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Fremanezumab for chronic and episodic migraine

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LAY SUMMARY

Migraine is a type of headache that can be moderate to severe. It is the third most common condition in the world. It is further subtyped into chronic or episodic migraine. This classification depends on the number of headache days per month. The symptoms of migraine include throbbing pain, feeling sick, vomiting, and sensitivity to sound and light. There are other symptoms that may be associated with migraine such as sight problems, numbness or tingling sensation, dizziness, difficulty speaking and sometimes fainting. Migraine is a disabling illness that can have big impacts on the patient's normal activities and quality of life. There is a significant unmet need for the treatment of migraine.

Fremanezumab is a new medicine under development for preventative treatment of chronic and episodic migraine. It acts by targeting a very specific type of protein called the human calcitonin gene-related peptide (CGRP) which is a well-known to be involved in migraine. Therefore, if licensed it will offer a potential new treatment option for patients with migraine.

TARGET GROUP

Migraine (chronic migraine (CM) and episodic migraine (EM))

TECHNOLOGY

DESCRIPTION

Fremanezumab (TEV-48125) is under development for the treatment of chronic and episodic migraine and cluster headache. It is a fully humanised monoclonal antibody that selectively blocks the binding of human calcitonin gene-related peptide (CGRP) to the CGRP receptor. CGRP is released from trigeminal ganglia cells. CGRP transcription is increased under conditions mimicking neurogenic inflammation. In migraine, activation of trigeminal nerves involves the release of CGRP and other peptides that cause the release of pro-inflammatory mediators.[1]

In the Phase III clinical trial (HALO CM; NCT02621931), fremanezumab was given subcutaneously at 675 mg at initiation followed by monthly 225 mg of fremanezumab for two months (monthly dose regimen), or followed by placebo for two months (quarterly dose regimen).[2,3] In the Phase III clinical trial (HALO EM; NCT02629861), fremanezumab was given as subcutaneous injections at 225 mg as a monthly dose for three months, or at 675 mg at initiation followed by placebo for two months.[4,5]

Fremanezumab does not currently have Marketing Authorisation in the EU for any indication.

INNOVATION and/or ADVANTAGES

Fremanezumab is a fully humanised monoclonal antibody targeting the CGRP ligand, a well-validated target in migraine.[6] It was reported that currently, there are a limited number of preventive treatments for migraine. There are issues of efficacy, tolerance, safety, adherence, pharmacophobia and nocebo response, all suggesting the need for better treatments.[7] Efficacy of fremanezumab was demonstrated for both monthly and quarterly dosing. For both dose regimens in EM and CM, a significant reduction in the number of monthly migraine days were observed both during 4-weeks and 12-weeks period. With limited availability of preventive treatment options, fremanezumab, presents a potential new option to address a significant unmet medical need.[6]

DEVELOPER

Teva Pharmaceuticals Ltd

PATIENT GROUP

BACKGROUND

Migraine is a primary headache disorder that most often begins at puberty and mostly affects those aged between 35 and 45 years. Migraine is more common in women, with a ratio of about 2:1. It is caused by the activation of a mechanism deep in the brain that leads to the release of pain-producing inflammatory substances around the nerves and blood vessels of the head. Migraine is often life-long and characterised by recurring attacks.[8]

The most common symptoms of a migraine attack include throbbing headache in one side of the head, sensitivity to light and noise, nausea, vomiting and lethargy (lack of energy). Other symptoms that might be associated with migraine include sweating, poor concentration, feeling very hot or very cold, abdominal pain, and diarrhoea. About one in three people with migraines experience transient

neurological symptoms before the migraine phase starts, which occurs due to changes in the cortex area. These symptoms are known as aura and include: visual disturbances (such as seeing flashing lights, zig-zag patterns or coloured spots, blind spots), numbness or tingling sensation like pins and needles, dizziness, vertigo (the feeling of everything spinning), speech and hearing disturbance, memory changes, feelings of fear and confusion, and loss of consciousness (although this is unusual).[9,10]

Migraines can be sub-typed as chronic migraine (CM) or episodic migraine (EM) based on the frequency of headache days.[11] The International Headache Society defines CM as 15 or more headache days per month over a three month period of which more than eight are migrainous, in the absence of medication over use. EM is defined as less than 15 headache days per month.[12]

Of the two sub-types, CM is regarded as the more debilitating disorder following the findings from various population and clinical studies. For example, CM compared to EM patients are more likely to be unemployed, overweight and tend to experience more depression and anxiety.[13] Remarkable impairment of daily activities is also associated with CM.[14] A large population-based study showed that psychiatric, respiratory, cardiovascular and chronic pain disorders were all more commonly associated with CM than with EM.[11]

Despite there being a lack of understanding surrounding the exact mechanism at play when a migraine attack is initiated, dysfunction in the central nervous system (CNS) leading to release of inflammatory mediators is proposed to cause sensitisation and excitation of trigeminal nerves that promote neurogenic inflammation and generation of painful stimuli.[15] Furthermore elevated levels of CGRP, but not of other neuropeptides, were found in the external jugular vein during the headache phase of migraine whereas these levels normalised when headache improved.[16] The importance of CGRP is further highlighted as infusion of human CGRP was found to trigger a migraine attack in susceptible individuals, while CGRP levels returned to normal after migraine treatment with triptans.[15] These findings provide insight into a putative role of CGRP in the pathophysiology of migraine, opening newer pathways for therapeutic intervention.[17]

CLINICAL NEED and BURDEN OF DISEASE

Migraine is the third most common condition in the world[18] and affects 15% of the UK adult population.[19] In a Single Technology Appraisal about Botulinum toxin type A published by NICE in 2011, it is estimated that there are 190,000 migraine attacks experienced every day in England and 6 million people suffer from migraine in the UK. Prevalence has been reported to be 5–25% in women and 2–10% in men. Prevalence of CM in the UK is unknown, although some clinicians consider the rate could be 1 in 1000 people.[20]

In 2015-16, there were 25,360 hospital admissions for migraine (ICD 10 G43), resulting in 27,698 bed days and 31,279 finished consultant episodes.[21] In the UK, 43% of people with CM visit a neurologist or headache specialist compared to only 18% of people with EM. It is estimated that between 2.5% and 4.6% of people with EM experience progression to CM. However, approximately the same proportion regress from CM to EM spontaneously. Migraine is ranked globally as the seventh most disabling disease among all diseases and the leading cause of disability among all neurological disorders.[12]

The World Health Organisation (WHO) has recognised the impact of migraine worldwide and categorised it as the same level of disability as dementia, quadriplegia and acute psychosis. Furthermore WHO classified CM as more disabling than blindness, paraplegia, angina or rheumatoid arthritis. The cost of migraine in terms of medications are estimated at £150 million annually in the UK, however it is thought that overall costs are well in excess of this figure. It is estimated that the UK

population loses 25 million working days each year due to migraine this costs the UK £2.25 billion *per annum*.[22]

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal. Botulinum toxin type A for the prevention of headaches in adults with chronic migraine (TA260). June 2012.
- NICE guidelines. Headaches in over 12s: diagnosis and management (CG150). September 2012. (Updated November 2015).
- NICE quality standard. Headaches in over 12s (QS42). August 2013.
- NICE interventional procedure guidance in development. Transcutaneous electrical stimulation of the supraorbital nerve for treating and preventing migraine (GID-IP1293). May 2016.
- NICE interventional procedure guidance. Transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine (IPG552). March 2016.
- NICE interventional procedure guidance Implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache (IPG527). June 2015.
- NICE interventional procedure guidance. Transcranial magnetic stimulation for treating and preventing migraine (IPG477). January 2014.
- NICE interventional procedure guidance. Occipital nerve stimulation for intractable chronic migraine (IPG452). April 2013.
- NICE interventional procedure guidance. Percutaneous closure of patent foramen ovale for recurrent migraine (IPG370). December 2010.

NHS ENGLAND and POLICY GUIDANCE

- NHS England. NHS standard contract. Occipital nerve stimulation for intractable headaches and migraine D08/P/c.
- NHS England. NHS standard contract for specialised pain. Specialised services for pain management (Adult). D08/S/a.

OTHER GUIDANCE

- American Headache Society. How to Apply the AHS Evidence Assessment of the Acute Treatment of Migraine in Adults to your Patient with Migraine. 2016.[23]
- Management of chronic headache. Australian family physician. March 2014.[24]
- Headache Classification Committee of the International Headache Society (HIS). The international classification of headache disorders, (beta version).3rd ed. 2013.[25]
- British Association for the Study of Headache. Guidelines for All Healthcare Professionals in the Diagnosis and Management of Migraine, Tension-Type, Cluster and Medication-Overuse Headache. 3rd ed. 2010.[26]
- Scottish Intercollegiate Guidelines Network (SIGN). Diagnosis and management of headaches in adults (SIGN Publication no. 107). November 2008.[27]

CURRENT TREATMENT OPTIONS

Based on discussions regarding the benefits and risks of the prophylactic treatment of migraine, including consideration of individual preferences, comorbidities, risk of adverse events, and the

impact of the headache on the person's quality of life, the following options are recommended by NICE: [28]

- Offer topiramate or propranolol according to the person's preference, comorbidities and risk of adverse events. Advise women and girls of childbearing potential that topiramate is associated with a risk of foetal malformations and can impair the effectiveness of hormonal contraceptives. Ensure they are offered suitable contraception if needed
- Consider amitriptyline according to the person's preference, comorbidities and risk of adverse events
- If both topiramate and propranolol are unsuitable or ineffective, consider a course of up to 10 sessions of acupuncture over 5–8 weeks according to the person's preference, comorbidities and risk of adverse events
- Advise people with migraine that riboflavin (400 mg once a day) may be effective in reducing migraine frequency and intensity for some people
- Flunarizine: this is not licensed in the UK but it is licensed in other countries, including Ireland, for migraine prophylaxis. NICE has published an evidence summary on migraine prophylaxis: flunarizine.[29]

Botulinum toxin type A is recommended as an option for the prophylaxis of headaches in adults with CM (defined as headaches on at least 15 days *per* month of which at least 8 days are with migraine) in those:[28]

- That have not responded to at least three prior pharmacological prophylaxis therapies and
- Whose condition is appropriately managed for medication overuse

Treatment with botulinum toxin type A that is recommended above should be stopped in people whose condition is not adequately responding to treatment (defined as less than a 30% reduction in headache days *per* month after two treatment cycles) or has changed to EM.

NICE also has published guidance on interventional procedures with special arrangements for clinical governance, consent and audit or research:[28]

- Transcutaneous electrical stimulation of the supraorbital nerve for treating and preventing migraine
- Transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine
- Transcranial magnetic stimulation for treating and preventing migraine
- Occipital nerve stimulation for intractable CM
- Percutaneous closure of patent foramen ovale for recurrent migraine

EFFICACY and SAFETY

Trial	**HALO CM, NCT02621931; fremanezumab (monthly dose regimen) vs fremanezumab (quarterly dose regimen) vs placebo; phase III**
Sponsor	Teva Branded Pharmaceutical Products, R&D Inc.
Status	Completed.
Source of Information	Trial registry,[30] manufacturer,[3] global data.[2]
Location	EU (not UK), USA, Canada, Russia, Japan, and Israel.
Design	Randomised, double-blind, placebo-controlled, parallel-group.
Participants	n= 1,134; aged 18-70 years; males or females; history of migraine according to International Classification of Headache Disorders, or clinical judgment suggests a migraine diagnosis; Patient fulfils the criteria for CM (headache occurring on ≥15 days, with features of migraine headache on ≥8 days) in prospectively collected baseline information during the 28-day run-in period, 85% e-diary compliance; total body weight between 99 and 250 lbs, inclusive.
Schedule	Randomised in a 1:1:1 ratio to receive subcutaneous injections of fremanezumab at 675 mg at initiation followed by monthly 225 mg for two months (monthly dose regimen), fremanezumab at 675 mg at initiation followed by placebo for two months (quarterly dose regimen), or three monthly doses of matching placebo.[3]
Follow-up	Active treatment for 12 weeks, follow-up 12 weeks.
Primary Outcomes	• Mean change from baseline in the monthly average number of headache days of at least moderate severity [Time Frame: Baseline, 12 weeks] • Percentage of participants with adverse events [Time Frame: 12 weeks]
Secondary Outcomes	• Proportion of patients reaching at least 50% reduction in the monthly average number of headache days of at least moderate severity [Time Frame: 12 weeks] • Mean change from baseline in the monthly average number of days of use of any acute headache medications [Time Frame: Baseline, 12 weeks] • Mean change from baseline in the number of headache days of at least moderate severity [Time Frame: Baseline, 4 weeks] • Mean change from baseline in disability score, as measured by 6 item questionnaire (HIT-6) [Time Frame: Baseline, 4 weeks] • Mean change from baseline in the monthly average number of migraine days during the 12-week period after the 1st dose of study drug [Time Frame: Baseline, 12 weeks]
Key Results	Patients treated with fremanezumab experienced statistically significant reduction in the number of monthly headache days of at least moderate severity *vs.* placebo (-2.5 days) during the 12 week period after first dose, for both monthly (-4.6 days $p<0.0001$) and quarterly (-4.3 days $p<0.0001$) dosing regimens.

	In addition, patients treated with fremanezumab experienced significant improvement compared to placebo on all secondary endpoints for both monthly and quarterly dosing regimens, including: response rate, onset of efficacy, efficacy as monotherapy, and disability. The results were positive, and of 13 hierarchical comparisons, p<0.0001 in 12 of them, being 0.0004 in the remaining.[3]
Adverse effects (AEs)	The most commonly-reported adverse event in the study was injection site pain, with similar rates in the placebo and active groups.[3]
Expected reporting date	-

Trial	**HALO EM, NCT02629861; fremanezumab 225 mg as a monthly dose for three months, or 675 mg at initiation followed by placebo for two month, vs placebo; phase III**
Sponsor	Teva Branded Pharmaceutical Products, R&D Inc.
Status	Completed.
Source of Information	Trial registry,[31] manufacturer,[4,6] global data.[5]
Location	EU (not UK), USA, Canada, Russia, Japan, and Israel.
Design	Multicentre, Randomised, Double-Blind, Placebo-Controlled, Parallel-Group Study.
Participants	n= 878; aged 18-70 years; males or females; history of migraine according to International Classification of Headache Disorders, or clinical judgment suggests a migraine diagnosis; 85% e-diary compliance; are on monotherapy and stable doses of prophylactic medications; total body weight between 99 and 265 lbs, inclusive
Schedule	Randomised in a 1:1:1 ratio to receive subcutaneous injections of fremanezumab at 225 mg as a monthly dose for three months; or fremanezumab at 675 mg at initiation followed by placebo for two months; or three monthly doses of matching placebo.
Follow-up	3 months, follow-up 12 weeks.
Primary Outcomes	• Mean change from baseline in the monthly average number of migraine days [Time Frame: Baseline, 12 weeks] • Percentage of Participants with Adverse Events [Time Frame: 12 weeks]
Secondary Outcomes	• Proportion of patients reaching at least 50% reduction in the monthly average number of migraine days [Time Frame: 12 weeks] • Mean change from baseline in the monthly average number of days of use of any acute headache medications relative to baseline [Time Frame: Baseline, 12 Weeks] • Mean change from baseline of the number of migraine days [Time Frame: Baseline, 4-weeks] • Mean change from baseline in disability, as measured by the Migraine Disability Assessment (MIDAS) questionnaire [Time Frame: Baseline, 4-week]

Key Results	Participants in this trial had a mean of 9.1 migraine days per month and reported 39 days with functional impairment per quarter. In this severely affected population, Fremanezumab given monthly significantly improved the average number of migraine days, relative to baseline, by 41.6% for the duration of the trial (-3.7 days vs. -2.2 days for placebo, $p < 0.0001$), with 47.7% (monthly regimen) and 44.4% (quarterly regimen) of the patients achieving ≥50% reduction in the monthly average number of migraine days vs 27.9% in the placebo group. Number of days with disability were decreased by 64.7% ($p = 0.0021$) and use of medication was decreased by 39.0% ($p < 0.0001$). The quarterly SC dose, which was uniquely tested in this program, also yielded highly significant results for decrease in migraine days (-3.4 days or 37.0%, $p < 0.0001$) and for all other comparisons. Also unique to this development, both dose regimens highly significantly improved migraine in subjects on stable doses of other prophylactic medications (-4.0 days for monthly dose vs -2.0 days for placebo, $p = 0.001$; -3.7 days for quarterly dose, $p = 0.006$).[4,6]
Adverse effects (AEs)	The most commonly-reported adverse event in the study was injection site pain, with similar rates in the placebo and active groups.[4]
Expected reporting date	-

Trial	**HALO, NCT02638103; fremanezumab dose regimen 1 vs fremanezumab dose regimen 2; phase III**
Sponsor	Teva Branded Pharmaceutical Products, R&D Inc.
Status	Ongoing
Source of Information	Trial registry,[32] global data.[33]
Location	EU (not UK), USA, Canada, Russia, Japan, and Israel.
Design	Multicentre, Randomized, Double-Blind, Parallel-Group Study
Participants	n= 1,578; aged 18-70 years; males and females; have completed the pivotal efficacy study without major protocol violations; history of migraine or clinical judgment suggests a migraine diagnosis; fulfil the criteria for EM or CM; total body weight between 99 and 265 lbs., inclusive; must be of non-childbearing potential; female patients of childbearing potential must have a negative serum beta-human chorionic gonadotropin (β-HCG) pregnancy test prior to randomisation.
Schedule	Randomised to fremanezumab -1 subcutaneously; or fremanezumab -2 subcutaneously.
Follow-up	Active treatment period is not reported; follow-up 533 days (±15 days).
Primary Outcomes	Percentage of participants with adverse events [Time Frame: 533 days (±15 days)]
Secondary Outcomes	Other outcomes: • Mean change from baseline in the number of migraine days [Time Frame: 533 days (±15 days)] • Mean change from baseline in the monthly average of migraine days [Time Frame: 533 days (±15 days)] • Mean change from baseline in the number of headache days of any severity [Time Frame: 533 days (±15 days)]

	• Mean change from baseline in the monthly average of headache days of any severity [Time Frame: 533 days (±15 days)]
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study completion date reported as April 2018.

Trial	**NCT02021773 CM; fremanezumab 900mg dose vs fremanezumab 675/225mg dose vs placebo; phase II.**
Sponsor	Teva Pharmaceutical Industries.
Status	Completed.
Source of Information	Trial registry,[34] publication,[35] manufacturer,[36] global data[37]
Location	USA
Design	A Multicenter, Randomized, Double-Blind, Double-Dummy, Placebo-Controlled, Parallel Group, Multi-Dose Study.
Participants	n=264; aged 18-65 years; males and females; chronic migraine meeting the diagnostic criteria listed in the International Classification of Headache Disorders; Body Mass Index (BMI) of 17.5 to 37.5 kg/m2, and a total body weight between 50 kg and 120 kg inclusive, demonstrated compliance with the electronic headache diary during the run-in period headache data on a minimum of 22/28 days (80% diary compliance).
Schedule	Randomised in a 1:1:1 ratio to receive subcutaneous injections of fremanezumab at 900 mg as a monthly dose for three months; or fremanezumab at 675 mg at initiation followed by 225 mg for two months; or three monthly doses of matching placebo.
Follow-up	Active treatment for 3 months, follow-up 12 weeks.
Primary Outcomes	• Mean change from baseline in the number of monthly cumulative headache hours of any severity on headache days relative to the 28-day post-treatment period ending with week 12 [Time Frame: 12 weeks after first dose of blinded study drug] • Safety as determined by the presence of Adverse events by treatment group [Time Frame: 12 weeks after first dose of blinded study drug]
Secondary Outcomes	• Mean change from baseline in the number of headache days of at least moderate severity relative to the 28-day post-treatment period ending with week 12. [Time Frame: 12 weeks after first dose of blinded study drug]
Key Results	The mean change from baseline in number of headache-hours during weeks 9-12 was -59.84 h (SD 80.38) in the 675/225 mg group and -67.51 h (79.37) in the 900 mg group, compared with -37.10 h (79.44) in the placebo group. The least square mean difference in the reduction of headache-hours between the placebo and 675/225 mg dose groups was -22.74 h (95% CI -44.28 to -1.21; p=0.0386), whereas the difference between placebo and 900 mg dose groups was -30.41 h (-51.88 to -8.95; p=0.0057). Adverse events were reported by 36 (40%) patients in the placebo group, 47 (53%) patients in the 675/225 mg dose group, and 41 (47%) patients in the 900 mg dose group, whereas treatment-

	related adverse events were recorded in 15 (17%) patients, 25 (29%) patients, and 28 (32%) patients, respectively.[35]
Adverse effects (AEs)	The most common adverse events were mild injection-site pain and pruritus. Four (1%) patients had serious non-treatment-related adverse events (one patient in the placebo group, one patient in the 675/225 mg group, and two patients in the 900 mg group); no treatment-related adverse events were serious and there were no relevant changes in blood pressure or other vital signs.[35]
Expected reporting date	-

Trial	**NCT02025556 EM; fremanezumab 225 mg (low dose) vs fremanezumab 675 mg (high dose) *vs* placebo; phase II**
Sponsor	Teva Pharmaceutical Industries
Status	Completed.
Source of Information	Publication,[38] trial registry,[39] manufacturer,[40] global data.[41]
Location	USA
Design	Multicentre, Randomised, Double-Blind, Placebo-Controlled, Parallel-Group.
Participants	n=297; aged 18-65 years; males and females; fulfilling criteria for episodic migraine as per the Second Edition of The International Headache Society; Body Mass Index (BMI) of 17.5 to 37.5 kg/m^2, and a total body weight between 50 kg and 120 kg, inclusive; compliance with the electronic headache diary during the run-in period by entry of headache data on a minimum of 22/28 days (80% compliance).
Schedule	Randomized to high dose fremanezumab (675 mg), low dose fremanezumab (225 mg) or placebo, administered subcutaneously once a month.
Follow-up	Active treatment for months, follow-up 12 weeks.
Primary Outcomes	• Efficacy of two distinct doses of subcutaneous fremanezumab in the preventive treatment of high frequency episodic migraine (HFEM), measured by mean change from baseline in the monthly migraine days during the 28-day post treatment period ending with week 12 [Time Frame: 12 weeks after first dose of blinded study drug] • Evaluate the safety and tolerability (*i.e.* by measuring the change from baseline in the frequency and severity of adverse events) of fremanezumab in the preventive treatment of HFEM. [Time Frame: 12 weeks after first dose of blinded study drug]
Secondary Outcomes	Efficacy of two distinct doses of subcutaneous fremanezumab in the preventive treatment of HFEM, measured by mean change from baseline on the number of days with headache of any severity during the 28-day post treatment period ending with week 12 [Time Frame: 12 weeks after first dose of blinded study drug]
Key Results	Between Jan 8, 2014, and Oct 15, 2014, 297 participants were enrolled: 104 were randomly assigned to receive placebo, 95 to receive 225 mg fremanezumab, and 96 to receive 675 mg fremanezumab. The least square mean (LSM) change in number of migraine-days from baseline to weeks 9-12 was -3.46 days (SD 5.40) in the placebo group, -6.27 days (5.38) in the 225 mg

	dose group, and -6.09 days (5.22) in the 675 mg dose group. The LSM difference in the reduction of migraine-days between the placebo and 225 mg dose groups was -2.81 days (95% CI -4.07 to -1.55; p<0.0001), whereas the difference between the placebo and 675 mg dose group was -2.64 days (-3.90 to -1.38; p<0.0001). LSM differences in the reduction of headache-days were -2.63 days (-3.91 to -1.34; p<0.0001) between the placebo group and 225 mg dose group and -2.58 days (-3.87 to 1.30; p <0.0001) between the placebo group and the 675 mg dose group.[38]
Adverse effects (AEs)	Adverse events occurred in 58 (56%) patients in the placebo group, 44 (46%) patients in the 225 mg dose group, and 57 (59%) patients in the 675 mg dose group; moderate or severe adverse events were reported for 29 (27%) patients, 24 (25%) patients, and 26 (27%) patients, respectively.[38]
Expected reporting date	-

ESTIMATED COST and IMPACT

COST

The cost of fremanezumab is not yet known.

IMPACT – SPECULATIVE

IMPACT ON PATIENTS AND CARERS

☐ Reduced mortality/increased length of survival

☒ Reduced symptoms or disability

☒ Other: *improved quality of life for carers, improved patient convenience, wider societal benefits (e.g. earlier return to normal activities, including employment) etc.*

☐ No impact identified

IMPACT ON HEALTH and SOCIAL CARE SERVICES

☐ Increased use of existing services

☒ Decreased use of existing services

☐ Re-organisation of existing services

☒ Need for new services: if injection needs to be administered by a health care professional.

☐ Other

☐ None identified

IMPACT ON COSTS and OTHER RESOURCE USE

☒ Increased drug treatment costs

☐ Reduced drug treatment costs

☒ Other increase in costs: *there might be additional costs for administration in clinic*

☐ Other reduction in costs

☐ Other

☐ None identified

OTHER ISSUES

☐ Clinical uncertainty or other research question identified

☒ None identified

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