NICE National Institute for Health and Care Excellence

Slides for public – ACIC redacted

Fremanezumab for preventing migraine
Lead team presentation

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Company: Teva UK

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Key issues

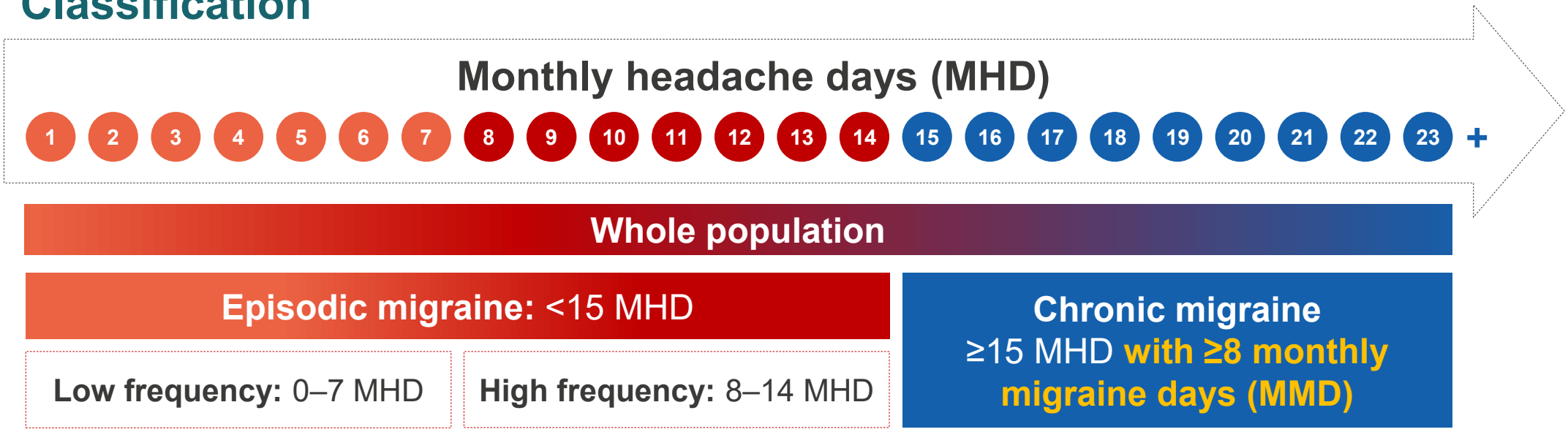
- Will fremanezumab treatment effect continue indefinitely after treatment is stopped?
- Would treatment be restarted if treatment effect (after stopping) diminishes?
- The model time horizon should be: 10 years or lifetime?
- How is the treatment effectiveness (effect on monthly migraine days) of fremanezumab and best supportive care expected to change after treatment stops?
- Are quality of life improvements beyond that achieved by reducing monthly migraine days plausible for people on treatment?
- Should the high frequency episodic migraine subgroup be considered separately to episodic and chronic migraine?
- What proportion of people will self-administer fremanezumab: 100%; 95%; 90%?
- Is there sufficient evidence to support a benefit for fremanezumab over onabotulinumtoxin A?
- Would fremanezumab be considered as an option once onabotulinumtoxin A has been used?
- Equality considerations

[redacted]

Migraine

- Headache disorder with recurring attacks usually lasting 4–72 hours
- Often accompanied by nausea, vomiting, sensitivity to light/sound
- Factors triggering attacks can include stress, change in sleep pattern, overtiredness, menstruation, caffeine/alcohol consumption
- Prevalence 5-25% in women; 2-10% in men

Classification



Fremanezumab (Ajovy, Teva)

Description of technology	Fremanezumab (Ajovy, Teva) is a fully humanised monoclonal antibody that inhibits the action of calcitonin gene-related peptide (CGRP) which is believed to transmit signals that can cause severe pain
Marketing authorisation	Fremanezumab is indicated for prophylaxis of migraine in adults who have at least 4 migraine days per month
Dosage and administration	Fremanezumab is administered by subcutaneous injection and has two dosing options available: • 225 mg once monthly (monthly dosing) or, • 675 mg every three months (quarterly dosing)
List price	The list price of fremanezumab is £450 per 225 mg injection (£1350 per 675 mg). Costs may vary in different settings because of negotiated procurement discounts

Background

Comparators	Best supportive care episodic migraine [EM] and chronic migraine [CM] onabotulinumtoxin A [OBA] CM only
Subgroups	High-frequency episodic migraine HFEM
Main clinical trial	FOCUS: compared fremanzumab with placebo in adults with migraine EM or CM who had 2 to 4 failed preventative therapies
Key results	[redacted]
Comparison with OBA	Network meta-analysis in chronic migraine
Key result	[redacted]
Model	Semi-Markov model. 28 MMD health states → model split by responders and non-responders → non-responders discontinue → exclusive cost and utilities for each MMD health state → MMDs driven by response status
Company ICER	EM: £13,954 CM: £11,825 v BSC; £16,227 v OBA
Technical teams most plausible ICER	EM: £53,309 CM v BSC: £21,529; CM v OBA: Dominated

Key trial results

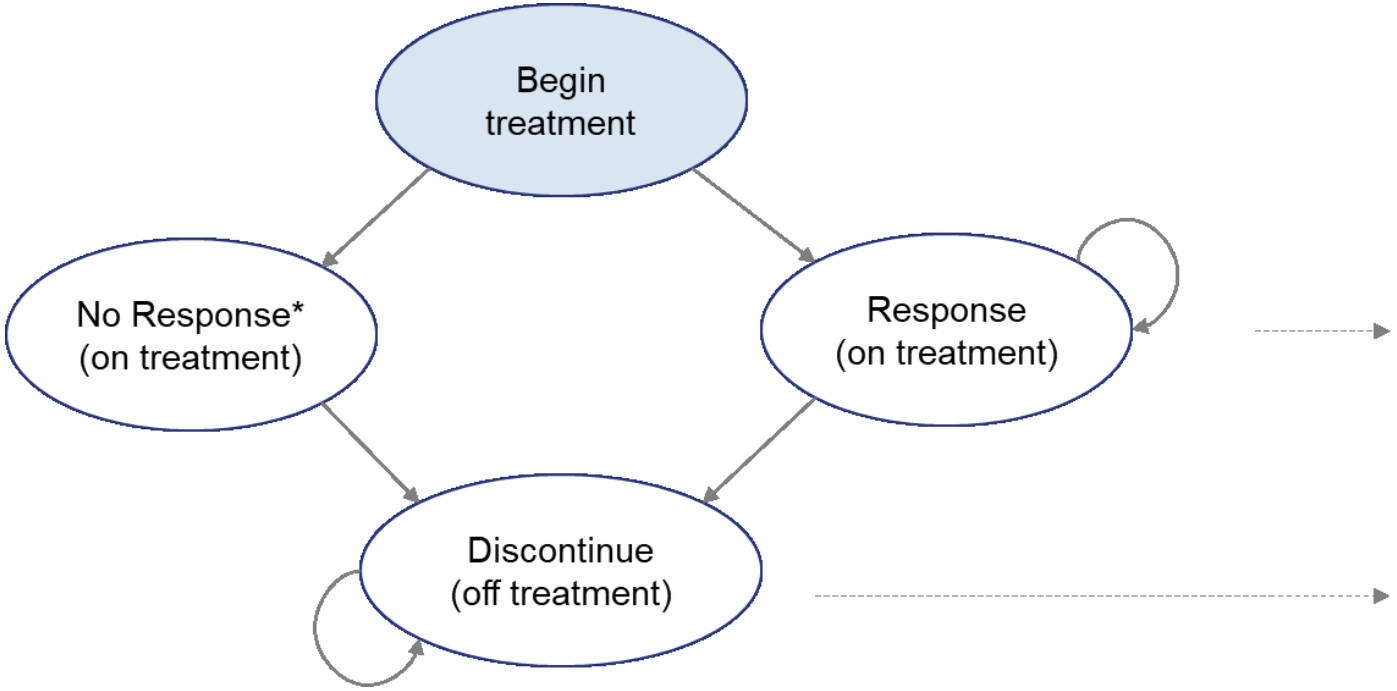
FOCUS trial efficacy outcomes at week 12

	Episodic migraine			Chronic migraine		
	Placebo (n=**)	Frem 3-mthly (n=**)	Frem monthly (n=**)	Placebo (n=**)	Frem 3-mthly (n=**)	Frem monthly (n=**)
Mean monthly migraine days						
Baseline (SD)	****	****	****	****	****	****
LSM change (95% CI)	****	****	****	****	****	****
Difference vs placebo (95% CI)		****	****		****	****
Patients with at least 50% reduction in monthly average migraine days						
Responder rate (n)	****	****	****	****	****	****
Odds ratio vs placebo (95% CI)		****	****		****	****
Mean monthly days of use of any acute headache medication						
Baseline (SD)	****	****	****	****	****	****
LSM change (95% CI)	****	****	****	****	****	****
Difference vs placebo (95% CI)		****	****		****	****

Source: adapted from tables 25 and 29 company submission. Note: LSM = log-square mean

Economic model

- Semi-markov model
- EM and CM are analysed separately with dedicated input parameters for each
- People in the model are split into treatment responders and non-responders
  - Responders remain on treatment and non-responders discontinue
- Cost and utilities are exclusive to each health state
  - Separately calculated for responders and non-responders based on the proportion of patients in each MMD health state



Markov Model
(28 MMD health states)

1	2	3	4
5	6	7	8
9	10	11	12
13	14	15	16
17	18	19	20
21	22	23	24
25	26	27	28

Patient perspectives

Comments: Migraine Trust (based on 1,838 survey responses), OUCH (UK), patient

Migraine:

- Throbbing headaches with many other potential symptoms (e.g. visual, sensory, nausea, fatigue)

Especially debilitating when chronic:

- "I had to give up work because of chronic migraine four years ago. There are days when I feel useless, hopeless and a failure"
- "Chronic migraine infiltrates all parts of my life. On the odd day when I'm not in pain, I worry about being in pain."
- "I developed bad anxiety and depression with suicidal thoughts"

Current treatment experience

- 67% of people living with migraine had tried five or more NHS treatments
- Only 19% of chronic migraine respondents were happy with treatment now
- "The preventative medicines have side effects which actually outweigh any positive impact they have on reducing the pain"
- There is a need a preventative treatment that reduces MMDs

Patient perspectives: *Migraine Trust*

Advantages of Fremanezumab

- *"…can significantly reduce the frequency and severity of migraine attacks"*
- faster rapidity of onset compared with current preventative treatmentsI
- well tolerated → improves wellbeing and quality of life
- single monthly or quarterly treatment (unlike Botox, which requires multiple injections by a healthcare professional)
- Reduced use of acute treatments and painkillers → alleviates headaches induced by medication overuse

Disadvantages

- Potential injection site reactions and phobias
- Long-term tolerability unknown

[redacted]

Clinician perspectives

Submissions:

- Association of British Neurologists (ABN)
- British Association for Study of Headache (BASH), 2 submissions

Current treatment experience

- "very significant unmet need"
- "Headache services are extremely patchy... neurologists are extremely busy and oversubscribed"

Fremanezumab experience:

- Self-administered monthly injections: better compliance and less burden on healthcare resources compared to Botox
- "Patients will require injection training that could best be provided through industry support"
- "As the treatment is expensive, it is reasonable to restrict to those who have failed three treatments"
- Stop after three months if migraine days not reduced by 30%...re-evaluation after one year
- "Overall benefit will fall off following stopping"

[redacted]

Outstanding issues after technical engagement

- **Issue 1:** Treatment stopping rules [slides 12-14]
- **Issue 2:** Model time horizon [s15-17]
- **Issue 3:** Model utility values [s18]
- **Issue 4:** High frequency episodic migraine (HFEM) subgroup [s19]
- **Issue 5:** Resource use and costs [s20-21]
- **Issue 6:** Network-meta analysis in chronic migraine [s22-23]
- **Issue 7:** fremanezumab use post-onabotulinumtoxin A [s24]

[redacted]

Issue 1: Treatment stopping rules

Background

- *Company:* base-case assumes 20% stop treatment (every 64 weeks) following a positive response → indefinitely continuing treatment benefit (at zero cost) → reducing the ICER
- *Technical team:* Lack of evidence to support the long-term efficacy and usage of fremanezumab → unrealistic to assume all treatment responders stop indefinitely
  - When migraines do not respond to treatment, treatment should be stopped

Stakeholder comments: *Company*

- Conservative to assume only 20% stop treatment following a positive response → expert opinion is that the majority will stop treatment within 2yrs
- Expert opinion suggests fremanezumab will control migraines → once control is gained, improvements will be maintained
- Restarting treatment is plausible
- Non-responders will stop treatment

Stakeholder comments: *Allergan (OBA)*

- Assuming continued efficacy at zero cost is highly optimistic → underestimates the ICERs
- After a loss of efficacy there may be a need for people to restart treatment

[redacted]

Issue 1: Treatment stopping rules

Stakeholder comments: *Novartis (erenumab)*

- Positive discontinuation scenarios were considered inappropriate in the appraisal of erenumab
- Evidence demonstrating maintenance of treatment effect upon positive discontinuation has not been provided

Stakeholder comments: *professional groups*

- Treatment is stopped after negative response OR when MMDs fall below 8 or 10
- 'Drug holidays' are recommended to determine if continued treatment is necessary
- Limited data follow those who discontinue following a positive response
- Treatment would be restarted (for a further 6 – 12 months) if effect diminishes

Stakeholder comments: *NHSE*

- "…agreement of and adherence to stopping rules is important"
  - At a minimum people should be assessed 3 months after initiating treatment → treatment stopped in non-responders

[redacted]

Issue 1: Treatment stopping rules

ERG comments:

- For people who respond to treatment after 12 weeks the need to continue therapy would then be assessed annually → in line with OBA
- The following is reasonable given current clinical practice and experience
  - An assessment period of 3 months to monitor migraine frequency
  - A proportion with continued treatment effect after stopping treatment
- Satisfied with the approach used to estimate the proportion (20%) positively stopping treatment each year, however, this figure is still uncertain
- Highly uncertain whether treatment effect will continue after stopping treatment
- Response rates from FOCUS can be used to implement a negative stopping rule

Final technical report judgements:

- Assuming continued treatment effectiveness after stopping treatment is unrealistic and is not supported by evidence → assuming continued effectiveness at zero cost is optimistic and underestimates the ICER
- Treatment would likely be restarted if MMDs increase after stopping treatment

- ***After stopping treatment would the benefit continue indefinitely?***
- ***Would treatment be restarted if treatment effect (after stopping) diminishes?***

Issue 2: Model time horizon

Background

- Company used a 10 year time horizon in its base-case
- Tech team stated a preference for a lifetime time horizon
  - In the company's model people discontinuing fremanezumab reverted to BSC MMDs → this is overly optimistic and resulted in unrealistic lifetime ICERs
  - The ERG explored the implications of using a lifetime horizon in 2 scenarios:
    - **Scenario A:** Assuming people who respond to fremanezumab revert to baseline fremanezumab MMDs after stopping treatment (with or without linear waning of the BSC effect over 5yrs)
    - **Scenario B:** Reverting to BSC MMDs after discontinuation but also applying BSC responder/non-responder rates where non-responders revert to baseline

Stakeholder comments: *Company*

- All meaningful benefits and costs are sufficiently captured by 10 years
- Data not available to model the natural history of migraine → extending time horizon increases modelling uncertainty
- The company considered the ERG scenarios (above) exploring a lifetime horizon:
  - **Scenario A:** "not clinically justifiable" that people who respond to frem would revert to baseline (non-responder) MMDs
  - **Scenario B:** "is a more reasonable and justifiable approach"

Issue 2: Model time horizon

Stakeholder comments: *Allergan*

- Lifetime model time horizon less appropriate given the uncertainty in key model assumptions → a shorter time horizon would result in more robust estimates

Stakeholder comments: *Novartis*

- Lifetime horizon was preferred in the appraisal of erenumab

Stakeholder comments: *professional groups*

- Lifetime horizon preferable, 5 yrs reasonable (difficult to model natural history)

Stakeholder comments: *NHSE*

- Lifetime horizon is reasonable

ERG comments:

- A 10-year time horizon is reasonable to capture most costs and benefits as longer time horizons require extrapolation of short term data
- Extending the time horizon exacerbates uncertainty in the model

Final technical report judgements:

- Lifetime time horizon is preferred

- ***The model time horizon should be: 10 years or lifetime?***

[redacted]

Issue 2: Model time horizon

Post all-cause discontinuation scenarios

Background

- Lifetime ICERs using the company model were unrealistic
- After discontinuation (per-cycle) treatment effectiveness was maintained long-term
- ERG scenarios adjust treatment effect after stopping → more realistic ICERs

	Scenario A	Scenario A *(BSC effect waning)*	Scenario B
Fremanezumab non-responder	Residual effect over frem baseline MMDs (1 fewer MMDs than baseline)		
Fremanezumab responder	Continues treatment full fremanezumab effect (-7 MMDs [EM]; -9 MMDs [CM])		
Fremanezumab responder: ***following per cycle discontinuation***	Revert to baseline fremanezumab MMD • baseline = 16 MMDs for responders		Revert to BSC responder /non-responder MMDs • responders (see below) • non-responders revert to BSC baseline
BSC responder	Maintain BSC responder MMDs (-7 MMDs [EM]; -8 MMDs [CM])	Revert to baseline BSC non-responder MMDs (effect linearly waned over 5 years)	Maintain BSC responder MMDs (-7 MMDs [EM]; -8 MMDs [CM])
BSC non-responder	Remain at baseline BSC MMDs		

- ***What is the most plausible assumption after all-cause discontinuation?***

Issue 3: Model utility values

Background

Company

- Mapped from the Migraine-Specific Quality of Life Questionnaire (MSQoL) to EQ-5D-3L
- Clinical experts stated there was anecdotal evidence to support an additional utility premium (benefit) for people on treatment

Technical team

- Insufficient evidence to support an on treatment utility benefit
- Requested utility values at engagment:
  1. Re-analysed base-case utility values accounting for baseline characteristics
  2. EQ-5D-5L mapped to EQ-5D-3L

Stakeholder comments:

Company

- MSQoL is the most appropriate quality of life (QoL) measure
- EQ-5D misses QoL impacts
- Evidence of on treatment utility benefits from FOCUS and experts

Allergan

- Improvements in QoL beyond reductions in MMDs on OBA

Professional groups

- Preventatives reduce severity and duration of migraines
- HIT-6 and MIDAS are preferred

ERG comments:

- MSQoL is more appropriate than HIT-6 and MIDAS in this population
- Using utility data mapped from MSQoL instead of EQ-5D-5L is reasonable
- Unclear if additional HRQoL benefits were not captured by the MSQoL

Final technical report judgements:

- On and off treatment utility values should be equivalent → no additional benefit

Are on treatment QoL improvements beyond that achieved by reducing MMDs plausible?

Issue 4: High-frequency episodic migraine subgroup

Background

- The HFEM subgroup has particularly high unmet need as they are not eligible for OBA (CM only)
- No consensus on the definition of HFEM
- HFEM subgroup from FOCUS is from a post-hoc analyses

Stakeholder comments: *Company*

- HFEM can be defined as between 8 and 14 MMDs
- HFEM subgroup is recognised and clinically distinct
- HFEM has a substantial QoL impact with limited treatment options → high unmet need
- Lack of definition should not prevent consideration

Stakeholder comments: *Allergan*

- There is no agreed definition for HFEM

Stakeholder comments: *Novartis*

- HFEM not considered in the erenumab appraisal

Stakeholder comments: *Professional groups*

- HFEM is recognised and is challenging to treat
- HFEM is believed to cause similar disability to CM

Stakeholder comments: *NHS England*

- HFEM is 10 or more (within the EM definition < 15)

ERG comments:

- Experts advice: HFEM is clinically relevant and biologically distinct from CM

Final technical report judgements:

- HFEM does not need separate consideration

Should HFEM be considered separately to episodic and chronic migraine?

Issue 5: Resource use and costs

Background

- Company: assumed that 100% of people self-administer fremanezumab
- Technical team: it's appropriate to assume an administration cost for (10%) of people receiving fremanezumab

Stakeholder comments: *Company*

- Assuming 10% need their treatment administered is too high → 5%, in line with expert opinion, should be explored
- Changing this assumption has a negligible impact on the ICER

Stakeholder comments: *Allergan*

- A better reflection of real world resource use would assume:
  1. people won't self-administered from the start
  2. some will need treatment administering for them
  3. compliance and response will be monitored

Stakeholder comments: *Novartis*

- Needle phobic patients won't be able to self administer
- The clinical trials do not demonstrate any self administration
- Fremanezumab needs appropriate storage (refrigeration)

Stakeholder comments: *Professional groups*

- 5% / 10% may need their treatment administered
- Vast majority will self-administer (>95%)

Stakeholder comments: *NHS England*

- Reasonable to assume some will not be able/willing to self-administer → exact proportion unknown

[redacted]

Issue 5: Resource use and costs

ERG comments:

- Scenarios provided where:
  - 5% or 10% cannot self-administer fremanezumab
  - A weighted cost for oral and injectable triptan was modelled

Final technical report judgements:

- Assuming all people receiving fremanezumab will be able/willing to self-administering treatment is unrealistic → assuming 10% of people have their treatment administered is reasonable
- Applying an administration cost has a minimal impact on the ICER

What proportion of people will self-administer treatment: 100%; 95%; 90%?

[redacted]

Issue 6: Network meta-analysis for chronic migraine

Background

- No direct comparison of frem and OBA in CM
- Concerns with the evidence in the NMA limit its robustness
  - Placebo-adjusted analysis requested
- Improvements estimated from the NMA are not statistically significant
  - Equal efficacy should be considered
- Concern that prior OBA use could bias results
- Assuming equivalence in monthly headache days (MHDs) and MMDs may flatten response

Stakeholder comments

Company

- No RCT data → NMA is the best evidence available
- Placebo-adjusted NMA was not feasible
- Different assessment time points (24 weeks [OBA] and 12 weeks [FOCUS) and outcomes (reduction in MHDs [OBA] and reduction in MMDs [FOCUS]) favour OBA → NMA effect estimate is conservative
- NMA shows additional benefit for frem across all endpoints despite data limitations → assuming equal efficacy is unreasonable
- NMA effect estimates which were not statistically significant have been accepted in previous appraisals
- Including people who had prior OBA use in the NMA has a minimal effect on the results
- Due to data limitations MHDs and MMDs assumed equivalent → reduction in MHDs is easier to achieve than MMDs → this assumption could underestimate frem relative efficacy

[redacted]

Issue 6: Network meta-analysis for chronic migraine

Stakeholder comments: *Allergan*

- No robust evidence that fremanezumab is more clinically effective than OBA
- Data limitations prevent a robust indirect comparison

Stakeholder comments: *Novartis*

- Same NMA limitations as in erenumab v OBA NMA (not accepted by committee)
- No robust evidence of a treatment benefit over OBA

Stakeholder comments: *Professional groups*

- No head to head studies → relative efficacy is unknown
- Assuming equivalence of MHDs and MMDs is unreasonable → different severity
- No evidence of benefit, however patients may prefer frem administration

ERG comments:

- Frem effectiveness (compared to OBA) appears reduced for people previously treated with OBA
- Reasonable to assume MHDs are equivalent to MMDs
- Scenario provided assuming equal the efficacy of frem and OBA

Final technical report judgements:

- Estimates from the NMA are not robust
- The possibility of no comparative benefit cannot be ruled out

Is there sufficient evidence to support a benefit for fremanezumab over OBA?

Issue 7: Use of fremanezumab after OBA (CM)

Background

- Fremanezumab is positioned as a treatment option after 3 or more failed preventative therapies
- FOCUS included patients who had previously received OBA at various lines of treatment that may not be available in England
- At technical engagement, company provided subgroup analyses of effectiveness of fremanezumab in those previously treated with OBA
  - Results: similar efficacy to full trial population; however, small patient numbers and uncertainty relating to how many preventative treatments those with prior-OBA exposure have failed

ERG comments:

- Efficacy appears reduced for participants who have had prior OBA treatment in the fremanezumab monthly group → differences in MMD changes versus placebo
  - Prior OBA use ([redacted] v placebo); no prior OBA use ([redacted] v placebo)

Final technical report judgements:

- There is clinical evidence to suggest that fremanezumab may be effective in a subgroup of people with CM who have had prior OBA
- No cost-effectiveness evidence provided to support this positioning

Would fremanezumab be considered as an option in those who have had OBA?

Cost effectiveness results (1):

Episodic migraine (frem v BSC)

Scenario (issue)	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Company base case	[redacted]	[redacted]	£13,954
ERG fixes	[redacted]	[redacted]	£13,535
No positive stopping rule (1)	[redacted]	[redacted]	£20,214
Lifetime time horizon (2) [see slides 15,17]			
Scenario A	[redacted]	[redacted]	£71,789
Scenario A (BSC effect waning)	[redacted]	[redacted]	£25,957
Scenario B	[redacted]	[redacted]	£8,933
No additional on treatment utility benefit (3)	[redacted]	[redacted]	£16,435
Administration costs for 10% (5)	[redacted]	[redacted]	£14,022
Technical team's preferred ICER (all above + scenario A)	[redacted]	[redacted]	£243,684*
Technical team's preferred ICER (all above + scenario A [BSC waning])	[redacted]	[redacted]	£53,309*
Technical team's preferred ICER (all above + scenario B)	[redacted]	[redacted]	£16,902*

**probabilistic ICERs consistent with deterministic*

Cost effectiveness results (2):

Chronic migraine (frem v BSC)

Scenario (issue)	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Company base case	[redacted]	[redacted]	£11,825
ERG fixes	[redacted]	[redacted]	£11,487
No positive stopping rule (1)	[redacted]	[redacted]	£16,951
Lifetime time horizon (2) [see slides 15,17]			
Scenario A	[redacted]	[redacted]	£194,498
Scenario A (BSC effect waning)	[redacted]	[redacted]	£12,078
Scenario B	[redacted]	[redacted]	£23,464
No additional on treatment utility benefit (3)	[redacted]	[redacted]	£13,363
Administration costs for 10% (5)	[redacted]	[redacted]	£11,881
Technical team's preferred ICER (all above + scenario A)	[redacted]	[redacted]	Dominated
Technical team's preferred ICER (all above + scenario A [BSC waning])	[redacted]	[redacted]	£21,529*
Technical team's preferred ICER (all above + scenario B)	[redacted]	[redacted]	£43,754*

**probabilistic ICERs consistent with deterministic*

Cost effectiveness results (3):

Chronic migraine (frem v OBA)

Scenario (issue)	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Company base case	[redacted]	[redacted]	£16,227
ERG fixes	[redacted]	[redacted]	£16,118
No positive stopping rule (1)	[redacted]	[redacted]	£24,756
Lifetime time horizon (2) [see slides 15,17]			
Scenario A	[redacted]	[redacted]	£17,905
Scenario A (BSC effect waning)	[redacted]	[redacted]	£17,905
Scenario B	[redacted]	[redacted]	£18,700
No additional on treatment utility benefit (3)	[redacted]	[redacted]	£20,681
Administration costs for 10% (5)	[redacted]	[redacted]	£16,332
Equal efficacy frem v OBA (6)	[redacted]	[redacted]	Dominated
Technical team's preferred ICER (all above + scenario A)	[redacted]	[redacted]	Dominated
Technical team's preferred ICER (all above + scenario A [BSC waning])	[redacted]	[redacted]	Dominated
Technical team's preferred ICER (all above + scenario B)	[redacted]	[redacted]	Dominated

Scenario analyses: *scenario A*

Scenario (issue)	ICER (£/QALY)		
	EM: frem v BSC	CM: frem v BSC	CM: frem v OBA
Company base case	£13,954	£11,825	£16,227
Tech team assumptions	£243,684	Dominated	Dominated
Starting from the technical teams preferred assumptions			
Positive stoppers restart if effect diminishes by 50%	Not reported	Dominated	Not reported
No administration costs	£242,644	Dominated	£39,823
Administration cost for 5%	£243,134	Dominated	£39,938
Weighted oral and injectable triptan costs	£240,933	Dominated	£36,993
Use NMA frem v OBA effectiveness estimate	N/A	N/A	Dominated

[redacted]

Scenario analyses: *scenario A, BSC waning*

Scenario (issue)	ICER (£/QALY)		
	EM: frem v BSC	CM: frem v BSC	CM: frem v OBA
Company base case	£13,954	£11,825	£16,227
Tech team assumptions	£53,309	£21,529	Dominated
Starting from the technical teams preferred assumptions			
Positive stoppers restart if effect diminishes by 50%	Not reported	£28,501	Not reported
No administration costs	£53,701	£21,432	Dominated
Administration cost for 5%	£53,190	£21,481	Dominated
Weighted oral and injectable triptan costs	£50,856	£19,239	Dominated
Use NMA frem v OBA effectiveness estimate	N/A	N/A	£40,053

[redacted]

Scenario analyses: *scenario B*

Scenario (issue)	ICER (£/QALY)		
	EM: frem v BSC	CM: frem v BSC	CM: frem v OBA
Company base case	£13,954	£11,825	£16,227
Tech team assumptions	£16,902	£43,754	Dominated
Starting from the technical teams preferred assumptions			
Positive stoppers restart if effect diminishes by 50%	Not reported	£57,049	Not reported
No administration costs	£16,818	£43,568	Dominated
Administration cost for 5%	£16,860	£43,661	Dominated
Weighted oral and injectable triptan costs	£14,352	£41,677	Dominated
Use NMA frem v OBA effectiveness estimate	N/A	N/A	£42,179

[redacted]

Equality

Migraine trust

- Migraine can be classed as a disability
- Women are 3 times more likely to be affected by migraine
- Current access to migraine treatments varies across regions in England

Company

- Migraine is more common in women → approximately twice the migraine prevalence compared to men (18% vs 7%)
- Restricting access to fremanezumab disadvantages women to a greater extent

Technical team

- The technical team concluded that these are not issues that can be addressed by NICE guidance on fremanezumab

[redacted]

Key issues

- Will fremanezumab treatment effect continue indefinitely after treatment is stopped?
- Would treatment be restarted if treatment effect (after stopping) diminishes?
- The model time horizon should be: 10 years or lifetime?
- How is the treatment effectiveness (effect on monthly migraine days) of fremanezumab and best supportive care expected to change after treatment stops?
- Are quality of life improvements beyond that achieved by reducing monthly migraine days plausible for people on treatment?
- Should the high frequency episodic migraine subgroup be considered separately to episodic and chronic migraine?
- What proportion of people will self-administer fremanezumab: 100%; 95%; 90%?
- Is there sufficient evidence to support a benefit for fremanezumab over onabotulinumtoxin A?
- Would fremanezumab be considered as an option once onabotulinumtoxin A has been used?
- Equality considerations

[redacted]