Cost-Consequence Analysis of Fremanezumab Treatment in Patients With Migraine and Comorbid Major Depressive Disorder in the UK Using Results From the UNITE Study

Additional methodology/ results accessible via QR code

Modeling assumptions

1. The number of eligible patients does not change in the base year
2. No treatment switch is assumed after patients enter the model
3. A time horizon of only 1 year is taken for cost comparison
4. No administration costs are considered for subcutaneous injections
5. Costs are taken from UK sources and inflated to 2023
6. Costs are not discounted
7. Due to data unavailability, costs and healthcare utilization are assumed to be the same for episodic and chronic migraine

Direct costs

1. Drug costs

Drug acquisition costs

Acquisition costs for calcitonin gene-related peptide (CGRP) pathway monoclonal antibodies (mAbs) are derived from MIMS UK and the 2021/22 National Cost Collection Data Publication (National Health Service [NHS] England) and the recommended dosing, as described in the relevant Summary of Product Characteristics documents, and do not include any confidential commercial discounts that may exist between suppliers and payers.[1–6]
Adherence is assumed to be 100% for all the drugs.

Drug administration costs

Fremanezumab, erenumab, and galcanezumab are available as subcutaneous injections, thus it is assumed that there are no administration costs. In comparison, eptinezumab is administered by intravenous infusion (drip) over 30 minutes once every 12 weeks, thereby leading to an additional cost of £356.00 per administration.

2. Disease management costs

The components of disease management included in the model were as follows:

- Emergency room (ER) visits
- Hospitalizations
- General practitioner (GP) visits
- Nurse practitioner visits
- Neurologist visits
- Mental health visits (psychiatrist, psychologist, therapist)

Migraine-specific and depression-specific medications were not considered separately in the model, as a single concomitant medication prescribed for the treatment of depression was permitted in the trial.

The unit costs employed in the model for each of the disease management components are presented in **Table 1.**

Table 1: Disease Management Costs Used in the Analysis

Healthcare resource	Unit costs (£)	Source	Description
ER visit	290.7	NHS Tariff 2021[2]	Average of Health Resource Group code "VB08Z" in the EC worksheet of the 2021/2022 National tariffs
Hospitalization (per stay)	1,184.7	NHS Tariff 2021[2]	Calculated as an average of the non-elective tariff for code AA31E (Headache, Migraine, or Cerebrospinal Fluid Leak, with CC Score 0–6) in worksheet "APC" of the 2021/2023 tariffs
GP visit	48.4	PSSRU 2021[7]	Cost of a surgery consultation lasting 9.22 minutes (Table 10.3b GP – unit costs, chapter 10, pages 110–116, PSSRU, 2021). A consultation length of 11.7 minutes was used in the NICE costing template (NICE-TA260 2012)
Nurse visit	48.6	PSSRU 2021[7]	Cost per hour of a nurse, PSSRU, 2021
Neurologist visit	261.9	NHS Tariff 2021[2]	Assumed to be the "Non-Admitted Face-to-Face Attendance, Follow-up for a consultant led (WF01A)" for a Neurology outpatient visit (code 400) in the 2021/2022 NHS tariffs
Mental health visit (psychiatrist, psychologist, therapist)	319.6	NHS Tariff 2021[2]	Assumed to be the "Other Mental Health Specialist Teams, Adult and Elderly (MHSTOTHA)" for a Mental Health Specialist Team in the 2021/2022 NHS tariffs

ER, emergency room; GP, general practitioner; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; PSSRU, Personal Social Services Research Unit.

- The mean management costs due to healthcare resource utilization (HRU) associated with a particular patient on a drug are represented by the average of the costs per average number of monthly migraine days (MMDs).

- HRU calculations were based on a separate cross-sectional analysis using National Health and Wellness Survey (NHWS) 2022 data from France, Germany, Italy, Spain, and the UK.[8] Direct HRU costs associated with migraine and depression were compared for adult patients with migraine and depression with adult patients with migraine only.
- In the analysis, aggregated HRU and costs per mean headache days were calculated, therefore, adjustments were made to convert the aggregate level data to the HRU per MMD frequency. Although headache days and migraine days are separate outcomes, it was assumed that HRU per headache day frequency would provide a good approximation for HRU per migraine day frequency. The trend in HRU per MMD frequency was based on results from the American Migraine Prevalence and Prevention study, wherein mean patient-reported HRU over 12 months was divided by the reported annual number of headache days to estimate the HRU cost per headache day in the model.[9] This trend was adjusted so that the mean of the trend fell close to the average HRU as observed in the NHWS 2022 data. The adjustment was done separately for patients with migraine only (**Table 2**) and patients with both migraine and depression (**Table 3**) in accordance with their reported MMDs.

Methodology to calculate total disease management cost per patient

Total disease management costs were calculated in the following steps:

Step 1: Determine HRU for patients with both migraine and MDD at baseline

- At baseline, all patients had symptoms of both migraine and MDD in both scenarios. For these patients, HRU was estimated using **Table 3**, based on the mean MMD.
- Upon treatment with a CGRP pathway mAb, the mean MMD of the patients decreased, and patients started utilizing less resources per the decreased MMDs obtained from the same table.

Step 2: Determine whether patients get treated for symptoms of both migraine and MDD or only migraine with the use of CGRP pathway mAb

- Based on the decrease in the HAM-D 17 or PHQ-9 score, it was estimated that either patients had full remission (i.e., no depression) or partial remission (depression symptoms still exist).

Step 3: Determine HRU for patients with full remission versus patients with partial remission of depression

- If migraine patients with comorbid depression achieved full remission, then it was assumed that patients would utilize resources only due to migraine (**Table 2**). Whereas in cases of partial remission, patients would continue to have resource use (as per **Table 3**) corresponding to only a decrease in MMDs.

Step 4: HRU was multiplied with unit costs to get total costs

Table 2: Summary of HRU Frequency (Per Quarter) in Patients With Migraine Only Using NHWS 2022 Data

MMD	Hospitalizations	ER visits	GP visits	Nurse practitioner visits	Neurologist visits	Mental health visits
0	0.15	0.02	0.02	0.03	0.01	0.01
1	0.21	0.05	0.03	0.05	0.03	0.05
2	0.21	0.05	0.03	0.05	0.03	0.05
3	0.21	0.05	0.03	0.05	0.03	0.05
4	0.30	0.05	0.03	0.08	0.02	0.04
5	0.30	0.05	0.03	0.08	0.02	0.04
6	0.30	0.05	0.03	0.08	0.02	0.04
7	0.30	0.05	0.03	0.08	0.02	0.04
8	0.40	0.07	0.03	0.02	0.07	0.12
9	0.40	0.07	0.03	0.02	0.07	0.12
10	0.40	0.07	0.03	0.02	0.07	0.12
11	0.40	0.07	0.03	0.02	0.07	0.12
12	0.40	0.07	0.03	0.02	0.07	0.12
13	0.40	0.07	0.03	0.02	0.07	0.12
14	0.40	0.07	0.03	0.02	0.07	0.12
15	0.42	0.10	0.03	0.06	0.13	0.24
16	0.42	0.10	0.03	0.06	0.13	0.24
17	0.42	0.10	0.03	0.06	0.13	0.24
18	0.42	0.10	0.03	0.06	0.13	0.24
19	0.42	0.10	0.03	0.06	0.13	0.24
20	0.42	0.10	0.03	0.06	0.13	0.24
21	0.42	0.10	0.03	0.06	0.13	0.24
22	0.42	0.10	0.03	0.06	0.13	0.24
23	0.42	0.10	0.03	0.06	0.13	0.24
24	0.42	0.10	0.03	0.06	0.13	0.24
25	0.42	0.10	0.03	0.06	0.13	0.24
26	0.42	0.10	0.03	0.06	0.13	0.24
27	0.42	0.10	0.03	0.06	0.13	0.24
28	0.42	0.10	0.03	0.06	0.13	0.24

ER, emergency room; GP, general practitioner; HRU, healthcare resource utilization; MMD, monthly migraine days; NHWS, National Health and Wellness Survey.

Table 3: Summary of HRU Frequency (Per Quarter) in Patients With Migraine and Depression Using NHWS 2022 Data

MMD	Hospitalizations	ER visits	GP visits	Nurse practitioner visits	Neurologist visits	Mental health visits
0	0.25	0.06	0.03	0.04	0.02	0.13
1	0.36	0.13	0.05	0.06	0.09	0.59
2	0.36	0.13	0.05	0.06	0.09	0.59
3	0.36	0.13	0.05	0.06	0.09	0.59
4	0.52	0.11	0.05	0.10	0.08	0.53
5	0.52	0.11	0.05	0.10	0.08	0.53
6	0.52	0.11	0.05	0.10	0.08	0.53
7	0.52	0.11	0.05	0.10	0.08	0.53
8	0.70	0.18	0.05	0.03	0.24	1.52
9	0.70	0.18	0.05	0.03	0.24	1.52
10	0.70	0.18	0.05	0.03	0.24	1.52
11	0.70	0.18	0.05	0.03	0.24	1.52
12	0.70	0.18	0.05	0.03	0.24	1.52
13	0.70	0.18	0.05	0.03	0.24	1.52
14	0.70	0.18	0.05	0.03	0.24	1.52
15	0.74	0.23	0.07	0.07	0.46	2.90
16	0.74	0.23	0.07	0.07	0.46	2.90
17	0.74	0.23	0.07	0.07	0.46	2.90
18	0.74	0.23	0.07	0.07	0.46	2.90
19	0.74	0.23	0.07	0.07	0.46	2.90
20	0.74	0.23	0.07	0.07	0.46	2.90
21	0.74	0.23	0.07	0.07	0.46	2.90
22	0.74	0.23	0.07	0.07	0.46	2.90
23	0.74	0.23	0.07	0.07	0.46	2.90
24	0.74	0.23	0.07	0.07	0.46	2.90
25	0.74	0.23	0.07	0.07	0.46	2.90
26	0.74	0.23	0.07	0.07	0.46	2.90
27	0.74	0.23	0.07	0.07	0.46	2.90
28	0.74	0.23	0.07	0.07	0.46	2.90

ER, emergency room; GP, general practitioner; HRU, healthcare resource utilization; MMD, monthly migraine days; NHWS, National Health and Wellness Survey.

Indirect costs

- Indirect costs were calculated using wage rates sourced from Eurostat[10] or other available data.
- Among employed respondents, the number of hours missed in the last week because of health and the number of hours missed in the last week because of health impairment while at work (based on work productivity and activity impairment responses from the 2022 NHWS) were each multiplied by the hourly wage rate and then multiplied by the number of work weeks in a year (i.e., 50) to annualize the estimates of costs.

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