptability	Riboflavin (50 mg/day)	-	-	Placebo Carotene capsules	migraine with and without aura	ICHD second edition	Riboflavin: 9.9 (1.89) Placebo: 9.5 (1.63)	Riboflavin: 40 Placebo: 45.5	Netherlan ds	Low
Fallah 2013	Efficacy Acceptability Safety	Topiramate (3 mg/kg/day)	Propranolol (1 mg/kg/day)	-	-	migraine with and without aura	n.r.	Topiramate: 10.1 (2.24) Propranolol: 10.7 (2.35)	Topiramate: 58 Propranolol: 46	Iran	Low
Fallah 2018 ^b	Acceptability	Amitriptylin (1 mg/kg/day; max. 50 mg/day)	Melatonin (0.3 mg/kg/day; max. 6 mg/day)	-	-	migraine with and without aura	ICHD second edition	Amitriptylin: 10.1 (2.13) Melatonin: 10.6 (2.44)	Amitriptylin: 47.5 Melatonin: 55.0	Iran	Low
Gelfand 2017°	Acceptability	Melatonin (3 mg/day)	-	-	Placebo	migraine	ICHD third edition (beta version)	-	-	USA	Low

eTable 1a. Demographics and Study Characteristics. Continued.

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Biasª
Lakshmi 2007	Efficacy Acceptability	Topiramate (25-100 mg/day in 2 doses [baseline] 100 mg in 2 doses [maintenance phase])	-	-	Placebo Pill	migraine with and without aura	ICHD second edition	Topiramate: 10.95 (1.53) Placebo: 10.14 (1.35)	Topiramate: 14.29 Placebo: 47.62	India	Low
Lewis 2009	Efficacy Acceptability Safety	Topiramate 50 mg/day	Topiramate 100 mg/day	-	Placebo Capsule	migraine	ICHD second edition	Topiramate 50mg: 14.2 (1.6) Topiramate 100mg: 14.2 (1.5) Placebo: 14.4 (1.70)	Topiramate 50mg: 71.43 Topiramate 100mg: 48.57 Placebo: 63.64	US and non-US	Moderate
Ludvigsson 1974	Efficacy	Propranolol (<35kg: max. 60 mg/day in 3 doses; >35kg max 120 mg/day in 3 doses)	-	-	Placebo Pill	migraine	Ad hoc Committe e on classificati on of headache	n.r.	Propranolol:43 .75 Placebo: 43.75	Sweden	Moderate
MacLennan 2008	Efficacy Acceptability Safety	Riboflavin (200 mg/day)	-	-	Placebo Pill	migraine with and without aura	ICHD second edition	Riboflavin: 11.1 (2.1) Placebo: 11.5 (2.5)	Riboflavin: 44.44 Placebo: 57.14	Australia	Low

eTable 1a. Demographics and Study Characteristics. Continued.

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Biasª
Oelkers 2008	Efficacy Acceptability Safety	Butterbur root extract (8-9 years: 50mg/day in 2 doses [if no improvement: 75mg/day]; 10-12 years: 100mg/d in 2 doses [if no improvement: 150mg/day])		-	Placebo	migraine with and without aura	ICHD first edition (24h-rule replaced with 18h- rule)	Butterbur root extract: 10.6 (1.2) Placebo: 10.6 (1.5)	Butterbur root extract: 47.4 Placebo: 31.6	Germany	Moderate
Santucci 1986	Efficacy	L-5- Hydroxytrypto phan (5mg/kg/day in 3 doses)	-	-	Placebo Identical gelatine capsules	common migraine	In accordanc e with the ad hoc Committe e on classificati on of headache	Age range? 6- 11	< 50% female	Italy	Moderate
Slater 2011	Efficacy Acceptability	CoEnzyme Q10 as chewable tablets (100mg/day)	-	-	Placebo Chewable tablets	migraine with and without aura	ICHD second edition	CoEnzyme Q10: 13.3 (3) Placebo: 14 (2.6)	CoEnzyme Q10: 66.7 Placebo: 63.3	USA	Moderate
Sorge 1985	Efficacy Acceptability Safety	Flunarizine (5 mg/day)	-	-	Placebo	common and classical migraine	Valquist's criteria, clinical observatio n	Flunarizine: 10.6 (3.25) Placebo: 10.7 (3.29)	Flunarizine: 58.3 Placebo: 54.6	Italy	Moderate

eTable 1a. Demographics and Study Characteristics. Continued.

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Biasª
Talebian 2018	Efficacy Acceptability	Riboflavin 100mg	Riboflavin 200mg	-	Placebo Capsule	migraine with and without aura	ICHD second edition	Riboflavin 100mg: 8.47 (n.r.) Riboflavin 200mg: 8.97 (n.r.) Placebo: 7.9 (n.r.)	Riboflavin 100mg: 43.3 Riboflavin 200mg: 43.3 Placebo 50	Iran	Low
Togha 2012	Efficacy Acceptability Safety	Cinnarizine (6-12years: 37.5mg/day; 12-17 years: 50mg/day in 2 doses)	Propranolol (1 mg/kg/day)	-	-	migraine with and without aura	ICHD second edition	Cinnarizine: 9.8 (2.3) Propranolol: 8.9 (2.7)	Cinnarizine: 33.3 Propranolol: 32.1	Iran	Moderate
Tonekaboni 2013	Efficacy Acceptability Safety	Topiramate (50-100 mg/day)	Propranolol (20-80 mg/day)	-	-	migraine	ICHD second edition	Topiramate: 8.5 (2.9) Propranolol: 8.3 (2.8)	Topiramate: 50 Propranolol: 52.5	Iran	Moderate
Winner 2005 ^d	Efficacy Acceptability Safety	Topiramate (15 mg/day [week 1], 30 mg/day [week 2], 50 mg/day [week 3], in 2 doses)	-	-	Placebo	migraine with and without aura	ICHD 1997 proposed revision	Topiramate: 11.3 (2.5) Placebo: 10.7 (2.6)	Topiramate: 53.1 Placebo: 53.1	USA	Moderate

eTable 1a. Demographics and Study Characteristics. Continued.

eTable 1a. Demographics and Study Characteristics. Continued.

Study ID	Main Outcome	Intervention 1	Intervention 2	Intervention 3	Control	Diagnosis	Diagnosis criteria	Mean age per group, years (SD)	% Female per group	Country	Risk of Bias ^a
Powers	Efficacy	Amitriptylin	Topiramate	-	Placebo	migraine	ICHD	Amitriptylin:	Amitriptylin: 67	USA	Low
2017 ^d	Acceptability	(1 mg/kg/day	(2			with and	second	14.2 (2.4)	Topiramate:		
	Safety	in 2 doses)	mg/kg/day in			without	edition	Topiramate:	69.7		
			2 doses)			aura		14.2 (2.5)	Placebo: 68.06		
								Placebo: 14.2			
								(2.5)			

Note. *ICHD* = International Classification of Headache Disorders

^a Based on adequacy of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, usage of observer-rated outcomes, completeness of outcome data, specification of main outcomes a priori, reporting on all outcomes, and conduction of ITT-analyses. Individual items were summarized to produce a total score of 1 (low risk of bias), 2 (moderate/unclear risk of bias), or 3 (high risk of bias).

^b This study did not report efficacy data in a usable way (i.e., no baseline data reported).

[°]This study did report efficacy data; however, the study was unconnected to the efficacy network.

^d These studies reported long-term outcomes and were not included in the main analysis but only in the long-term analysis

eTable 1b. Study design and outcomes

						Dichotomous outco	ome	Continuous outcome		
Study ID	Number of study sites	Study design	Treatment duration	Co- intervention	Randomized per group	Responder criterion	Reported time point(s)	Types of outcome	Reported time point(s)	
Apostol 2008	38	Parallel	10 weeks plus 2 weeks titration	No	250 mg: 83 500 mg: 74 1000 mg: 75 Placebo: 73	≥50% reduction in migraine frequency within 4 weeks	2-4 months	Migraine frequency within 3 months prior to screening	2-4 months	
Ashrafi 2005	n.r.	Parallel	≥ 12 weeks	No	Sodium Valporate: 60 Propranolol: 60	≥ 50% reduction of baseline headache frequency per month	up to 2 months	Headache frequency	2-4 months	
Ashrafi 2014	1	Parallel	12 weeks	No	Cinnarizine: 34 Placebo: 34	≥50% reduction of baseline headache frequency per month	2-4 months	Headache frequency per month	2-4 months	
Bakhshand eh Bali 2015	1	Parallel	at least 8 weeks	Yes	Pregabalin: 46 Propranolol: 45	>=50% reduction of severity and frequency of headache per month	up to 2 months	Headache frequency per month	up to 2 months	
Battistella 1990	n.r.	Crossov er	12 weeks, 4 weeks washout crossover, 12 weeks	No	Nimodipine: 18 Placebo: 19	n.r.	n.r.	Headache frequency (attacks per month)	2-4 months	
Bidabadi 2010	1	Parallel	4 to 6 months	No	Propranolol: 32 Sodium Valpoate: 31	Headache frequency: Reduction of baseline headache frequency by >50%	2-4 months	Headache frequency per month	2-4 months	
Bruijn 2010	2	Crossov er	16 weeks, 4 weeks washout, 16 weeks	Yes	Riboflavin: 20 Placebo: 22	n.r.	n.r.	Mean frequency of migraine attacks in the last 4 weeks at the end of the riboflavin and placebo phase	2-4 months	

eTable 1b	Study	design	and	outcomes.	Continued.
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						Dichotomous outco	ome	Continuous outcome		
Study ID	Number of study sites	Study design	Treatment duration	Co- intervention	Randomized per group	Responder criterion	Reported time point(s)	Types of outcome	Reported time point(s)	
Fallah 2013	1	Parallel	3 months	No	Topiramate: 50 Propranolol: 50	≥50% reduction in monthly headache frequency	2-4 months	Headache frequency monthly	2-4 months	
Fallah 2018	1	Parallel	12 weeks	No	Melatonin: 45 Amitriptylin: 46	More than 50% decrease in monthly headache frequency during the follow-up period	n.r.	Monthly headache frequency	n.r.	
Gelfand 2017	1	Parallel	12 weeks	Yes	Melatonin: 13 Placebo: 13	n.r.	n.r.	Mean migraine days	2-4 months	
Lakshmi 2007	1	Parallel	12 weeks	No	Topiramate: 22 Placebo: 22	≥50% reduction in monthly migraine days	2-4 months	Migraine frequency	2-4 months	
Lewis 2009	31	Parallel	4 weeks titration and 12 weeks maintenance	No	Topiramate 50mg: 35 Topiramate 100mg: 35 Placebo: 33	≥50% reduction in the monthly migraine attack rate (48-hour-rule: a single migraine episode defined as all recurrences of migraine symptoms within 48 hours after onset)	2-4 months	Migraine attacks per month	2-4 months	
Ludvigsson 1974	n.r.	Crossov er	2 x13 weeks including titration phase of 1 week each	No	Propranolol: 16 Placebo: 16	Headache frequency reduction responder (66,6% reduction)	2-4 months	Frequency of headache attacks during a 3-month period	2-4 months	
MacLennan 2008	1	Parallel	12 weeks	No	Riboflavin: 27 Placebo: 21	≥50% reduction in the number of migraine attacks per 4 weeks at the end of the study period, compared with the baseline month	up to 2 months	Migraine frequency per month	n.r.	

						Dichotomous outco	me	Continuous o	utcome
Study ID	Number of study sites	Study design	Treatment duration	Co- intervention	Randomized per group	Responder criterion	Reported time point(s)	Types of outcome	Reported time point(s)
Oelkers 2008	1	Parallel	12 weeks	Yes	Butterbur root extract: 20 Placebo: 19	≥50% reduction of headache frequency compared with baseline	n.r.	Attack frequency per 28 days	Up to 2 months and 5-6 months
Santucci 1986	n.r.	Crossov er	4 weeks	No	n.r.	n.r.	n.r.	Frequency of migraine attacks per 4 weeks	2-4 months
Slater 2011	1	Crossov er	2 x16 weeks	No	CoEnzyme Q10: 60 Placebo: 60	CoEnzyme Q10: Migraine episodes -50% or more Placebo: n.r.	n.r.	Headache frequency	Up to 2 months and 2-4 months
Sorge 1985	1	Parallel	12 weeks	No	Flunarizine: 24 Placebo: 24	>50% reduction in migraine frequency	n.r.	Headache frequency	2-4 months
Talebian 2018	1	Parallel	12 weeks	No	Riboflavin 100mg: 30 Riboflavin 200mg: 30 Placebo: 30	≥50% reduction in headache days	2-4 months	Frequency of migraine attacks	2-4 months
Togha 2012	3	Parallel	12 weeks	No	Cinnarizine: 60 Propranolol: 60	≥ 50% reduction of baseline headache frequency per month	Up to 2 months and 2-4 months	Migraine frequency attacks per month	2-4 months
Tonekaboni 2013	1	Parallel	4weeks/16w eeks	No	Topiramate: 44 Propranolol: 42	n.r.	n.r.	Frequency, average number of headaches	up to 2 months and 2-4 months

						Dichotomous outco	ome	Continuous o	utcome
Study ID	Number of study sites	Study design	Treatment duration	Co- intervention	Randomized per group	Responder criterion	Reported time point(s)	Types of outcome	Reported time point(s)
Powers 2017*	31	Crossov er	12 weeks	unclear	Amitriptylin: 144 Topiramate: 145 Placebo: 72	≥50%reduction in number of headache days compared with baseline	4-6 months	Headache days per 28 days	4-6 months
Winner 2005*	17	Parallel	8 weeks titration (increasing dose), 12 weeks maintenance	No	Topiramate: 112 Placebo: 50	>50% baseline vs. last 28 days	4-6 months	Number of migraine days per months	4-6 months

eTable 1b. Study design and outcomes. Continued.

* These studies reported long-term outcomes and were not included in the main analysis but only in the long-term analysis

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]
Butterbur root extract [1]							0.00 [- 1.15; 1.15]					
Cinnarizine [2]	-0.52 [- 1.88; 0.85]						0.23 [- 0.74; 1.20]		0.17 [- 0.74; 1.08]			
CoEnzyme Q10 [3]	-0.30 [- 1.76; 1.17]	0.22 [- 0.94; 1.38]					0.30 [- 0.61; 1.21]					
Flunarizine [4]	-0.93 [- 2.49; 0.63]	-0.41 [- 1.69; 0.87]	-0.63 [- 2.02; 0.75]				0.93 [- 0.12; 1.98]					
L-5-Hydroxytryptophan (L-5HTP) [5]	0.21 [- 1.45; 1.87]	0.73 [- 0.68; 2.13]	0.51 [- 1.00; 2.01]	1.14 [- 0.45; 2.73]			-0.21 [- 1.40; 0.99]					
Nimodipine [6]	-0.00 [- 1.56; 1.56]	0.52 [- 0.76; 1.80]	0.30 [- 1.09; 1.69]	0.93 [- 0.55; 2.42]	-0.21 [- 1.80; 1.39]		0.00 [- 1.05; 1.05]					
Placebo [7]	-0.00 [- 1.15; 1.15]	0.52 [- 0.21; 1.25]	0.30 [- 0.61; 1.21]	0.93 [- 0.12; 1.98]	-0.21 [- 1.40; 0.99]	-0.00 [- 1.05; 1.05]			-1.51 [- 2.81; - 0.20]	-0.19 [- 0.78; 0.39]	-0.10 [- 0.98; 0.77]	-0.55 [- 1.25; 0.14]
Pregabalin [8]	-0.81 [- 2.40; 0.77]	-0.30 [- 1.47; 0.88]	-0.52 [- 1.93; 0.90]	0.12 [- 1.40; 1.63]	-1.02 [- 2.64; 0.60]	-0.81 [- 2.33; 0.70]	-0.81 [- 1.90; 0.28]		0.21 [- 0.72; 1.14]			
Propranolol [9]	-0.60 [- 1.89; 0.68]	-0.08 [- 0.80; 0.63]	-0.30 [- 1.37; 0.77]	0.33 [- 0.86; 1.52]	-0.81 [- 2.13; 0.52]	-0.60 [- 1.80; 0.60]	-0.60 [- 1.17; - 0.03]	0.21 [- 0.72; 1.14]			0.32 [- 0.35; 0.98]	-0.02 [- 0.68; 0.63]

eTable 2a. Head-to-head comparisons of efficacy of the included prophylactic treatments

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]
Riboflavin [10]	-0.19 [- 1.49; 1.10]	0.32 [- 0.61; 1.26]	0.10 [- 0.97; 1.18]	0.74 [- 0.46; 1.94]	-0.40 [- 1.73; 0.93]	-0.19 [- 1.40; 1.01]	-0.19 [- 0.78; 0.39]	0.62 [- 0.62; 1.86]	0.41 [- 0.41; 1.22]			
Sodium Valproate [11]	-0.22 [- 1.54; 1.10]	0.30 [- 0.55; 1.15]	0.08 [- 1.03; 1.19]	0.71 [- 0.52; 1.94]	-0.42 [- 1.78; 0.93]	-0.22 [- 1.45; 1.01]	-0.22 [- 0.86; 0.42]	0.60 [- 0.49; 1.69]	0.38 [- 0.19; 0.95]	-0.02 [- 0.89; 0.84]		
Topiramate [12]	-0.59 [- 1.87; 0.69]	-0.07 [- 0.89; 0.75]	-0.29 [- 1.36; 0.78]	0.34 [- 0.85; 1.53]	-0.80 [- 2.12; 0.52]	-0.59 [- 1.78; 0.60]	-0.59 [- 1.15; - 0.03]	0.22 [- 0.85; 1.30]	0.01 [- 0.54; 0.56]	-0.40 [- 1.21; 0.42]	-0.37 [- 1.09; 0.34]	

Note: Column headers are identical to row headers and are indicated by the number in the respective square brackets. Cells contain the network estimates (SMDs) from network meta-analysis in the lower triangle and the direct treatment estimates (SMDs) from pairwise comparisons in the upper triangle.

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Amitriptylin [1]						1.17 [0.39; 3.57]							
Butterbur root extract [2]	0.62 [0.02; 25.02]							0.95 [0.06; 14.13]					
Cinnarizine [3]	0.52 [0.03; 8.60]	0.84 [0.04; 16.20]						2.00 [0.39; 10.20]		0.75 [0.18; 3.21]			
CoEnzyme Q10 [4]	0.70 [0.05; 8.98]	1.13 [0.07; 17.17]	1.35 [0.37; 4.84]					0.84 [0.58; 1.22]					
Flunarizine [5]	0.59 [0.03; 11.12]	0.95 [0.04; 20.82]	1.14 [0.16; 7.87]	0.84 [0.18; 3.94]				1.00 [0.22; 4.47]					
Melatonin [6]	1.17 [0.39; 3.57]	1.90 [0.06; 64.83]	2.27 [0.17; 30.11]	1.69 [0.17; 16.89]	2.00 [0.13; 30.44]			0.50 [0.05; 4.86]					
Nimodipine [7]	0.74 [0.04; 13.07]	1.20 [0.06; 24.56]	1.44 [0.23; 8.90]	1.07 [0.26; 4.32]	1.26 [0.17; 9.49]	0.63 [0.04; 8.90]		0.79 [0.21; 3.06]					
Placebo [8]	0.59 [0.05; 7.38]	0.95 [0.06; 14.13]	1.14 [0.33; 3.87]	0.84 [0.58; 1.22]	1.00 [0.22; 4.47]	0.50 [0.05; 4.86]	0.79 [0.21; 3.06]				2.03 [0.51; 8.12]	0.58 [0.25; 1.32]	1.31 [0.58; 2.96]
Pregabalin [9]	0.62 [0.04; 10.97]	1.00 [0.05; 20.61]	1.20 [0.28; 5.25]	0.89 [0.22; 3.64]	1.06 [0.14; 7.97]	0.53 [0.04; 7.46]	0.84 [0.12; 5.68]	1.06 [0.27; 4.10]		0.98 [0.40; 2.38]			

eTable 2b. Head-to-head comparisons of acceptability of the included prophylactic treatments

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Propranolol [10]	0.61 [0.04; 9.32]	0.98 [0.05; 17.63]	1.18 [0.36; 3.81]	0.87 [0.29; 2.59]	1.03 [0.17; 6.34]	0.52 [0.04; 6.26]	0.82 [0.15; 4.46]	1.03 [0.37; 2.88]	0.98 [0.40; 2.38]			0.98 [0.24; 3.98]	0.40 [0.10; 1.69]
Riboflavin [11]	1.19 [0.07; 21.37]	1.93 [0.09; 40.12]	2.31 [0.36; 14.68]	1.71 [0.41; 7.18]	2.03 [0.26; 15.62]	1.02 [0.07; 14.56]	1.61 [0.23; 11.13]	2.03 [0.51; 8.12]	1.92 [0.28; 13.36]	1.96 [0.35; 11.00]			
Sodium Valproate [12]	0.39 [0.03; 5.51]	0.63 [0.04; 10.48]	0.76 [0.20; 2.88]	0.56 [0.24; 1.31]	0.67 [0.12; 3.58]	0.33 [0.03; 3.67]	0.53 [0.11; 2.49]	0.67 [0.31; 1.43]	0.63 [0.16; 2.49]	0.65 [0.23; 1.83]	0.33 [0.07; 1.60]		
Topiramate [13]	0.58 [0.04; 8.18]	0.94 [0.06; 15.55]	1.13 [0.30; 4.29]	0.84 [0.36; 1.93]	0.99 [0.19; 5.30]	0.50 [0.05; 5.45]	0.79 [0.17; 3.69]	0.99 [0.47; 2.10]	0.94 [0.24; 3.72]	0.96 [0.34; 2.75]	0.49 [0.10; 2.36]	1.49 [0.54; 4.07]	

eTable 2b. Head-to-head comparisons of acceptability of the included prophylactic treatments. Continued.

Note: Column headers are identical to row headers and are indicated by the number in the respective square brackets.

Cells contain the network estimates (RRs) from network meta-analysis in the lower triangle and the direct treatment estimates (RRs) from pairwise comparisons in the upper triangle. Shaded Area = Direct Comparisons

Butterbur root extract	Cinnarizine	Flunarizine	Nimodipine	Placebo	Propranolol	Riboflavin	Sodium Valproate	Topiramate
				0.95 [0.02; 45.63]				
0.54 [0.00; 201.21]		_			1.00 [0.02; 49.59]			
0.14 [0.00; 17.23]	0.25 [0.00; 52.10]			7.00 [0.38; 128.47]				
0.90 [0.00; 214.72]	1.66 [0.00; 616.22]	6.64 [0.05; 840.10]		1.05 [0.02; 50.43]				
0.95 [0.02; 45.63]	1.75 [0.02; 153.87]	7.00 [0.38; 128.47]	1.05 [0.02; 50.43]			1.28 [0.03; 61.88]	0.35 [0.05; 2.74]	0.35 [0.04; 2.82]
0.54 [0.01; 46.23]	1.00 [0.02; 49.59]	3.99 [0.10; 151.99]	0.60 [0.01; 51.11]	0.57 [0.06; 5.08]			0.98 [0.06; 15.48]	0.45 [0.07; 3.12]
1.22 [0.01; 291.78]	2.24 [0.01; 836.87]	8.95 [0.07; 1142.76]	1.35 [0.01; 322.72]	1.28 [0.03; 61.88]	2.24 [0.03; 192.64]			
0.40 [0.01; 28.53]	0.73 [0.01; 63.41]	2.92 [0.09; 90.18]	0.44 [0.01; 31.54]	0.42 [0.07; 2.57]	0.73 [0.08; 6.36]	0.33 [0.00; 23.63]		
0.28 [0.00; 20.59]	0.52 [0.01; 37.59]	2.09 [0.07; 65.21]	0.31 [0.00; 22.77]	0.30 [0.05; 1.87]	0.52 [0.09; 2.98]	0.23 [0.00; 17.06]	0.72 [0.08; 6.49]	
	root extract 0.54 [0.00; 201.21] 0.14 [0.00; 17.23] 0.90 [0.00; 214.72] 0.95 [0.02; 45.63] 0.54 [0.01; 46.23] 1.22 [0.01; 291.78] 0.40 [0.01; 28.53] 0.28 [0.00;	root extract Cinnarizine 0.54 [0.00; 201.21]	root extract Cinnarizine Flunarizine 0.54 [0.00; 201.21]	root extractCinnarizineFlunarizineNimodipine $0.54 [0.00;$ $201.21]0.55 [0.00;201.21]0.25 [0.00;52.10]0.25 [0.00;52.10]0.14 [0.00;17.23]0.25 [0.00;52.10]0.25 [0.00;52.10]0.90 [0.00;616.22]6.64 [0.05;840.10]0.90 [0.00;214.72]1.66 [0.00;616.22]6.64 [0.05;840.10]1.05 [0.02;50.43]0.95 [0.02;45.63]1.75 [0.02;153.87]7.00 [0.38;128.47]1.05 [0.02;50.43]0.54 [0.01;49.59]1.00 [0.02;49.59]3.99 [0.10;151.99]0.60 [0.01;51.11]1.22 [0.01;2.94 [0.01;836.87]8.95 [0.07;1142.76]1.35 [0.01;322.72]0.40 [0.01;28.53]0.73 [0.01;63.41]2.92 [0.09;90.18]0.44 [0.01;31.54]0.28 [0.00;0.52 [0.01;2.09 [0.07;0.31 [0.00;$	root extractCinnarizineFlunarizineNimodipinePlacebo0.54 [0.00; 201.21]0.25 [0.00; 52.10]0.25 [0.00; 52.10]0.25 [0.00; 17.23]7.00 [0.38; 128.47]0.90 [0.00; 214.72]0.25 [0.00; 52.10]6.64 [0.05; 840.10]7.00 [0.38; 128.47]0.90 [0.00; 214.72]1.66 [0.00; 616.22]6.64 [0.05; 840.10]1.05 [0.02; 50.43]0.95 [0.02; 45.63]1.75 [0.02; 153.87]7.00 [0.38; 128.47]1.05 [0.02; 50.43]0.54 [0.01; 46.23]1.00 [0.02; 49.59]3.99 [0.10; 151.99]0.60 [0.01; 51.11]0.57 [0.06; 5.08]1.22 [0.01; 291.78]2.24 [0.01; 836.87]8.95 [0.07; 1142.76]1.35 [0.01; 322.72]1.28 [0.03; 61.88]0.40 [0.01; 28.53]0.73 [0.01; 63.41]2.92 [0.09; 90.18]0.44 [0.01; 31.54]0.42 [0.07; 2.57]0.28 [0.00; 0.052 [0.01;0.52 [0.01; 2.09 [0.07;0.31 [0.00; 0.30 [0.05;	root extractCinnarizineFlunarizineNimodipinePlaceboPropranolol $0.54 [0.00;$ $201.21]$ $1.00 [0.02;$ $45.63]$ $0.95 [0.02;$ $45.63]$ $1.00 [0.02;$ $49.59]$ $0.14 [0.00;$ $201.21]$ $0.25 [0.00;$ $52.10]$ $7.00 [0.38;$ $128.47]$ $1.00 [0.02;$ $49.59]$ $0.90 [0.00;$ $214.72]$ $1.66 [0.00;$ $616.22]$ $6.64 [0.05;$ $840.10]$ $1.05 [0.02;$ $50.43]$ $0.95 [0.02;$ $214.72]$ $1.75 [0.02;$ $153.87]$ $7.00 [0.38;$ $128.47]$ $1.05 [0.02;$ $50.43]$ $0.95 [0.02;$ $49.59]$ $1.75 [0.02;$ $128.47]$ $1.05 [0.02;$ $50.43]$ $2.24 [0.03;$ $128.47]$ $0.95 [0.02;$ $49.59]$ $1.05 [0.02;$ $151.99]$ $1.05 [0.02;$ $50.43]$ $2.24 [0.03;$ $128.47]$ $0.54 [0.01;$ $49.59]$ $2.24 [0.01;$ $151.99]$ $3.99 [0.10;$ $1142.76]$ $0.57 [0.06;$ $5.08]$ $1.22 [0.01;$ $2.24 [0.01;$ $836.87]$ $8.95 [0.07;$ $1142.76]$ $1.35 [0.01;$ $322.72]$ $2.24 [0.03;$ $128.61]$ $0.40 [0.01;$ $2.57]$ $0.73 [0.01;$ $0.31 [0.02;$ $2.57]$ $0.73 [0.08;$ $6.36]$ $0.28 [0.00;$ $0.52 [0.01;$ $2.09 [0.07;$ $0.31 [0.00;$ $0.30 [0.05;$ $0.52 [0.09;$	root extract Cinnarizine Flunarizine Nimodipine Placebo Propranolol Riboflavin 0.54 [0.00; 201.21]	root extract Cinnarizine Flunarizine Nimodipine Placebo Propranolol Riboflavin Valproate 0.54 [0.00; 201.21]

eTable 2c. Head-to-head comparisons of safety of the included prophylactic treatments

Cells contain the network estimates (RRs) from network meta-analysis in the lower triangle and the direct treatment estimates (RRs) from pairwise comparisons in the upper triangle. Shaded Area = Direct Comparisons

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Amitriptylin [1]								0.14 [- 0.72; 1.00]					0.00 [- 0.84; 0.84]
Butterbur root extract [2]	0.22 [- 1.15; 1.59]							0.00 [- 1.13; 1.13]					
Cinnarizine [3]	-0.21 [- 1.23; 0.80]	-0.43 [- 1.77; 0.90]						0.23 [- 0.72; 1.18]		0.17 [- 0.72; 1.06]			
CoEnzyme Q10 [4]	-0.08 [- 1.25; 1.09]	-0.30 [- 1.73; 1.14]	0.13 [- 1.00; 1.26]					0.30 [- 0.58; 1.18]					
Flunarizine [5]	-0.71 [- 1.99; 0.57]	-0.93 [- 2.46; 0.60]	-0.50 [- 1.75; 0.75]	-0.63 [- 1.99; 0.72]				0.93 [- 0.10; 1.96]					
L-5- Hydroxytryptophan (L- 5HTP) [6]	0.43 [- 0.98; 1.83]	0.21 [- 1.43; 1.84]	0.64 [- 0.73; 2.01]	0.51 [- 0.97; 1.98]	1.14 [- 0.43; 2.70]			-0.21 [- 1.38; 0.97]					
Nimodipine [7]	-0.24 [- 1.53; 1.05]	-0.46 [- 1.99; 1.08]	-0.03 [- 1.28; 1.23]	-0.16 [- 1.52; 1.20]	0.47 [- 0.99; 1.94]	-0.66 [- 2.24; 0.91]		0.46 [- 0.58; 1.50]					
Placebo [8]	0.22 [- 0.54; 0.98]	0.00 [- 1.13; 1.13]	0.43 [- 0.27; 1.14]	0.30 [- 0.58; 1.18]	0.93 [- 0.10; 1.96]	-0.21 [- 1.38; 0.97]	0.46 [- 0.58; 1.50]			-1.51 [- 2.79; - 0.22]	-0.20 [- 0.77; 0.37]	-0.10 [- 0.95; 0.75]	-0.21 [- 0.66; 0.24]
Pregabalin [9]	-0.43 [- 1.69; 0.83]	-0.65 [- 2.19; 0.89]	-0.22 [- 1.36; 0.92]	-0.35 [- 1.72; 1.02]	0.28 [- 1.18; 1.75]	-0.86 [- 2.43; 0.72]	-0.19 [- 1.66; 1.28]	-0.65 [- 1.69; 0.39]		0.21 [- 0.69; 1.12]			

eTable 3a. Head-to-head comparisons of long-term efficacy of the included prophylactic treatments

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Propranolol [10]	-0.22 [- 1.09; 0.65]	-0.44 [- 1.68; 0.81]	-0.01 [- 0.70; 0.69]	-0.14 [- 1.16; 0.89]	0.49 [- 0.66; 1.65]	-0.64 [- 1.93; 0.64]	0.02 [- 1.14; 1.18]	-0.44 [- 0.96; 0.08]	0.21 [- 0.69; 1.12]			0.32 [- 0.34; 0.97]	-0.02 [- 0.66; 0.62]
Riboflavin [11]	0.02 [- 0.93; 0.98]	-0.20 [- 1.47; 1.07]	0.23 [- 0.67; 1.14]	0.10 [- 0.95; 1.15]	0.73 [- 0.44; 1.91]	-0.40 [- 1.71; 0.90]	0.26 [- 0.92; 1.45]	-0.20 [- 0.77; 0.37]	0.45 [- 0.74; 1.64]	0.24 [- 0.53; 1.01]			
Sodium Valproate [12]	0.11 [- 0.84; 1.05]	-0.11 [- 1.40; 1.17]	0.32 [- 0.51; 1.15]	0.18 [- 0.89; 1.26]	0.82 [- 0.38; 2.01]	-0.32 [- 1.65; 1.01]	0.34 [- 0.86; 1.55]	-0.11 [- 0.73; 0.50]	0.54 [- 0.52; 1.60]	0.32 [- 0.23; 0.87]	0.08 [- 0.75; 0.92]		
Topiramate [13]	-0.07 [- 0.83; 0.69]	-0.29 [- 1.50; 0.91]	0.14 [- 0.62; 0.89]	0.00 [- 0.97; 0.98]	0.64 [- 0.47; 1.75]	-0.50 [- 1.75; 0.75]	0.16 [- 0.95; 1.28]	-0.29 [- 0.70; 0.12]	0.36 [- 0.68; 1.39]	0.14 [- 0.36; 0.65]	-0.10 [- 0.80; 0.61]	-0.18 [- 0.83; 0.47]	

eTable 3a. Head-to-head comparisons of long-term efficacy of the included prophylactic treatments. Continued.

Note: Column headers are identical to row headers and are indicated by the number in the respective square brackets. Cells contain the network estimates (SMDs) from network meta-analysis in the lower triangle and the direct treatment estimates (SMDs) from pairwise comparisons in the upper triangle. Shaded Area = Direct Comparisons

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Amitriptylin [1]						1.17 [0.39; 3.57]		1.46 [0.83; 2.57]					0.89 [0.61; 1.29]
Butterbur root extract [2]	1.29 [0.08; 19.92]							0.95 [0.06; 14.13]					
Cinnarizine [3]	1.00 [0.28; 3.59]	0.78 [0.04; 15.01]						2.00 [0.39; 10.20]		0.75 [0.18; 3.21]			
CoEnzyme Q10 [4]	1.45 [0.81; 2.60]	1.13 [0.07; 17.17]	1.45 [0.41; 5.15]					0.84 [0.58; 1.22]					
Flunarizine [5]	1.22 [0.26; 5.85]	0.95 [0.04; 20.82]	1.22 [0.18; 8.40]	0.84 [0.18; 3.94]				1.00 [0.22; 4.47]					
Melatonin [6]	1.35 [0.50; 3.69]	1.05 [0.06; 19.13]	1.35 [0.27; 6.70]	0.93 [0.30; 2.88]	1.11 [0.18; 6.94]			0.50 [0.05; 4.86]					
Nimodipine [7]	1.55 [0.37; 6.44]	1.20 [0.06; 24.56]	1.54 [0.25; 9.49]	1.07 [0.26; 4.32]	1.26 [0.17; 9.49]	1.14 [0.20; 6.39]		0.79 [0.21; 3.06]					
Placebo [8]	1.22 [0.78; 1.93]	0.95 [0.06; 14.13]	1.22 [0.36; 4.12]	0.84 [0.58; 1.22]	1.00 [0.22; 4.47]	0.90 [0.31; 2.63]	0.79 [0.21; 3.06]				2.03 [0.51; 8.12]	0.58 [0.25; 1.32]	0.78 [0.53; 1.14]
Pregabalin [9]	1.14 [0.29; 4.45]	0.88 [0.04; 17.86]	1.13 [0.26; 4.93]	0.78 [0.20; 3.10]	0.93 [0.13; 6.86]	0.84 [0.16; 4.49]	0.74 [0.11; 4.88]	0.93 [0.25; 3.49]		0.98 [0.40; 2.38]			

eTable 3b. Head-to-head comparisons of long-term acceptability of the included prophylactic treatments

	[1]	[2]	[3]	[4]	[5]	[6]	[7]	[8]	[9]	[10]	[11]	[12]	[13]
Propranolol [10]	1.11 [0.40; 3.13]	0.86 [0.05; 15.27]	1.11 [0.35; 3.57]	0.77 [0.27; 2.19]	0.91 [0.15; 5.44]	0.82 [0.20; 3.40]	0.72 [0.14; 3.82]	0.91 [0.34; 2.42]	0.98 [0.40; 2.38]			0.98 [0.24; 3.98]	0.40 [0.10; 1.69]
Riboflavin [11]	2.49 [0.58; 10.69]	1.93 [0.09; 40.12]	2.48 [0.39; 15.66]	1.71 [0.41; 7.18]	2.03 [0.26; 15.62]	1.84 [0.32; 10.55]	1.61 [0.23; 11.13]	2.03 [0.51; 8.12]	2.19 [0.32; 14.86]	2.23 [0.41; 12.21]			
Sodium Valproate [12]	0.79 [0.33; 1.89]	0.61 [0.04; 10.13]	0.79 [0.21; 2.99]	0.54 [0.23; 1.26]	0.65 [0.12; 3.46]	0.58 [0.16; 2.14]	0.51 [0.11; 2.41]	0.65 [0.30; 1.38]	0.69 [0.18; 2.69]	0.71 [0.26; 1.97]	0.32 [0.07; 1.54]		
Topiramate [13]	0.92 [0.64; 1.31]	0.71 [0.05; 10.85]	0.91 [0.26; 3.17]	0.63 [0.37; 1.07]	0.75 [0.16; 3.50]	0.68 [0.24; 1.93]	0.59 [0.15; 2.41]	0.75 [0.51; 1.09]	0.80 [0.21; 3.04]	0.82 [0.31; 2.21]	0.37 [0.09; 1.55]	1.16 [0.51; 2.65]	

eTable 3b. Head-to-head comparisons of long-term acceptability of the included prophylactic treatments. Continued.

Note: Column headers are identical to row headers and are indicated by the number in the respective square brackets. Cells contain the network estimates (RRs) from network meta-analysis in the lower triangle and the direct treatment estimates (RRs) from pairwise comparisons in the upper triangle. Shaded Area = Direct Comparisons

	Amitriptylin	Butterbur root extract	Cinnarizine	Flunarizine	Nimodipine	Placebo	Propranolol	Riboflavin	Sodium Valproate	Topiramate
Amitriptylin						3.50 [0.44; 27.91]				0.88 [0.33; 2.37]
Butterbur root extract	2.43 [0.04; 145.18]					0.95 [0.02; 45.63]				
Cinnarizine	1.65 [0.02; 129.09]	0.68 [0.00; 224.72]					1.00 [0.02; 49.59]			
Flunarizine	0.33 [0.01; 8.07]	0.14 [0.00; 17.23]	0.20 [0.00; 36.62]			7.00 [0.38; 128.47]				
Nimodipine	2.19 [0.04; 130.69]	0.90 [0.00; 214.72]	1.33 [0.00; 438.70]	6.64 [0.05; 840.10]		1.05 [0.02; 50.43]				
Placebo	2.31 [0.61; 8.70]	0.95 [0.02; 45.63]	1.40 [0.02; 105.46]	7.00 [0.38; 128.47]	1.05 [0.02; 50.43]			1.28 [0.03; 61.88]	0.35 [0.05; 2.74]	0.43 [0.15; 1.24]
Propranolol	1.65 [0.24; 11.52]	0.68 [0.01; 49.65]	1.00 [0.02; 49.59]	5.00 [0.16; 157.52]	0.75 [0.01; 54.89]	0.71 [0.11; 4.56]			0.98 [0.06; 15.48]	0.45 [0.07; 3.12]
Riboflavin	2.95 [0.05; 178.06]	1.22 [0.01; 291.78]	1.79 [0.01; 595.87]	8.95 [0.07; 1142.76]	1.35 [0.01; 322.72]	1.28 [0.03; 61.88]	1.79 [0.02; 131.92]			
Sodium Valproate	1.04 [0.13; 8.47]	0.43 [0.01; 30.30]	0.63 [0.01; 51.51]	3.16 [0.10; 95.30]	0.48 [0.01; 33.50]	0.45 [0.08; 2.65]	0.63 [0.08; 4.82]	0.35 [0.00; 25.10]		

eTable 3c. Head-to-head comparisons of long-term safety of the included prophylactic treatments

eTable 3c. Head-to-head comparisons of long-term safety of the included prophylactic treatments. Continued.

	Amitriptylin	Butterbur root extract	Cinnarizine	Flunarizine	Nimodipine	Placebo	Propranolol	Riboflavin	Sodium Valproate	Topiramate
Topiramate	0.93 [0.35; 2.44]	0.38 [0.01; 20.92]	0.56 [0.01; 39.73]	2.81 [0.13; 61.39]	0.42 [0.01; 23.12]	0.40 [0.14; 1.12]	0.56 [0.10; 3.08]	0.31 [0.01; 17.33]	0.89 [0.13; 5.96]	

Note: The league table contains the network estimates (RRs) from network meta-analysis in the lower triangle and the direct treatment estimates (RRs) from pairwise comparisons in the upper triangle. Shaded Area = Direct Comparisons

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