National Institute for Health and Care Excellence

4-year surveillance (2017) – Neuropathic pain in adults: pharmacological management in non-specialist settings (2013) NICE guideline CG173

Appendix B: stakeholder consultation comments table

Consultation dates: 22 June to 5 July 2017

Do you agree with the proposal not to update the guideline?

Stakeholder	Overall response	Comments	NICE response
University Hospitals Birmingham	Yes	No comment	Thank you for your comment.
Sheffield Teaching Hospitals	Yes	No comment	Thank you for your comment.
Professional Standards Committee of FPM	Yes	No comment	Thank you for your comment.
British Pain Society	No	1.1.12 The guideline needs to include oxycodone and tapentadol to the list because they are promoted and often used for neuropathic pain The BPS has been contacted by the Cochrane Pain, Palliative and Supportive Care Review Group who are working on an overview of Cochrane reviews on pharmacological intervention for neuropathic pain. This is due to be published this summer (date TBC). They would be willing to share a pre-publication summary of this piece of work with the NICE guideline committee as they feel it is directly relevant to the guideline. Members have commented as follows: In view of the lack of useful medicines to treat Neuropathic pains the use of cannabinoids should be promoted as a safe medicine to be used outside of medical control. The last NICE reports on NP and on MS have condemned a large number of patients to ongoing and intractable pain.	Thank you for your comment. Oxycodone and tapentadol were not considered in CG173 recommendations and evidence on these drugs during this surveillance review is limited and judged insufficient to trigger an update at present. There was no convincing evidence that lidocaine plasters are effective for treating neuropathic pain. New evidence on cannabinoids was also judged insufficient to trigger an update of this topic. This area will be monitored by future surveillance reviews. Thank you for notifying us of the Cochrane Pain, Palliative and Supportive Care Review Group overview of Cochrane

		Having used cannabinoids in clinical practice and in research for over 20 years and also seen the increasing use of cannabinoids worldwide I feel that NICE have to start to consider the problem of NP and medications that are currently being used. Lidocaine plasters (Versatis) were left out, because of not enough studies. Perhaps that needs reconsidering, especially as it is used inappropriately and so often	reviews on pharmacological intervention for neuropathic pain. We will add this review to our event tracker and consider the evidence at the next surveillance point.
Royal College of Nursing	No	1.1.12 Need to add oxycodone and tapentadol to the list	Thank you for your comment. Oxycodone and tapentadol were not considered in CG173 recommendations and evidence identified during the surveillance review is limited and judged as insufficient to trigger an update. This area will be monitored by future surveillance reviews.
Cochrane Pain Palliative and Supportive Care Review Group	No	We are developing an overview of Cochrane reviews on interventions for neuropathic pain. We copy below an extract from this pre-publication draft, which is confidential. On request, we are happy to share the draft document in full, and/or additional information such as references. This overview captures the latest evidence from Cochrane reviews in this area and may inform changes to the NICE guideline. This overview will be submitted this summer (2017), with publication expected before the end of the year. **Overview review: assessment of Cochrane reviews of neuropathic pain treatments** **Methods (Removed due to confidentiality)**	Thank you for notifying us of the Cochrane Pain, Palliative and Supportive Care Review Group on an overview of Cochrane reviews on pharmacological intervention for neuropathic pain. We will add this review to our event tracker and consider the evidence at the next surveillance point.

Do you agree with the proposal to put the guideline on the static list?

Stakeholder	**Overall response**	**Comments**	**NICE response**

University Hospitals Birmingham	Yes	No comment	Thank you for your comment. However, following consideration of all comments received during consultation, we will not place the guideline on the static list.
Sheffield Teaching Hospitals	Yes	No comment	Thank you for your comment. However, following consideration of all comments received during consultation, we will not place the guideline on the static list.
Professional Standards Committee of FPM	No answer	No comment	
British Pain Society	No	No comment	Thank you for your comment. Following consideration of all comments received during consultation, we will not place the guideline on the static list.
Royal College of Nursing	No	No comment	Thank you for your comment. Following consideration of all comments received during consultation, we will not place the guideline on the static list.
Cochrane Pain Palliative and Supportive Care Review Group	No answer	There is no compelling new evidence for any intervention, and the bulk of the evidence is for duloxetine, gabapentin, and pregabalin for effective therapies, and lamotrigine for an ineffective therapy. What is new is the recognition that there is no good evidence for opioids, and it may be that the current guidance should be written with a clearer steer on opioids before being put on the static list. It is less about what to use, and more about what to avoid. What the guideline cannot do at the moment is to recommend a pathway though the drugs to provide the largest degree of benefit to most people in the shortest time. It needs new research to provide evidence to help make these decisions.	Thank you for your comment. Following consideration of all comments received during consultation, we will not place the guideline on the static list. Your feedback will be logged for consideration at the next surveillance point.

Do you agree with the proposal to remove the research recommendation:

RR–02 Is response to pharmacological treatment predicted more reliably by underlying aetiology or by symptom characteristics?

Stakeholder	Overall response	Comments	NICE response
University Hospitals Birmingham	Yes	No comment	Thank you for your comment. However, upon identification of new evidence we will retain the research

			recommendation at this time and review it again at the next surveillance of the guideline.
Sheffield Teaching Hospitals	No	There have been a number of papers showing that certain pain phenotypes may respond to certain treatments. I think this area of research is exciting and is pointing a mechanism based treatment – tailored treatment for individual patients – which is promising: I have attached recent papers that may be useful: Demant DT, Lund K, Vollert J, Maier C, Segerdahl M, Finnerup NB, Jensen TS, Sindrup SH. The effect of oxcarbazepine in peripheral neuropathic pain depends on pain phenotype: a randomised, double-blind, placebo-controlled phenotype-stratified study. Pain. 2014 Nov;155(11):2263-73. Bouhassira D et al. Neuropathic pain phenotyping as a predictor of treatment response inpainful diabetic neuropathy: data from the randomized, double-blind, COMBO-DN study. Pain. 2014 Oct;155(10):2171-9. Marchettini P et al. Are there different predictors of analgesic response between antidepressants and anticonvulsants in painful diabetic neuropathy? Eur J Pain. 2016 Mar;20(3):472-82. Jensen TS, Finnerup NB. Allodynia and hyperalgesia in neuropathic pain: clinical manifestations and mechanisms. Lancet Neurol. 2014 Sep;13(9):924-35. Attal N, Bouhassira D, Baron R, Dostrovsky J, Dworkin RH, Finnerup N, Gourlay G, Haanpaa Assessing symptom profiles in neuropathic pain clinical trials: can it improve outcome? Attal N, de Andrade DC, Adam F, Ranoux D, Teixeira MJ, Galhardoni R, Raicher I, Üçeyler N, Sommer C, Bouhassira D. Safety and efficacy of repeated injections of botulinum toxin A in peripheral neuropathic pain (BOTNEP): a randomised, double-blind, placebo-controlled trial. Safety and efficacy of repeated injections of botulinum toxin A in peripheral neuropathic pain (BOTNEP): a randomised, double-blind, placebo-controlled trial. Katz NP, Mou J, Paillard FC, Turnbull B, Trudeau J, Stoker M. Predictors of Response in Patients with Post-herpetic Neuralgia and HIV-associated Neuropathy Treated with the 8% Capsaicin Patch (Qutenza(R)). Clin J Pain 2015; Oct;31(10):859-66 Mainka T, Malewicz NM, Baron R, Enax-Krumova EK, Treede RD, Maier C. Presence of hyperalgesia predicts analgesic efficacy of topically applied capsaicin 8% in patients with peripheral neuropathic pain. Eur J Pain 2015.	Thank you for your comment. Upon identification of new evidence we will retain the research recommendation at this time and review it again at the next surveillance of the guideline. Thank you for these references which have been checked in order to be added to the summary of evidence. One reference is already included in the summary of evidence and the rest do not meet either the inclusion criteria specified in the original review protocol or are out of the surveillance search period (31 July 2012 to 24 January 2017). Any references before July 2012 would have been identified in the original guideline published November 2013.

		Gustorff, B., Poole, C., Kloimstein, H., Hacker, N., and Likar, R. Treatment of neuropathic pain with the capsaicin 8% patch: using quantitative sensory testing to investigate predictors of response to treatment. Scand J Pain. 2013; 4: 138–145 Simpson DM, Schifitto G, Clifford DB, Murphy TK, Durso-De Cruz E, Glue P, Whalen E, Emir B, Scott GN, Freeman R; 1066 HIV Neuropathy Study Group. Pregabalin for painful HIV neuropathy: a randomized, double-blind, placebo-controlled trial. Neurology 2010; 74(5):413-420. Yarnitsky D, Granot M, Nahman-Averbuch H, Khamaisi M, Granovsky Y. Conditioned pain modulation predicts duloxetine efficacy in painful diabetic neuropathy. Pain 2012; 153(6):1193-1198.	
Professional Standards Committee of FPM	No answer	No comment	
British Pain Society	Yes	No comment	Thank you for your comment. However, upon identification of new evidence we will retain the research recommendation at this time and review it again at the next surveillance of the guideline.
Royal College of Nursing	Yes	No comment	Thank you for your comment. However, upon identification of new evidence we will retain the research recommendation at this time and review it again at the next surveillance of the guideline.
Cochrane Pain Palliative and Supportive Care Review Group	Yes	Yes. While there is some evidence that some methods may have use in research terms, even the researchers do not currently consider this to be valuable (yet) for treatment decisions based on sensory phenotypes (see Pain. 2016 Aug;157(8):1810-8).	Thank you for your comment. However, upon identification of new evidence we will retain the research recommendation at this time and review it again at the next surveillance of the guideline.

Do you agree with the proposal to remove the research recommendation:

RR–04 What are the key factors, including additional care and support that influence participation and quality of life in people with neuropathic pain?

Stakeholder	Overall response	Comments	NICE response

University Hospitals Birmingham	Yes	No comment	Thank you for your comment. However, upon identification of new evidence we will retain the research recommendation at this time and review it again at the next surveillance of the guideline.
Sheffield Teaching Hospitals	Yes	No comment	Thank you for your comment. However, upon identification of new evidence we will retain the research recommendation at this time and review it again at the next surveillance of the guideline.
Professional Standards Committee of FPM	No answer	No comment	
British Pain Society	Yes	No comment	Thank you for your comment. However, upon identification of new evidence we will retain the research recommendation at this time and review it again at the next surveillance of the guideline.
Royal College of Nursing	Yes	No comment	Thank you for your comment. However, upon identification of new evidence we will retain the research recommendation at this time and review it again at the next surveillance of the guideline.
Cochrane Pain Palliative and Supportive Care Review Group	No	No. This a very important topic because of the link between pain reduction and improvement of quality of life in pain generally (**Pain** Pract. 2014 Jan;14(1):79-94), and neuropathic pain in particular (Pain. 2010 May;149(2):194-201). As large and prompt pain reduction is what people with pain want (Anaesthesia. 2013 Apr;68(4):400-12), the link between a patient-oriented outcome, quality of life, and work (Pain Pract. 2012 Sep;12(7):578-89) is of prime interest. It deserves more emphasis, and not be allowed to drop.	Thank you for your comment. Upon identification of new evidence we will retain the research recommendation at this time and review it again at the next surveillance of the guideline. Thank you for these references which have been checked in order to be added to the summary of evidence. The identified studies do not meet either the inclusion criteria specified in the original review protocol or are out of the surveillance search period (31 July 2012 to 24 January 2017). Any references before July 2012 would have been identified in the original guideline published November 2013.

Do you agree with the proposal to remove the research recommendation:

RR–05 What is the impact of drug-related adverse effects on health economics and quality of life in neuropathic pain?

Stakeholder	Overall response	Comments	NICE response
University Hospitals Birmingham	Yes	No comment	Thank you for your comment.
Sheffield Teaching Hospitals	Yes	No comment	Thank you for your comment.
Professional Standards Committee of FPM	No	We would suggest the recommendation remains as it continues to be a valid question even if no current research is under way.	Thank you for your comment. We proposed to remove the research recommendation from the NICE version of the guideline and the NICE database for research recommendations. The research recommendations will remain in the full versions of the guideline. See NICE's research recommendations process and methods guide 2015 for more information. As no new evidence relevant to the research recommendation was found and no ongoing studies were identified in this area we proposed to remove the recommendation.
British Pain Society	Uncertain	No comment	Thank you for your comment. As no new evidence relevant to the research recommendation was found and no ongoing studies were identified in this area we proposed to remove the recommendation.
Royal College of Nursing	Yes	No comment	Thank you for your comment.

Cochrane Pain Palliative and Supportive Care Review Group	No answer	There is good evidence that improved pain results in better quality of life, reduces healthcare costs and keeps people in work or allows them to look after families (**Pain** Pract. 2014 Jan;14(1):79-94; Pain Pract. 2012 Sep;12(7):578-89). However, more and more direct evidence is likely to be important, and it is possible to consider new research – or reevaluation of older research – that might help address these questions.	Thank you for your comment. We proposed to remove the research recommendation from the NICE version of the guideline and the NICE database for research recommendations. The research recommendations will remain in the full versions of the guideline. See NICE's research recommendations process and methods guide 2015 for more information. As no new evidence relevant to the research recommendation was found and no ongoing studies were identified in this area we proposed to remove the recommendation. Thank you for these references which have been checked. The identified studies are not related to the impact of drug-related adverse effects on health economics and quality of life in neuropathic pain.

Do you agree with the proposal to remove the research recommendation:

RR–06 Is there a potential for dependence associated with pharmacological agents for neuropathic pain?

Stakeholder	**Overall response**	**Comments**	**NICE response**
University Hospitals Birmingham	Yes	No comment	Thank you for your comment.
Sheffield Teaching Hospitals	Yes	No comment	Thank you for your comment.
Professional Standards Committee of FPM	No	Again, we would suggest the recommendation remains as it continues to be a valid question. There is strong anecdotal evidence of dependence and more formal research should be encouraged.	Thank you for your comment. We proposed to remove the research recommendation from the NICE version of the guideline and the NICE database for research recommendations. The research recommendations will remain in the full versions of the guideline. See NICE's research recommendations process and methods guide 2015 for more information.

			As no new evidence relevant to the research recommendation was found and no ongoing studies were identified in this area we proposed to remove the recommendation.
British Pain Society	No	Gabapentinoids are drugs of misuse and abuse, In clinical practice prescriptions are often diverted and patients with a substance use disorder describe how they tend to take 'handfuls' rather than small amounts especially pregabalin. With respect to dependence, pregabalin's anxiolytic effects make it a candidate for initial tolerance and potentially dependence. PHE and NHS England have published guidance for prescribers. It is relatively easy to buy online in the UK https://www.ukmeds.co.uk/treatments/neuropathic-pain/pregabalin-capsules/ and the US https://online-pharmacy-one.org/anti-convulsant/lyrica/	Thank you for your comment. Concerns also raised on the risk of addiction in 'Advice for prescribers on the risk of the misuse of pregabalin and gabapentin' published by Public Health England. However we have not found any evidence specifically to the patients with the neuropathic pain in the literature supporting this. As no new evidence relevant to the research recommendation was found and no ongoing studies were identified in this area we proposed to remove the recommendation.
Royal College of Nursing	No	Gabapentinoids are drugs of misuse and abuse, In clinical practice prescriptions are often diverted and patients with a substance use disorder describe how they tend to take 'handfuls' rather than small amounts especially pregabalin. With respect to dependence, pregabalin's anxiolytic effects make it a candidate for initial tolerance and potentially dependence. PHE and NHS England have published guidance for prescribers. It is relatively easy to buy online in the UK https://www.ukmeds.co.uk/treatments/neuropathic-pain/pregabalin-capsules/ and the US https://online-pharmacy-one.org/anti-convulsant/lyrica/	Thank you for your comment. Concerns also raised on the risk of addiction in 'Advice for prescribers on the risk of the misuse of pregabalin and gabapentin' published by Public Health England. However we have not found any evidence specifically to the patients with the neuropathic pain in the literature supporting this. As no new evidence relevant to the research recommendation was found and no ongoing studies were identified in this area we proposed to remove the recommendation.

Cochrane Pain Palliative and Supportive Care Review Group	Yes	Yes. This is largely known for the gabapentinoids. There have been two recent systematic reviews on the topic (Drugs. 2017 Mar;77(4):403-426; Pharmacopsychiatry. 2016 Jul;49(4):155-61).	Thank you for these references which have been checked. The populations in these studies are not exclusive to patients with neuropathic pain.

Do you have any comments on areas excluded from the scope of the guideline?

Stakeholder	Overall response	Comments	NICE response
University Hospitals Birmingham	Yes	The paragraph heading 1.1.12 "Treatments that are not recommended" should be modified to "Treatments which may be indicated following review in a specialist setting". NICE guidance is very good at the mixed message. To most readers this paragraph is what it says it is (treatments not recommended for initiationin primary care but which may be indicated following specialist review); however, commissioning bodies only ever get as far as "Treatments which are not indicated" which is unhelpful for selected patients as these specialist treatments are no longer commissioned on the basis of a guideline which is aimed at primary care	Thank you for your comment. Assessment of neuropathic pain in a specialist setting is not within the scope of this guideline, however, recommendation1.1.12 states that certain treatments can be started in non-specialist settings if advised by a specialist to do so.
Sheffield Teaching Hospitals	No	No comment	Thank you for your comment.
Professional Standards Committee of FPM	No answer	No comment	
British Pain Society	No	No comment	Thank you for your comment.
Royal College of Nursing	No	No comment	Thank you for your comment.
Cochrane Pain Palliative and Supportive Care Review Group	No	No comment	Thank you for your comment.

Do you have any comments on equalities issues?

Stakeholder	Overall response	Comments	NICE response
University Hospitals Birmingham	No	No comment	Thank you for your comment.
Sheffield Teaching Hospitals	No	No comment	Thank you for your comment.
Professional Standards Committee of FPM	No answer	No comment	
British Pain Society	No	No comment	Thank you for your comment.
Royal College of Nursing	No	No comment	Thank you for your comment.
Cochrane Pain Palliative and Supportive Care Review Group	Yes	There is anecdotal evidence that the guidelines are not applied, and that interventions with known efficacy are not available in some localities because of perceived cost. That raises issues of equity, and it is perhaps surprising that it has not yet arisen.	Thank you for your comment. Provision and commissioning of services delivery and implementation were outside the original scope of the guideline which focused on the pharmacological management of neuropathic pain.