

Supplementary Information: The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for rating the quality of estimates of treatment effect size

- **Study Limitations:** Determining risk of bias; the rating was downgraded by one level when the studies with high risk of bias in at least one domain contributed to the comparisons.
- **Imprecision:** Focusing on width of the confidence interval; the rating was downgraded by one level when the null value lies within the 95% Credible Intervals. The null value is zero for continuous outcomes.
- **Inconsistency:** Judging the extent of heterogeneity; tau-squared values were very low with little suggestion of heterogeneity for all outcomes. Also, evaluating the inconsistent loops of evidence which in our six NMA models, there was no evidence of close loops to assess local inconsistency. Global inconsistency test showed a consistent evidence of data points.
- **Indirectness:** Evaluating indirectness of populations, interventions and outcomes; these were assured in the network by limiting the included outcomes specific to adult with chronic migraine at week 12 and only for double blind phase of RCTs. Effect modifiers are balanced across the network. Thus, there is no evidence of intransitivity.
- **Publication Bias:** Non-statistical consideration of likelihood of non-publication of evidence, was assured through comprehensive searching in registered trials in the clinicaltrials.gov.

The quality of the head-to-head comparison of each outcome were rated as High ($\oplus\oplus\oplus\oplus$), Moderate ($\oplus\oplus\oplus\circ$), Low ($\oplus\oplus\circ\circ$) and Very low quality ($\oplus\circ\circ\circ$)

Table 1: Change from baseline in MHD (Rating down)

Outcome: Change from baseline in MHD (Rating down)								
Comparisons	MDs (95% CrIs)	Study Limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading	
FRE675 vs PBO	-1.79 (-2.62, -0.98)						High	⊕⊕⊕⊕
FRE225 vs PBO	-2.10 (-2.95, -1.23)						High	⊕⊕⊕⊕
GAL120 vs PBO	-1.82 (-2.91, -0.73)						High	⊕⊕⊕⊕
GAL240 vs PBO	-1.61 (-2.68, -0.54)						High	⊕⊕⊕⊕
TOP100 vs PBO	-1.10 (-2.38, 0.16)	↓	↓				Low	⊕⊕○○
EPT100 vs PBO	-1.84 (-2.60, -1.08)						High	⊕⊕⊕⊕
EPT300 vs PBO	-2.46 (-3.24, -1.67)						High	⊕⊕⊕⊕
EPT30 vs PBO	-2.19 (-3.63, -0.74)						High	⊕⊕⊕⊕
EPT10 vs PBO	-0.48 (-2.02, 1.01)		↓				Moderate	⊕⊕⊕○
BTA vs PBO	-1.87 (-2.55, -1.18)						High	⊕⊕⊕⊕
FRE225 vs FRE675	-0.30 (-1.60, 0.55)		↓				Moderate	⊕⊕⊕○
GAL120 vs FRE675	-0.02 (-1.44, 1.33)		↓				Moderate	⊕⊕⊕○
GAL240 vs FRE675	0.19 (-1.20, 1.56)		↓				Moderate	⊕⊕⊕○
TOP100 vs FRE675	0.69 (-0.78, 2.19)	↓	↓				Low	⊕⊕○○
EPT100 vs FRE675	-0.05 (-1.18, 1.10)		↓				Moderate	⊕⊕⊕○
EPT300 vs FRE675	-0.67 (-1.85, 0.49)		↓				Moderate	⊕⊕⊕○
EPT30 vs FRE675	-0.39 (-2.04, 1.23)		↓				Moderate	⊕⊕⊕○
EPT10 vs FRE675	1.31 (-0.47, 3.03)		↓				Moderate	⊕⊕⊕○
BTA vs FRE675	-0.07 (-1.16, 0.98)		↓				Moderate	⊕⊕⊕○
GAL120 vs FRE225	0.28 (-1.16, 1.67)		↓				Moderate	⊕⊕⊕○
GAL240 vs FRE225	0.49 (-0.86, 1.89)		↓				Moderate	⊕⊕⊕○
TOP100 vs FRE225	0.99 (-0.52, 2.50)	↓	↓				Low	⊕⊕○○
EPT100 vs FRE225	0.26 (-0.92, 1.39)		↓				Moderate	⊕⊕⊕○
EPT300 vs FRE225	-0.36 (-1.52, 0.81)		↓				Moderate	⊕⊕⊕○
EPT30 vs FRE225	-0.09 (-1.74, 1.54)		↓				Moderate	⊕⊕⊕○
EPT10 vs FRE225	1.62 (-0.13, 3.34)		↓				Moderate	⊕⊕⊕○

Outcome: Change from baseline in MHD (Rating down)								
Comparisons	MDs (95% CrIs)	Study Limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading	
BTA vs FRE225	0.23 (-0.84, 1.34)		↓				Moderate	⊕⊕⊕○
GAL240 vs GAL120	0.21 (0.85, 1.29)		↓				Moderate	⊕⊕⊕○
TOP100 vs GAL120	0.71 (-0.99, 2.37)	↓	↓				Low	⊕⊕○○
EPT100 vs GAL120	-0.02 (-1.35, 1.31)		↓				Moderate	⊕⊕⊕○
EPT300 vs GAL120	-0.64 (-2.02, 0.74)		↓				Moderate	⊕⊕⊕○
EPT30 vs GAL120	-0.37 (-2.22, 1.48)		↓				Moderate	⊕⊕⊕○
EPT10 vs GAL120	1.34 (-0.50, 3.27)		↓				Moderate	⊕⊕⊕○
BTA vs GAL120	-0.05 (-1.33, 1.23)		↓				Moderate	⊕⊕⊕○
TOP100 vs GAL240	0.50 (-1.18, 2.15)	↓	↓				Low	⊕⊕○○
EPT100 vs GAL240	-0.23 (-1.56, 1.08)		↓				Moderate	⊕⊕⊕○
EPT300 vs GAL240	-0.86 (-2.25, 0.49)		↓				Moderate	⊕⊕⊕○
EPT30 vs GAL240	-0.58 (-2.37, 1.20)		↓				Moderate	⊕⊕⊕○
EPT10 vs GAL240	1.13 (-0.70, 3.00)		↓				Moderate	⊕⊕⊕○
BTA vs GAL240	-0.26 (-1.54, 1.04)		↓				Moderate	⊕⊕⊕○
EPT100 vs TOP100	-0.74 (-2.21, 0.75)	↓	↓				Low	⊕⊕○○
EPT300 vs TOP100	-1.36 (-2.89, 0.14)	↓	↓				Low	⊕⊕○○
EPT30 vs TOP100	-1.08 (-3.08, 0.79)	↓	↓				Low	⊕⊕○○
EPT10 vs TOP100	0.62 (-1.36, 2.69)	↓	↓				Low	⊕⊕○○
BTA vs TOP100	-0.76 (-2.21, 0.70)	↓	↓				Low	⊕⊕○○
EPT300 vs EPT100	-0.62 (-1.42, 0.17)		↓				Moderate	⊕⊕⊕○
EPT30 vs EPT100	-0.35 (-1.81, 1.05)		↓				Moderate	⊕⊕⊕○
EPT10 vs EPT100	1.36 (-0.13, 2.87)		↓				Moderate	⊕⊕⊕○
BTA vs EPT100	-0.02 (-1.05, 1.02)		↓				Moderate	⊕⊕⊕○
EPT30 vs EPT300	0.28 (-1.18, 0.79)		↓				Moderate	⊕⊕⊕○
EPT10 vs EPT300	1.98 (0.52, 3.52)		↓				Moderate	⊕⊕⊕○
BTA vs EPT300	0.60 (-0.47, 1.67)		↓				Moderate	⊕⊕⊕○
EPT10 vs EPT30	1.70 (0.85, 3.32)		↓				Moderate	⊕⊕⊕○

Outcome: Change from baseline in MHD (Rating down)								
Comparisons	MDs (95% CrIs)	Study Limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading	
BTA vs EPT30	0.32 (-1.25, 1.95)		↓				Moderate	⊕⊕⊕○
BTA vs EPT10	-1.38 (0.85, 0.29)		↓				Moderate	⊕⊕⊕○

Abbreviations: MDs (95% CrIs), Mean Differences (95% Credible Intervals); FRE675, Fremanezumab-quarterly; PBO, Placebo; FRE225, Fremanezumab-monthly; GAL120, Galcanezumab 120mg; GAL240, Galcanezumab 240mg, TOP100, Topiramate 100mg, EPT100, Eptinezumab 100mg; EPT300, Eptinezumab 300mg; EPT30, Eptinezumab 30mg; EPT10, Eptinezumab 10mg; BTA, OnabotulinumtoxinA

Table 2: Change from baseline in MMD (Rating down)

Outcome: Change from baseline in MMD (Rating down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading of comparisons	
FRE675 vs PBO	-2.31 (-2.97, -1.70)						High	⊕⊕⊕⊕
FRE225 vs PBO	-2.76 (-3.36, -2.15)						High	⊕⊕⊕⊕
GAL120 vs PBO	-2.11 (-3.22, -1.03)						High	⊕⊕⊕⊕
GAL240 vs PBO	-1.91 (-3.01, -0.78)						High	⊕⊕⊕⊕
ERE70 vs PBO	-2.46 (-3.56, -1.37)						High	⊕⊕⊕⊕
ERE140 vs PBO	-2.45 (-3.52, -1.37)						High	⊕⊕⊕⊕
TOP100 vs PBO	-1.49 (-2.84, -0.12)	↓					Moderate	⊕⊕⊕○
EPT100 vs PBO	-2.10 (-2.98, -1.18)						High	⊕⊕⊕⊕
EPT300 vs PBO	-2.61 (-3.64, -1.63)						High	⊕⊕⊕⊕
EPT30 vs PBO	-2.31 (-4.36, -0.27)						High	⊕⊕⊕⊕
EPT10 vs PBO	-1.08 (-3.77, -0.86)						High	⊕⊕⊕⊕
BTA vs PBO	-1.96 (-2.69, -1.24)						High	⊕⊕⊕⊕
FRE225 vs FRE675	-0.45 (-1.06, 0.17)		↓				Moderate	⊕⊕⊕○
GAL120 vs FRE675	0.20 (-1.09, 1.46)		↓				Moderate	⊕⊕⊕○
GAL240 vs FRE675	0.40 (-0.85, 1.70)		↓				Moderate	⊕⊕⊕○
ERE70 vs FRE675	-0.15 (-1.42, 1.16)		↓				Moderate	⊕⊕⊕○
ERE140 vs FRE675	-0.13 (-1.41, 1.13)		↓				Moderate	⊕⊕⊕○
TOP100 vs FRE675	0.82 (-0.68, 2.37)	↓	↓				Low	⊕⊕○○
EPT100 vs FRE675	0.21 (-0.89, 1.37)		↓				Moderate	⊕⊕⊕○
EPT300 vs FRE675	-0.30 (-1.48, 0.88)		↓				Moderate	⊕⊕⊕○
EPT30 vs FRE675	0.00 (-1.60, 1.66)		↓				Moderate	⊕⊕⊕○
EPT10 vs FRE675	1.19 (-0.37, 2.90)		↓				Moderate	⊕⊕⊕○
BTA vs FRE675	0.35 (-0.62, 1.32)		↓				Moderate	⊕⊕⊕○
GAL120 vs FRE225	0.65 (-0.61, 1.88)		↓				Moderate	⊕⊕⊕○
GAL240 vs FRE225	0.85 (-0.40, 2.12)		↓				Moderate	⊕⊕⊕○
ERE70 vs FRE225	0.30 (-0.96, 1.57)		↓				Moderate	⊕⊕⊕○

Outcome: Change from baseline in MMD (Rating down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading of comparisons	
ERE140 vs FRE225	0.31 (-0.94, 1.57)		↓				Moderate	⊕⊕⊕○
TOP100 vs FRE225	1.27 (-0.20, 2.78)	↓	↓				Low	⊕⊕○○
EPT100 vs FRE225	0.66 (-0.43, 1.77)		↓				Moderate	⊕⊕⊕○
EPT300 vs FRE225	0.15 (-1.04, 1.31)		↓				Moderate	⊕⊕⊕○
EPT30 vs FRE225	0.45 (-1.13, 2.05)		↓				Moderate	⊕⊕⊕○
EPT10 vs FRE225	1.64 (0.08, 3.30)		↓				Moderate	⊕⊕⊕○
BTA vs FRE225	0.80 (-0.15,1.75)		↓				Moderate	⊕⊕⊕○
GAL240 vs GAL120	0.20 (-0.89, 1.29)		↓				Moderate	⊕⊕⊕○
ERE70 vs GAL120	-0.35 (-1.89, 1.21)		↓				Moderate	⊕⊕⊕○
ERE140 vs GAL120	-0.34 (-1.87, 1.24)		↓				Moderate	⊕⊕⊕○
TOP100 vs GAL120	0.62 (-1.13, 2.38)	↓	↓				Low	⊕⊕○○
EPT100 vs GAL120	0.01 (-1.43, 1.43)		↓				Moderate	⊕⊕⊕○
EPT300 vs GAL120	-0.50 (-1.93, 0.97)		↓				Moderate	⊕⊕⊕○
EPT30 vs GAL120	-0.21 (-2.01, 1.57)		↓				Moderate	⊕⊕⊕○
EPT10 vs GAL120	0.99 (-0.85, 2.85)		↓				Moderate	⊕⊕⊕○
BTA vs GAL120	0.15 (-1.16, 1.47)		↓				Moderate	⊕⊕⊕○
ERE70 vs GAL240	-0.55 (-2.15, 0.96)		↓				Moderate	⊕⊕⊕○
ERE140 vs GAL240	-0.54 (-2.10, 0.98)		↓				Moderate	⊕⊕⊕○
TOP100 vs GAL240	0.42 (-1.32, 2.19)	↓	↓				Low	⊕⊕○○
EPT100 vs GAL240	-0.19 (-1.62, 1.20)		↓				Moderate	⊕⊕⊕○
EPT300 vs GAL240	-0.70 (-2.20, 0.76)		↓				Moderate	⊕⊕⊕○
EPT30 vs GAL240	-0.40 (-2.24, 1.42)		↓				Moderate	⊕⊕⊕○
EPT10 vs GAL240	0.79 (-1.03, 2.73)		↓				Moderate	⊕⊕⊕○
BTA vs GAL240	-0.05 (-1.36, 1.26)		↓				Moderate	⊕⊕⊕○
ERE140 vs ERE70	0.01 (-1.10, 1.11)		↓				Moderate	⊕⊕⊕○
TOP100 vs ERE70	0.97 (-0.78, 2.71)	↓	↓				Low	⊕⊕○○
EPT100 vs ERE70	0.36 (-1.09, 1.78)		↓				Moderate	⊕⊕⊕○

Outcome: Change from baseline in MMD (Rating down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading of comparisons	
EPT300 vs ERE70	-0.15 (-1.62, 1.33)		↓				Moderate	⊕⊕⊕○
EPT30 vs ERE70	0.15 (-1.70, 1.94)		↓				Moderate	⊕⊕⊕○
EPT10 vs ERE70	1.34 (-0.52, 3.23)		↓				Moderate	⊕⊕⊕○
BTA vs ERE70	0.50 (-0.79, 1.81)		↓				Moderate	⊕⊕⊕○
TOP100 vs ERE140	0.96 (-0.81, 2.71)	↓	↓				Low	⊕⊕○○
EPT100 vs ERE140	0.35 (-1.06, 1.75)		↓				Moderate	⊕⊕⊕○
EPT300 vs ERE140	-0.16 (-1.65, 1.28)		↓				Moderate	⊕⊕⊕○
EPT30 vs ERE140	0.13 (-1.65, 1.94)		↓				Moderate	⊕⊕⊕○
EPT10 vs ERE140	1.33 (-0.53, 3.16)		↓				Moderate	⊕⊕⊕○
BTA vs ERE140	0.49 (-0.80, 1.76)		↓				Moderate	⊕⊕⊕○
EPT100 vs TOP100	-0.61 (-2.27, 1.04)	↓	↓				Low	⊕⊕○○
EPT300 vs TOP100	-1.12 (-2.85, 0.56)	↓	↓				Low	⊕⊕○○
EPT30 vs TOP100	-0.83 (-2.83, 1.23)	↓	↓				Low	⊕⊕○○
EPT10 vs TOP100	-0.37 (-1.65, 2.39)	↓	↓				Low	⊕⊕○○
BTA vs TOP100	-0.47 (-2.01, 1.07)	↓	↓				Low	⊕⊕○○
EPT300 vs EPT100	-0.51 (-1.51, 0.48)		↓				Moderate	⊕⊕⊕○
EPT30 vs EPT100	-0.21 (-1.64, 1.24)		↓				Moderate	⊕⊕⊕○
EPT10 vs EPT100	0.98 (-0.49, 2.46)		↓				Moderate	⊕⊕⊕○
BTA vs EPT100	0.14 (-1.01, 1.33)		↓				Moderate	⊕⊕⊕○
EPT30 vs EPT300	0.30 (-1.20, 1.78)		↓				Moderate	⊕⊕⊕○
EPT10 vs EPT300	1.49 (-0.04, 3.01)		↓				Moderate	⊕⊕⊕○
BTA vs EPT300	0.65 (-0.53, 1.89)		↓				Moderate	⊕⊕⊕○
EPT10 vs EPT30	1.19 (-0.47, 2.88)		↓				Moderate	⊕⊕⊕○
BTA vs EPT30	0.36 (-1.24, 1.99)		↓				Moderate	⊕⊕⊕○
BTA vs EPT10	-0.84 (-2.44, 0.83)		↓				Moderate	⊕⊕⊕○

Abbreviations: MDs (95% CrIs), Mean Differences (95% Credible Intervals); FRE675, Fremanezumab-quarterly; PBO, Placebo; FRE225, Fremanezumab-monthly; GAL120, Galcanezumab 120mg; GAL240, Galcanezumab 240mg; TOP100, Topiramate 100mg; ERE70, Erenumab 70mg; ERE140, Erenumab 140mg; EPT100, Eptinezumab 100mg; EPT300, Eptinezumab 300mg; EPT30, Eptinezumab 30mg; EPT10, Eptinezumab 10mg; BTA, OnabotulinumtoxinA.

Table 3: Change from baseline in MSQ-Restrictive Role (Rating down)

Outcome: Change from baseline in MSQ-Restrictive Role (Rating down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading of comparisons	
FRE675 vs PBO	5.58 (2.68, 8.54)						High	⊕⊕⊕⊕
FRE225 vs PBO	6.27 (3.09, 9.28)						High	⊕⊕⊕⊕
GAL120 vs PBO	4.95(1.91, 8.08)						High	⊕⊕⊕⊕
GAL240 vs PBO	6.26(2.96, 9.49)						High	⊕⊕⊕⊕
ERE70 vs PBO	5.87 (2.03, 9.87)						High	⊕⊕⊕⊕
ERE140 vs PBO	7.28 (3.05, 11.65)						High	⊕⊕⊕⊕
TOP100 vs PBO	4.33 (-1.88, 10.50)	↓					Moderate	⊕⊕⊕○
BTA vs PBO	6.32 (2.51, 9.95)						High	⊕⊕⊕⊕
FRE225 vs FRE675	0.69 (-2.38, 3.66)		↓				Moderate	⊕⊕⊕○
GAL120 vs FRE675	-0.62 (-4.95, 3.81)		↓				Moderate	⊕⊕⊕○
GAL240 vs FRE675	0.68 (-3.68, 5.07)		↓				Moderate	⊕⊕⊕○
ERE70 vs FRE675	0.30 (-4.68, 5.26)		↓				Moderate	⊕⊕⊕○
ERE140 vs FRE675	1.71 (-3.49, 6.85)		↓				Moderate	⊕⊕⊕○
TOP100 vs FRE675	-1.24 (-7.91, 5.52)	↓	↓				Low	⊕⊕○○
BTA vs FRE675	0.75 (-4.04, 5.37)		↓				Moderate	⊕⊕⊕○
GAL120 vs FRE225	-1.31 (-5.72, 3.21)		↓				Moderate	⊕⊕⊕○
GAL240 vs FRE225	0.01 (-4.58, 4.60)		↓				Moderate	⊕⊕⊕○
ERE70 vs FRE225	-0.39 (-5.42, 4.53)		↓				Moderate	⊕⊕⊕○
ERE140 vs FRE225	1.02 (-4.15, 6.29)		↓				Moderate	⊕⊕⊕○
TOP100 vs FRE225	-1.93 (-8.75,4.92)	↓	↓				Low	⊕⊕○○
BTA vs FRE225	0.06(-4.78, 4.75)		↓				Moderate	⊕⊕⊕○
GAL240 vs GAL120	1.31 (-2.02, 4.76)		↓				Moderate	⊕⊕⊕○
ERE70 vs GAL120	0.92 (-4.06, 5.88)		↓				Moderate	⊕⊕⊕○
ERE140 vs GAL120	2.33 (-2.82, 7.76)		↓				Moderate	⊕⊕⊕○
TOP100 vs GAL120	-0.62 (-7.51, 6.17)	↓	↓				Low	⊕⊕○○
BTA vs GAL120	1.37 (-3.53, 6.16)		↓				Moderate	⊕⊕⊕○

Outcome: Change from baseline in MSQ-Restrictive Role (Rating down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading of comparisons	
ERE70 vs GAL240	-0.39 (-5.47, 4.59)		↓				Moderate	⊕⊕⊕○
ERE140 vs GAL240	1.02 (-4.32, 6.49)		↓				Moderate	⊕⊕⊕○
TOP100 vs GAL240	-1.93 (-8.71, 5.06)	↓	↓				Low	⊕⊕○○
BTA vs GAL240	0.06 (-4.79, 4.89)		↓				Moderate	⊕⊕⊕○
ERE140 vs ERE70	1.41 (-3.01, 5.86)		↓				Moderate	⊕⊕⊕○
TOP100 vs ERE70	-1.54 (-9.02, 5.87)	↓	↓				Low	⊕⊕○○
BTA vs ERE70	0.45 (-5.09, 5.81)		↓				Moderate	⊕⊕⊕○
TOP100 vs ERE140	-2.95 (-10.46, 4.43)	↓	↓				Low	⊕⊕○○
BTA vs ERE140	-0.96 (-6.59, 4.94)		↓				Moderate	⊕⊕⊕○
BTA vs TOP100	1.99 (-5.23, 9.11)	↓	↓				Low	⊕⊕○○

Abbreviations: MDs (95% CrIs), Mean Differences (95% Credible Intervals); FRE675, Fremanezumab-quarterly; PBO, Placebo; FRE225, Fremanezumab-monthly; GAL120, Galcanezumab 120mg; GAL240, Galcanezumab 240mg, TOP100, Topiramate 100mg, ERE70, Erenumab 70mg; ERE140, Erenumab 140mg, BTA, OnabotulinumtoxinA

Table 4: Change from baseline in MSQ-Preventative Role (Rating down)

Outcome: Change from baseline in MSQ-Preventative Role (Rating down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading of comparisons	
FRE675 vs PBO	4.29 (1.90, 6.81)						High	⊕⊕⊕⊕
FRE225 vs PBO	3.89 (1.39, 6.41)						High	⊕⊕⊕⊕
GAL120 vs PBO	6.97 (3.79, 10.24)						High	⊕⊕⊕⊕
GAL240 vs PBO	5.08 (1.84, 8.35)						High	⊕⊕⊕⊕
ERE70 vs PBO	4.09 (0.76, 7.31)						High	⊕⊕⊕⊕
ERE140 vs PBO	4.93 (1.70, 8.20)						High	⊕⊕⊕⊕
TOP100 vs PBO	3.78 (-2.37, 9.80)	↓	↓				Low	⊕⊕○○
BTA vs PBO	5.01 (1.99, 8.01)						High	⊕⊕⊕⊕
FRE225 vs FRE675	-0.39 (-2.81, 1.96)		↓				Moderate	⊕⊕⊕○
GAL120 vs FRE675	2.68 (-1.42, 6.73)		↓				Moderate	⊕⊕⊕○
GAL240 vs FRE675	0.79 (-3.28, 4.87)		↓				Moderate	⊕⊕⊕○
ERE70 vs FRE675	-0.20 (-4.47, 3.81)		↓				Moderate	⊕⊕⊕○
ERE140 vs FRE675	0.64 (-3.44, 4.63)		↓				Moderate	⊕⊕⊕○
TOP100 vs FRE675	-0.51 (-7.05, 6.02)	↓	↓				Low	⊕⊕○○
BTA vs FRE675	0.73 (-3.30, 4.55)		↓				Moderate	⊕⊕⊕○
GAL120 vs FRE225	3.08 (-1.06, 7.14)		↓				Moderate	⊕⊕⊕○
GAL240 vs FRE225	1.19 (-2.87, 5.17)		↓				Moderate	⊕⊕⊕○
ERE70 vs FRE225	0.20 (-3.88, 4.30)		↓				Moderate	⊕⊕⊕○
ERE140 vs FRE225	1.03 (-3.08, 5.21)		↓				Moderate	⊕⊕⊕○
TOP100 vs FRE225	-0.11 (-6.76, 6.27)	↓	↓				Low	⊕⊕○○
BTA vs FRE225	1.12 (-2.71, 5.08)		↓				Moderate	⊕⊕⊕○
GAL240 vs GAL120	-1.89 (-5.15, 1.44)		↓				Moderate	⊕⊕⊕○
ERE70 vs GAL120	-2.88 (-7.34, 1.49)		↓				Moderate	⊕⊕⊕○
ERE140 vs GAL120	-2.04 (-6.59, 2.51)		↓				Moderate	⊕⊕⊕○
TOP100 vs GAL120	-3.19 (-10.04, 3.51)	↓	↓				Low	⊕⊕○○
BTA vs GAL120	-1.95 (-6.41, 2.37)		↓				Moderate	⊕⊕⊕○

Outcome: Change from baseline in MSQ-Preventative Role (Rating down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading of comparisons	
ERE70 vs GAL240	-0.99 (-5.57, 3.64)		↓				Moderate	⊕⊕⊕○
ERE140 vs GAL240	-0.15 (-4.26, 4.30)		↓				Moderate	⊕⊕⊕○
TOP100 vs GAL240	-1.30 (-8.06, 5.64)	↓	↓				Low	⊕⊕○○
BTA vs GAL240	-0.07 (-4.56, 4.41)		↓				Moderate	⊕⊕⊕○
ERE140 vs ERE70	0.84 (-2.69, 4.29)		↓				Moderate	⊕⊕⊕○
TOP100 vs ERE70	-0.31 (-7.11, 6.38)	↓	↓				Low	⊕⊕○○
BTA vs ERE70	0.93 (-3.51, 5.37)		↓				Moderate	⊕⊕⊕○
TOP100 vs ERE140	-1.15 (-8.18, 5.69)	↓	↓				Low	⊕⊕○○
BTA vs ERE140	0.09 (-4.32, 4.60)		↓				Moderate	⊕⊕⊕○
BTA vs TOP100	1.24 (-5.50, 8.32)	↓	↓				Low	⊕⊕○○

Abbreviations: MDs (95% CrIs), Mean Differences (95% Credible Intervals); FRE675, Fremanezumab-quarterly; PBO, Placebo; FRE225, Fremanezumab-monthly; GAL120, Galcanezumab 120mg; GAL240, Galcanezumab 240mg, TOP100, Topiramate 100mg, ERE70, Erenumab 70mg; ERE140, Erenumab 140mg, BTA, OnabotulinumtoxinA

Table 5: Change from baseline in MSQ-Emotional Function (Rating Down)

Outcome: Change from baseline in MSQ-Emotional Function (Rating Down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading of comparisons	
FRE675 vs PBO	3.88 (1.06, 6.75)						High	⊕⊕⊕⊕
FRE225 vs PBO	3.31 (0.69, 5.95)						High	⊕⊕⊕⊕
GAL120 vs PBO	6.90 (3.42, 10.57)						High	⊕⊕⊕⊕
GAL240 vs PBO	6.59 (2.87, 10.23)						High	⊕⊕⊕⊕
ERE70 vs PBO	8.30 (2.10, 14.63)						High	⊕⊕⊕⊕
ERE140 vs PBO	8.89 (3.20, 14.55)						High	⊕⊕⊕⊕
TOP100 vs PBO	6.17 (0.02, 12.52)	↓					Moderate	⊕⊕⊕○
BTA vs PBO	7.34 (2.90, 11.72)						High	⊕⊕⊕⊕
FRE225 vs FRE675	-0.57 (-3.31, 2.21)		↓				Moderate	⊕⊕⊕○
GAL120 vs FRE675	3.02 (-1.73, 7.69)		↓				Moderate	⊕⊕⊕○
GAL240 vs FRE675	2.71 (-2.00, 7.39)		↓				Moderate	⊕⊕⊕○
ERE70 vs FRE675	4.42 (-2.31, 11.35)		↓				Moderate	⊕⊕⊕○
ERE140 vs FRE675	5.01 (-1.35, 11.35)		↓				Moderate	⊕⊕⊕○
TOP100 vs FRE675	2.29 (-4.60, 9.13)	↓	↓				Low	⊕⊕○○
BTA vs FRE675	3.46 (-1.88, 8.79)		↓				Moderate	⊕⊕⊕○
GAL120 vs FRE225	3.59 (-1.09, 8.25)		↓				Moderate	⊕⊕⊕○
GAL240 vs FRE225	3.28 (-1.31, 7.72)		↓				Moderate	⊕⊕⊕○
ERE70 vs FRE225	4.99 (-3.48, 11.74)		↓				Moderate	⊕⊕⊕○
ERE140 vs FRE225	5.58 (-0.77, 11.65)		↓				Moderate	⊕⊕⊕○
TOP100 vs FRE225	2.86 (-3.78, 9.31)	↓	↓				Low	⊕⊕○○
BTA vs FRE225	4.03 (-1.10, 9.18)		↓				Moderate	⊕⊕⊕○
GAL240 vs GAL120	-0.31 (-4.08, 3.49)		↓				Moderate	⊕⊕⊕○
ERE70 vs GAL120	1.41 (-5.89, 8.58)		↓				Moderate	⊕⊕⊕○
ERE140 vs GAL120	1.99 (-4.84, 8.74)		↓				Moderate	⊕⊕⊕○
TOP100 vs GAL120	-0.73 (-7.79, 6.61)	↓	↓				Low	⊕⊕○○
BTA vs GAL120	0.44 (-5.48, 6.13)		↓				Moderate	⊕⊕⊕○

Outcome: Change from baseline in MSQ-Emotional Function (Rating Down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	Indirectness	Publication Bias	Grading of comparisons	
ERE70 vs GAL240	1.71 (-5.70, 9.30)		↓				Moderate	⊕⊕⊕○
ERE140 vs GAL240	2.30 (-4.41, 9.12)		↓				Moderate	⊕⊕⊕○
TOP100 vs GAL240	-0.42(-7.52, 6.94)	↓	↓				Low	⊕⊕○○
BTA vs GAL240	0.74 (-4.96, 6.49)		↓				Moderate	⊕⊕⊕○
ERE140 vs ERE70	0.59 (-5.82, 7.14)		↓				Moderate	⊕⊕⊕○
TOP100 vs ERE70	-2.13 (-11.04,6.98)	↓	↓				Low	⊕⊕○○
BTA vs ERE70	-0.97 (-8.49, 6.75)		↓				Moderate	⊕⊕⊕○
TOP100 vs ERE140	-2.72 (-10.92, 5.49)	↓	↓				Low	⊕⊕○○
BTA vs ERE140	-1.55(-8.60, 5.55)		↓				Moderate	⊕⊕⊕○
BTA vs TOP100	1.17 (-6.56, 8.78)	↓	↓				Low	⊕⊕○○

Abbreviations: MDs (95% CrIs), Mean Differences (95% Credible Intervals); FRE675, Fremanezumab-quarterly; PBO, Placebo; FRE225, Fremanezumab-monthly; GAL120, Galcanezumab 120mg; GAL240, Galcanezumab 240mg, TOP100, Topiramate 100mg, ERE70, Erenumab 70mg; ERE140, Erenumab 140mg, BTA, OnabotulinumtoxinA

Table 6: Change from baseline in Headache Impact Test-6 (HIT-6) (Rating down)

Outcome: Change from baseline in Headache Impact Test-6 (HIT-6) (Rating down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	indirectness	Publication Bias	Grading of comparisons	
FRE675 vs PBO	-1.79 (-2.09, -0.94)						High	⊕⊕⊕⊕
FRE225 vs PBO	-1.99 (-2.29, -1.14)						High	⊕⊕⊕⊕
ERE140 vs PBO	-2.49 (-3.00, -1.04)						High	⊕⊕⊕⊕
ERE70 vs PBO	-2.49 (-3.00, -1.02)						High	⊕⊕⊕⊕
EPT100 vs PBO	-1.56 (-1.87, -0.62)						High	⊕⊕⊕⊕
EPT300 vs PBO	-3.22 (-3.59, -2.09)						High	⊕⊕⊕⊕
EPT30 vs PBO	-0.58 (-1.17, 1.11)		↓				Moderate	⊕⊕⊕○
EPT10 vs PBO	-0.59 (-1.18, 1.21)		↓				Moderate	⊕⊕⊕○
BTA vs PBO	-2.10 (-2.54, -0.86)						High	⊕⊕⊕⊕
FRE225 vs FRE675	-0.20 (-0.49, 0.65)		↓				Moderate	⊕⊕⊕○
ERE140 vs FRE675	-0.70 (-1.28, 1.01)		↓				Moderate	⊕⊕⊕○
ERE70 vs FRE675	-0.70 (-1.29, 1.01)		↓				Moderate	⊕⊕⊕○
EPT100 vs FRE675	0.23 (-0.23, 1.51)		↓				Moderate	⊕⊕⊕○
EPT300 vs FRE675	-1.42 (-1.93, 0.00)		↓				Moderate	⊕⊕⊕○
EPT30 vs FRE675	1.21 (0.55, 3.07)		↓				Moderate	⊕⊕⊕○
EPT10 vs FRE675	1.20 (0.52, 3.19)		↓				Moderate	⊕⊕⊕○
BTA vs FRE675	-0.31 (-0.86, 1.23)		↓				Moderate	⊕⊕⊕○
ERE140 vs FRE225	-0.50 (-1.09, 1.15)		↓				Moderate	⊕⊕⊕○
ERE70 vs FRE225	-0.50 (-1.09, 1.16)		↓				Moderate	⊕⊕⊕○
EPT100 vs FRE225	0.43 (0.00, 1.69)		↓				Moderate	⊕⊕⊕○
EPT300 vs FRE225	-1.23 (-1.72, 0.17)		↓				Moderate	⊕⊕⊕○
EPT30 vs FRE225	1.41 (0.76, 3.27)		↓				Moderate	⊕⊕⊕○
EPT10 vs FRE225	1.40 (0.73, 3.36)		↓				Moderate	⊕⊕⊕○
BTA vs FRE225	-0.11 (-0.64, 1.43)		↓				Moderate	⊕⊕⊕○
ERE70 vs ERE140	0.00 (-0.57, 1.68)		↓				Moderate	⊕⊕⊕○
EPT100 vs ERE140	0.93 (0.32, 2.66)		↓				Moderate	⊕⊕⊕○

Outcome: Change from baseline in Headache Impact Test-6 (HIT-6) (Rating down)								
Comparisons	MDs (95% CrIs)	Study limitations	Imprecision	Inconsistency	indirectness	Publication Bias	Grading of comparisons	
EPT300 vs ERE140	-0.72 (-1.34, 1.10)		↓				Moderate	⊕⊕⊕○
EPT30 vs ERE140	1.92 (1.13, 4.11)		↓				Moderate	⊕⊕⊕○
EPT10 vs ERE140	1.91 (1.12, 4.19)		↓				Moderate	⊕⊕⊕○
BTA vs ERE140	0.39 (-0.30, 2.32)		↓				Moderate	⊕⊕⊕○
EPT100 vs ERE70	0.93 (0.33, 2.67)		↓				Moderate	⊕⊕⊕○
EPT300 vs ERE70	-0.73 (-1.36, 1.15)		↓				Moderate	⊕⊕⊕○
EPT30 vs ERE70	1.91 (1.17, 4.11)		↓				Moderate	⊕⊕⊕○
EPT10 vs ERE70	1.90 (1.14, 4.20)		↓				Moderate	⊕⊕⊕○
BTA vs ERE70	0.39 (-0.29, 2.34)		↓				Moderate	⊕⊕⊕○
EPT300 vs EPT100	-1.66 (-2.03, -0.62)						High	⊕⊕⊕⊕
EPT30 vs EPT100	0.98 (0.41, 2.67)		↓				Moderate	⊕⊕⊕○
EPT10 vs EPT100	0.97 (0.37, 2.70)		↓				Moderate	⊕⊕⊕○
BTA vs EPT100	-0.54 (-1.07, 1.01)		↓				Moderate	⊕⊕⊕○
EPT30 vs EPT300	2.64 (2.04, 4.39)		↓				Moderate	⊕⊕⊕○
EPT10 vs EPT300	2.63 (2.01, 4.44)		↓				Moderate	⊕⊕⊕○
BTA vs EPT300	1.11 (0.52, 2.79)		↓				Moderate	⊕⊕⊕○
EPT10 vs EPT30	-0.01 (-0.67, 1.95)		↓				Moderate	⊕⊕⊕○
BTA vs EPT30	-1.52 (-2.24, 0.54)		↓				Moderate	⊕⊕⊕○
BTA vs EPT10	-1.52 (-2.24, 0.54)		↓				Moderate	⊕⊕⊕○

Abbreviations: MDs (95% CrIs), Mean Differences (95% Credible Intervals); FRE675, Fremanezumab-quarterly; PBO, Placebo; FRE225, Fremanezumab-monthly; GAL120, Galcanezumab 120mg; GAL240, Galcanezumab 240mg, TOP100, Topiramate 100mg, EPT100, Eptinezumab 100mg; EPT300, Eptinezumab 300mg; EPT30, Eptinezumab 30mg; EPT10, Eptinezumab 10mg; BTA, OnabotulinumtoxinA, ERE140, Erenumab 140mg, ERE70, Erenumab 70mg