REPORT VYEPTI® eptinezumab

<table>
<tr><th>Product &
Mechanism of action</th><th>Authorized indications
Licensing status</th><th>Essential therapeutic features</th><th>NHS impact</th></tr>
<tr>
<td>Substance: eptinezumab

Brand Name: Vyepti

Originator/licensee:
H. Lundbeck A/S

Classification: NCE

ATC code: N02CD05

Orphan Status:
Eu: No
Us: No

Mechanism of action:
Eptinezumab is a humanized mAb that binds to CGRP ligand andblocks its binding to the receptor[1].

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<td>Authorized Indication:
EMA:eptinezumab isindicated for the prophylaxis of migraine in adults who have at least 4 migraine days per month. [2]

FDA: eptinezumab isindicated for the preventive treatment of migraine in adults. [1]

Route of administration:IV

Licensing status
EU CHMP P.O. date: 11/11/2021
FDA M.A. date: 20/02/2020

EU Speed Approval Pathway:No
FDA Speed Approval Pathway: No

ABBREVIATIONS:
AEs: Adverse events
CGRP: calcitonin gene-related peptide
CHMP: Committee for Medicinal Products for Human Use
ISA: intrinsic sympathomimetic activity
M.A.: Marketing Authorization
mAb: monoclonal antibody
MMDs monthly migraine days
P.O.: Positive Opinion
Pts: patients
SAE: Serious adverse event
SOC: system organ class
TEAEs: treatment-emergent AEs</td>
<td>Summary of clinical EFFICACY:The efficacy of eptinezumab was evaluated in two randomized, double-blind, placebo-controlled, phase 3trials: one study in pts with episodic migraine (NCT02559895) and one in pts with chronic migraine (NCT02974153).In both studies, eptinezumab was administered by IV infusion every 12 weeks, andthe primary efficacy endpoint was the change from baseline over weeks 1 to 12 in MMDs.Pts were allowed to use concurrent migraine or headache medications with specific limitations [3-4].
NCT02559895 trial included adults with a history of migraine for ≥12 months with ≤14 headache days per month, including at least four migraine days, in the three months prior to screening.
NCT02974153 trial included adults with a history of chronic migraine for ≥12 months and experienced ≥15 to ≤26 headache days and ≥8 migraine days during the 28-day screening period.
In NCT02559895 trialpts were randomized to receive 30mg eptinezumab (n=223),100mg eptinezumab (n=221), 300mg eptinezumab (n=222)or placebo (n=222).Eptinezumab 100mg and 300mg demonstrated statistically significant reduction from baseline to 12th week in the frequency of migraine days compared to placebo.
In NCT02974153 trial pts. were randomized to receive 100mg eptinezumab (n=356), 300mg eptinezumab (n=350), or placebo (n=366). Both 100 and 300 mg of eptinezumab demonstrated statistically significant reductions in MMDs during weeks 1 to 12 compared to placebo.
Mean MMDs at baseline, change in MMDs from baseline to 12thweek and difference from placebo across the different groups for both studies are summarized in the following table.
[EPT: eptinezumab; PBO: placebo;[a]not statistically significant per testing hierarchy] [3,4]
<table>
<tr><th></th><th colspan="4">NCT02559895</th><th colspan="3">NCT02974153</th></tr>
<tr><td></td><td>EPT 30mg</td><td>EPT 100mg</td><td>EPT 300mg</td><td>PBO</td><td>EPT 100mg</td><td>EPT 300mg</td><td>PBO</td></tr>
<tr><td>Mean MMDs baseline</td><td>8.7</td><td>8.7</td><td>8.6</td><td>8.4</td><td>16.1</td><td>16.1</td><td>16.2</td></tr>
<tr><td>Change from baseline over weeks 1-12</td><td>-4.0</td><td>-3.9</td><td>-4.3</td><td>-3.2</td><td>-7.7</td><td>-8.2</td><td>-5.6</td></tr>
<tr><td>Difference from placebo</td><td>-0.8</td><td>-0.7</td><td>-1.1</td><td>-</td><td>-2.0</td><td>-2.6</td><td>-</td></tr>
<tr><td>p value</td><td>p=0.0046[a]</td><td>p = 0.0182</td><td>p = 0.0001</td><td>-</td><td><0.0001</td><td><0.0001</td><td>-</td></tr>
</table>
Summary of clinical SAFETY:In NCT02559895 trial, overall, 59.7% pts experienced ≥1 TEAEs and 2.8% pts had severe TEAEs. In particular, 12.6% pts who received eptinezumabvs8.6%pts who received placebohad ≥1 study drug-related TEAE.1.7%pts who received eptinezumab vs 2.7% who received placebo experienced a SAE. No SAEs were considered related to study treatment. 5.5% pts in the eptinezumab 30mg group, 2.7% in the eptinezumab 100mg group, 2.2% in the eptinezumab 300mg group, and 2.7% in the placebo group experienced a TEAE that led to study drug withdrawal. There were no deaths reported [3].
In NCT02974153 trial, overall, 47.4% pts experienced ≥1 TEAEs.In particular, 13.2% pts in the eptinezumab groups vs 7.9% in the placebo group had ≥1 TEAEs considered to be related to the study drug. A total of 10 pts (<1%) experienced a SAE (7 pts who received eptinezumab vs 3 who received placebo), and 13 pts (1.2%) experienced a TEAE that led tostudy drug withdrawal: 3 (<1%) in the eptinezumab 100mggroup, 8 (2.3%) in the eptinezumab 300mg group, and 2 (<1%)in the placebo group. No pts had life-threatening SAEs and no deaths were reported [4].

Ongoing studies:
● For the same indication: Yes
● For other indications: Yes

Discontinued studies (for the same indication): No

References:
1.https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761119s000lbl.pdf
2.https://www.ema.europa.eu/en/medicines/human/summaries-opinion/vyepti
3.https://pubmed.ncbi.nlm.nih.gov/32075406/
4.https://pubmed.ncbi.nlm.nih.gov/32209650/
5.https://www.drugs.com/price-guide/vyepti
6.http://www.neuro.it/web/eventi/NEURO/patologia.cfm?p=cefalee
7.https://pubmed.ncbi.nlm.nih.gov/22287564/
8.https://www.nature.com/articles/s41582-021-00509-5</td>
<td>Cost of therapy:The cost for Vyepti IV solution (100 mg/mL) is around $1,609[5].

Epidemiology:
Migraine prevalence in the worldis estimated to be 14.4%. In Italy, a survey among subjectsrepresentative of Parma's adult general population showed a prevalence of migraine of 24.7% (32.9% women and 13% men) [6,7].

POSSIBLE PLACE IN THERAPY
Pts are considered for preventive treatment depending on MMDs, severity and duration of attacks, migraine-related disability and in case of acute medication overuse.
CGRP mAbs represent 3rd-line preventive medications for migraine as well as OnabotulinumtoxinA [8].

OTHER INDICATIONS IN DEVELOPMENT: Cluster headache; dual diagnosis of migraine and medication overuse headache.

SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:No

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION: Zavegepant, Ubrogepant, Rimegepant, Atogepant, Lasmiditan.

*Service reorganization: No
*Possible off label use: No</td>
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