National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Esketamine for treatment-resistant depression [ID1414]

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

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Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Janssen	Janssen agrees that this topic is appropriate for referral to NICE.	Thank you for your comment.
Wording	Janssen	Janssen proposes using the term 'treatment resistant depression' (TRD) to provide clarity on the specific indication for which esketamine nasal spray will have marketing authorisation; thereby avoiding confusion with the broader population of individuals suffering with major depressive disorder. Janssen suggests using "esketamine nasal spray" in reference to the treatment throughout the scoping document to reinforce the particulars of the medicine and its unique formulation. Janssen proposes using the following wording for the remit, with the proposed changes in bold: "To appraise the clinical and cost effectiveness of esketamine nasal spray within its marketing authorisation for treatment resistant depression (Major Depressive Disorder in adults who have not responded to at least two	Thank you for your comment. Based on comments from the scoping workshop, the remit has been updated to refer to 'treatment-resistant depression' rather than 'major depressive disorder'. In order to allow flexibility, the remit for the scope has been kept broad. However, details about the technology's mode

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		different treatments with antidepressants in the current moderate to severe episode)."	of administration and the population are included in the scope.
Timing Issues	Janssen	The relative urgency of the proposed appraisal is high, as mental health has been declared a high priority by the NHS and the therapeutic area that has unfortunately been deprived of innovative new treatments in the last five decades. We would therefore suggest that guidance is generated as close to marketing authorisation as possible. We request that NICE considers esketamine nasal spray as soon as possible due to the high unmet medical need in TRD, and the considerable impact on patient quality of life, as well as on society due to a reduction in productivity. The current unmet need is for a rapid, effective, and safe treatment to sustain remission of depressive symptoms for patients with TRD. The overall impact of TRD on a patient is profound with symptoms including low mood, anhedonia and lack of energy. Many patients have impaired capacity and inability to work or participate in everyday activities. Esketamine is expected to receive marketing authorisation approval from the European Medicines Agency (EMA) in [redacted].	Thank you for your comment. This topic has been scheduled into the technology appraisal work programme with the aim of providing timely guidance as soon as possible after the company receives the marketing authorisation and introduces the technology in the UK.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Janssen	The background presented in the draft scope mainly references depression and MDD, however we believe a distinction should be made for TRD. We appreciate that whilst MDD, as a broad population, is relatively well described epidemiologically, there has been relatively little characterisation of the sub-population of individuals with TRD.	Thank you for your comment. The remit and population in the scope have been updated to focus on

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		We request that specific emphasis is made to distinguish between MDD and TRD as the latter will have greater duration and severity of illness, impairment/disability, suicidality, healthcare resource utilisation and mortality. For example, while the average duration of episode for the entire MDD population may be between 6-8 months as referenced in the draft scope, median duration of illness at baseline in the esketamine Phase 3 studies was considerably over 1 year. Additionally, we request that consideration is given to the greater unmet need among the elderly (aged ≥ 65 years) who have greater severity and lack of responsiveness. To estimate the prevalence of TRD, we propose the following proportions: • English population prevalence of MDD = 3.3% • Proportion receiving pharmacological treatment = 79.1% • Proportion with inadequate response to 2 antidepressant therapies = 10.6% (based on the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial; a large prospective US cohort study) To better characterise the overall burden, we suggest that the scope also describes the economic impact. McCrone et al (2008) has estimated the total cost of healthcare services for depression in England in 2007 to have been £1.7 billion per year. Compounded by loss of employment, the societal cost substantially increased to a total of £7.5 billion per year. References Johnston K., Powell L.C., Anderson IM, Szabo S., Cline S., The burden of treatment-resistant depression: a systematic review of the economic and quality of life literature, Journal of Affective Disorders (2018), doi: 10.1016/j.jad.2018.06.045	treatment-resistant depression. Inclusion of the subgroup of people aged ≥65 years was discussed at the scoping workshop. It is recognised that this subgroup may receive a different dose and have a different tolerance to esketamine compared to adults aged 18-64 years. However, the subgroup has not been included in the scope as specifying subgroups based on age may lead to equalities issues during the proposed appraisal because age is a protected characteristic. After receiving the company submission, NICE will assess the potential budget impact of esketamine by estimating the net annual cost to the NHS

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		Reutfors J, Andersson T.M-L, Brenner P, Brandt L, DiBernardo A, Li G, Hägga D, Wingård L, Bodén,R, Mortality in treatment-resistant unipolar depression: A register-based cohort study in Sweden. Journal of Affective Disorders 238 (2018) 674–679 Digital N. Mental Health and Wellbeing in England Adult Psychiatric Morbidity Survey. 2014 Kendrick T, Dowrick C, McBride A, Howe A, Clarke P, Maisey S, et al. Management of depression in UK general practice in relation to scores on depression severity questionnaires: analysis of medical record data. BMJ. 2009;338:b750 Rush J, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, et al. Acute and Longer-Term Outcomes in Depressed Outpatients Requiring One or Several Treatment Steps: A STAR*D Report. American Journal of Psychiatry. 2006;163(11):1905-17 Blazer DG. Depression in late life: review and commentary. J Gerontol A Biol Sci Med Sci. 2003 Mar;58(3):249-65. McCrone P, Dhanasiri, S., Patel, A., Knapp, M., Lawton-Smith, S. Paying the Price: the cost of mental health care in England to 2026: Kings Fund; 2008	(see the assessing resource impact process manual for further details).
The technology/ intervention	Janssen	To be accurate, the technology can best be described as: esketamine nasal spray. The brand name of esketamine nasal spray is [redacted]. Janssen requests the following wording to better and more accurately describe the proposed mechanism of action of this agent to be used in the scoping document: “Esketamine is a non-competitive, subtype non-selective, activity-dependent glutamate receptor modulator. Evidence suggests that through N-methyl-D-aspartate (NMDA) receptor antagonism, esketamine produces a transient	Thank you for your comment. Thank you for confirming the proposed brand name of the technology. The scope describes the mode of

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		increase in glutamate release leading to increases in α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) stimulation and subsequently to increases in neurotrophic signaling that restore synaptic function in these brain regions." In reference to the second paragraph under "The technology", we suggest that this be changed to better reflect the potential licensed indication (edits indicated in bold): "Esketamine nasal spray does not have a marketing authorisation in the UK for the treatment of major depressive disorder. It has been studied in randomised clinical trials in combination with a newly-initiated oral antidepressant in adults with treatment resistant depression (Major Depressive Disorder in adults who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode)."	administration in the description of the technology. The appraisal will focus on esketamine nasal spray. The scope now specifies that esketamine is a non-competitive, subtype non-selective, activity-dependent glutamate receptor modulator, and that it has been studied in trials in combination with a newly-initiated oral antidepressant.
Population	Janssen	The population would be more appropriately defined as: "Adults with treatment-resistant depression (Major Depressive Disorder in adults who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode)."	Thank you for your comment. The population has been updated to 'adults with treatment-resistant depression'.
	Royal College of Psychiatrists	The population should include patients with major depression as a comorbidity of other disorders.	Thank you for your comment. The population eligible for treatment with esketamine was discussed at the

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			scoping workshop. Following input from the company and clinical experts, the scope now refers to treatment-resistant depression rather than major depressive disorder.
Comparators	Janssen	There is no drug currently approved specifically for TRD by the European Medicines Agency. However, as certain MDD treatments are likely to be used on clinical grounds for the TRD-population, we agree that the antidepressant classes as well as the augmentation and combination treatments listed in the draft scope can be considered relevant comparators for esketamine nasal spray. The actual relevance of specific comparators will depend on the positioning of esketamine nasal spray within the TRD treatment pathway. We would also like to highlight that most comparators have not been studied in the specific TRD population. Therefore, comparator populations will be significantly heterogenous, weakening the robustness and feasibility of indirect comparisons with esketamine nasal spray. Furthermore, we believe for the indirect comparison it may be appropriate to analyse treatment classes (e.g. SSRI, MAOI, TCA, etc.) and modalities (i.e. augmentation, combination) rather than individual drugs/drug combinations as this may increase the evidence base for each comparison.	Thank you for your comment. The treatment pathway for major depressive disorder was discussed at the scoping workshop. Clinical experts suggested that esketamine may be used at different points in the treatment pathway (and that use is likely to depend on the safety profile of the treatment). The comparators in the scope have been amended accordingly.
	Royal College of Psychiatrists	An effective treatment for treatment resistant depression is ECT, which is particularly used in those with more serious disease. It is used in most mental health Trusts in the country. It is possible that Trusts will initially use	Based on discussion at the scoping workshop, electroconvulsive

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		the staff and facilities of ECT suites for the administration of esketamine. I would suggest that it is therefore included in the list of comparators. There is also evidence for the use of TMS in resistant depression, which is less widely available through the NHS but should nevertheless also be on the list of comparators.	therapy has been included as a comparator in the scope. However, clinical experts advised that transcranial magnetic stimulation is not widely used in the NHS and would not be a relevant comparator.
Outcomes	Janssen	To assess the full benefit of esketamine nasal spray, we would like to add the following outcome measures: 1) functioning and associated disability, 2) the impact on health-related quality of life of carers of patients with TRD, and 3) the (indirect) impact on productivity. TRD is a disorder that particularly impacts functioning and causes disability. Additionally, TRD associated disability has been associated with substantial indirect costs on employers. In a systematic literature review, Johnston et al found that increasing treatment resistance was associated with higher costs, reduced health-related quality of life and decreased health status. Furthermore, carers of patients with TRD experience high carer burden and high psychiatric caseness, which have a deteriorating impact on quality of life. In the esketamine phase 3 trials, esketamine has shown to have a positive effect on depressive symptoms, and other outcomes including the patient reported measure of functioning, measured by the Sheehan Disability Scale (SDS). Esketamine can have a beneficial effect on the three suggested outcomes mentioned above. For the definition of relapse, we would propose to include time from stable response to relapse, in addition to the already included relapse rate and time	Thank you for your comment. 'Functioning and associated disability' has been added to the outcomes in the scope. The impact on health-related quality life of carers of patients with treatment-resistant depression is assumed to be captured in the health-related quality of life outcome. Impact on productivity has not been included in the scope in line with the technology appraisals reference case section 5.1.10.

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		from remission to relapse, as this would more completely capture the full benefit of esketamine nasal spray as shown in the long-term clinical trial. References Petersen T, Papakostas GI, Mahal Y, Guyker WM, Beaumont EC, Alpert JE, Fava M, Nierenberg AA. Psychosocial functioning in patients with treatment resistant depression. European Psychiatry 19 (2004) 196–201 Corey-Lisle PK , Birnbaum HG , Greenberg PE , Marynchenko MB, Claxton AJ. Identification of a claims data "signature" and economic consequences for treatment-resistant depression. The Journal of Clinical Psychiatry 2002, 63(8):717-726 Johnston K, Powell LC, Anderson IM, Szabo S, Cline S. The burden of treatment-resistant depression: a systematic review of the economic and quality of life literature. Journal of Affective Disorders (2018), doi: 10.1016/j.jad.2018.06.045 Rane LJ, A. Fekadu, A. S. Papadopoulos (a1) (a2), S. C. Wooderson Psychological and physiological effects of caring for patients with treatment-resistant depression. Psychological Medicine Volume 42, Issue 9 2012 , pp. 1825-1833	
Economic analysis	Janssen	NICE indicated in the scientific advice on esketamine nasal spray shared with Janssen in 2013: “the appropriate time horizon for esketamine would depend on the anticipated benefits for which the model is to provide evidence of cost effectiveness. If it is expected that esketamine is associated with lower relapse rates and improved prognosis over a lifetime, then it is appropriate that the model time horizon is sufficiently long to account for this.” Janssen is still unclear as to the most appropriate time horizon for the cost effectiveness model as there are no precedents in TRD that have been assessed by NICE.	Thank you for your comment. The assumptions used in the economic modelling will be considered by the appraisal committee.
Equality and Diversity	Janssen	In relation to equality, Janssen would like to highlight the following key considerations:	Thank you for your comment. The

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		• Elderly population (aged ≥ 65 years): while there are already challenges with indirect comparison as highlighted above, this will be magnified with the relative lack of data about the elderly TRD sub-population. • Geographic access: esketamine nasal spray will require post- self-administration observation and there will be restrictions for driving. Additionally, some individuals with TRD may not be able to drive due to the nature of their condition. It will be important to consider how access will not inappropriately discriminate against individuals for whom geography may pose a challenge.	equalities issues raised are addressed in the Equalities Impact Assessment. The committee cannot make recommendations based on age because it is a protected characteristic, unless the marketing authorisation specifies otherwise. Issues relating to geographic access cannot be addressed in a technology appraisal.
Other considerations	Janssen	We would like to clarify whether the new (May 2018 draft) NICE Depression Clinical Guidelines will have an impact on the scoping, and specifically the comparators, if and when these are published.	Thank you for your comment. The update to the NICE Clinical Guideline on depression is expected to be published in February 2020.
	Royal College of Psychiatrists	The Oxford NIHR Biomedical Research Centre recently led a Patient and Public Involvement day on 22nd August to discuss the deployment of esketamine, ketamine and related rapidly acting antidepressants. This was exclusively focussed on PPI. The group of 40 participants included people who have received esketamine or ketamine as a treatment for depression, people with depression who have expressed interest in this form of treatment	Thank you for your comment. The appraisal committee will consider evidence from patient experts. NICE's public involvement programme

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		and carers of people with depression. The results are primarily qualitative, but also include quantitative data. If you think that these data might be of value in the NICE process, or if I can help with identifying patients with an interest or experience in this area for your meeting, do please let me know.	will also be involved in the appraisal.
Innovation	Janssen	Esketamine nasal spray is a major step-change in the management of TRD. It represents the first therapeutic option for TRD, and a new option in the field of MDD, which has had no novel pharmacological treatment approaches in the last 50 years. Esketamine is a novel antidepressant acting as a N-methyl-D-aspartate (NMDA) modulator. Thus, its mechanism of action is distinctively different compared to other widely used oral antidepressants, i.e. SSRIs, SNRIs, TCAs and MAOIs, which function through the prevention of reuptake or breakdown of monoamine neurotransmitters (serotonin, norepinephrine, and dopamine), or by alteration of their receptor pharmacodynamics. The clinical trial results demonstrate the potential of esketamine nasal spray to provide a fast acting, sustainable effective treatment option and fulfil an unmet need for individuals suffering from TRD. Compared to the initial delay to attain therapeutic effects for the currently widely used oral antidepressants, esketamine nasal spray has the potential to substantially improve health related quality of life from day 1. This benefit of the fast-acting nature of esketamine nasal spray may be not be adequately captured in the QALY calculation. Esketamine nasal spray plus a newly initiated oral antidepressant provides a rapid and transformative effect on patients' lives compared with a newly initiated oral antidepressant plus placebo nasal spray with superior reduction in depressive symptoms as early as day 1 and at 4 weeks. Additionally, esketamine nasal spray plus a newly initiated oral antidepressant has superior response and remission rates at 4 weeks,	Thank you for your comment. The appraisal committee will consider the innovative aspects of esketamine during the appraisal. You are therefore encouraged to describe the innovative nature of esketamine in your evidence submission to NICE.

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		significantly reduces the risk of relapse for stable remitters and stable responders by more than half, and delays time to relapse compared to a newly initiated oral antidepressant plus placebo nasal spray. The available clinical data suggests that esketamine nasal spray results in a rapid onset of action and durable efficacy compared to currently widely used oral antidepressants. References Iadarola ND, Niciu MJ, Richards EM, Vande Voort JL, Ballard ED, Lundin NB, et al. Ketamine and other N-methyl-D-aspartate receptor antagonists in the treatment of depression: a perspective review. Ther Adv Chronic Dis. 2015;6(3):97-114. Massart R, Mongeau R, Lanfumey L. Beyond the monoaminergic hypothesis: neuroplasticity and epigenetic changes in a transgenic mouse model of depression. Philos Trans R Soc Lond B Biol Sci. 2012;367(1601):2485-94. Popova V DE, Trivedi M, Cooper K, Lane R, Lim P, Mazzucco C, Hough D, Thase ME, Shelton RC, Molero P, Vieta E, Bajbouj M, Manji H, Drevets WC, Singh JB. Randomized, Double-Blind Study of Flexibly-Dosed Intranasal Esketamine Plus Oral Antidepressant vs. Active Control in Treatment-Resistant Depression. ASCP2018. Ochs-Ross R DE, Lane R, Zhang Y, Lim P, Foster K, Hough D, Manji H, Drevets WC, Sanacora G, Adler C, McShane R, Gaillard R, Singh JB. Efficacy and safety of esketamine nasal spray plus an oral antidepressant in elderly patients with treatment-resistant depression. ASCP2018. Daly EJ TM, Janik A, Li H, Zhang Y, Li X, Lane R, Lim P, Duca AR, Hough D, Thase ME, Zajecka J, Winokur A, Divacka I, Fagiolini A, Cubala WJ, Bitter I, Blier P, Shelton RC, Molero P, Manji H, Drevets WC, Singh JB. A Randomized Withdrawal, Double-blind, Multicenter Study of Esketamine	

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		Nasal Spray Plus an Oral Antidepressant for Relapse Prevention in Treatment-resistant Depression. ASCP2018. Wajs E AL, Morrison R, Daly E, Lane E, Lim P, Holder R, Sanacora G, Young AH, Kasper S, Sulaiman AH, Li CT, Paik JW, Manji H, Hough D, Drevets W, Singh JB. Long-Term Safety of Esketamine Nasal Spray Plus Oral Antidepressant in Patients with Treatment-Resistant Depression: Phase 3, Open-Label, Safety and Efficacy Study (SUSTAIN-2). ASCP2018.	
Questions for consultation		Have all relevant comparators for esketamine been included in the scope? Yes. Please see response for “comparators” above. Janssen would like to highlight that the relevance of comparators depends on the positioning of esketamine nasal spray within the treatment pathway. Which treatments are considered to be established clinical practice in the NHS for treatment-resistant depression? Please see response for “comparators” above. In addition to that, Lamy et al. shows that in UK clinical practice, a switch to a new antidepressant therapy is used most frequently as a third and fourth step for patients who were treated for an adequate length at an appropriate dose but did not respond to two prior lines of antidepressant therapy. Reference FX. Lamy, J. Chollet, E. Clay, M. Brignone, B. Rive & D. Saragoussi (2015) Pharmacotherapeutic strategies for patients treated for depression in UK primary care: a database analysis, Current Medical Research and Opinion, 31:4, 795-807 Would esketamine be used as a monotherapy, or in combination with an oral antidepressant, as a part of combination therapy, for treatment-resistant depression?	Thank you for your comment. The treatment pathway for major depressive disorder was discussed at the scoping workshop. Clinical experts suggested that esketamine may be used at different points in the treatment pathway (and that use is likely to depend on the safety profile of the treatment). The comparators in the scope have been amended accordingly. The committee cannot make recommendations based on age because it is a protected

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		Please see response for “technology” above. Esketamine nasal spray must be co-administered with a newly initiated oral antidepressant. Would esketamine be used before other combination or augmentation therapies would be considered? Esketamine nasal spray would potentially be an option before or alongside combination or augmentation therapies. Therefore, it could be used before depending on the position in the treatment pathway or based on clinical judgement. Are the outcomes listed appropriate? Please see response for “outcomes” above. Are the subgroups suggested in ‘other considerations appropriate? Are there any other subgroups of people in whom esketamine is expected to be more clinically effective and cost effective or other groups that should be examined separately? Janssen would suggest considering elderly (≥65 yrs) as a separate subgroup in this appraisal since the clinical effectiveness of esketamine nasal spray may be different from younger adults (18-64 yrs). Where do you consider esketamine will fit into the existing NICE pathway, Depression? Please see response for “comparators” above. In addition, the marketing authorisation population will be TRD, which is defined as MDD in adults who have not responded to at least two different treatments with antidepressants in the current moderate to severe episode. The clinical studies are also conducted in this TRD population, which is similar to the third and subsequent step in the existing NICE MDD treatment pathway. Janssen would therefore suggest that esketamine nasal spray in combination with an oral antidepressant will fit best as subsequent step after the first two steps in the existing NICE MDD treatment pathway.	characteristic, unless the marketing authorisation specifies otherwise. Issues relating to geographic access cannot be addressed in a technology appraisal. The appraisal committee will consider whether there are any benefits of esketamine that are not adequately captured by the QALY estimate.

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		NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope: • could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which esketamine will be licensed; • could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology; • could have any adverse impact on people with a particular disability or disabilities. Please see response for “equality” above. Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts. We would suggest that clinical evidence in elderly (≥65 yrs) should be appraised. In addition to that, we would suggest that evidence on the capacities to manage the observation requirements in the different regions in England will be collected Do you consider esketamine to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a ‘step-change’ in the management of the condition)? Please see response for “innovation” above.	

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		Do you consider that the use of esketamine can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? Please see response for “outcomes” and “innovation” above. We would suggest considering 1) the impact on health-related quality of life of carers of patients of TRD, and 2) the (indirect) impact on productivity and daily functioning as outcomes since we expect that esketamine nasal spray will have a potential significant and substantial health-related benefit on these parameters. In addition to that, the benefit of the fast-acting nature of esketamine nasal spray may be not be adequately captured in the QALY calculation. Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits. We would propose to consider UK-specific data on the impact of TRD on 1) health-related quality of life of carers of patients of TRD, and 2) the (indirect) impact on productivity and daily functioning that is generated by observational trials. To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly. A potential barrier to adoption of esketamine nasal spray would be the required observation period by a healthcare professional (HCP) after self-administration at the site of care. Currently, it is expected that during and after each occasion of esketamine nasal spray self-administration, individuals should be observed by a HCP until they are ready to leave based on clinical judgement. This is to ensure that all adverse events (e.g. potential transient blood pressure increases) are monitored and perceptual/dissociative effects have resolved. In addition to that, after administration of esketamine nasal	

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		spray, patients should not engage in potentially hazardous activities, such as driving a motor vehicle or operating machinery until the next day following a restful sleep. Esketamine nasal spray will be a Prescription Only Medicine with Schedule 2 controlled drug status. We would like to discuss these topics with NICE for additional adoption support. Would it be appropriate to use the cost comparison methodology for this topic? We think that a cost comparison methodology is not appropriate for this topic since clinical data on esketamine nasal spray has shown a clear benefit in terms of health-related quality of life compared to an active comparator. Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators? Please see response for “technology” and “innovation” above. The available clinical data demonstrates that esketamine nasal spray is superior in its clinical efficacy and will require additional resource use compared to any of the comparators. Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant? The primary outcome that was measured in the short-term clinical trials: change in MADRS from baseline to 4 weeks, as well as the secondary outcomes: remission rate and response rate, which are used to drive the model, are still considered clinically relevant. In addition to that, the primary outcome that was measured in the long-term trial: delaying relapse of depressive symptoms, is also used to drive the model, and is still considered clinically relevant. Data from studies of different treatments on these	

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		outcomes also form the evidence for the NICE CG90 as well as the new (May 2018 draft) NICE Depression Clinical Guidelines. Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year? No, there is no new substantial evidence for the comparator technologies expected in the next year.	

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Department of Health and Social Care
Merck Sharp & Dohme Limited