NICE National Institute for Health and Care Excellence

Appendix A: Stakeholder consultation comments table

2019 surveillance of Drug misuse in over 16s: opioid detoxification (2007)

Consultation dates: 7 to 20 November 2018

Do you agree with the proposal to not to update the guideline?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Turning Point	Yes	The only point queried was the idea that lofexidine will be 'available again soon'. Whilst this doesn't affect the guidance, we don't think it is accurate.	Thank you for your comments. Topic experts were not aware of the date of future availability of lofexidine or what its cost will be, but it is expected to become available again. The consultation document reflected this feedback, and did not stipulate a timeframe for availability. Experts highlighted a lack of research and innovation in this area, and that the related research recommendation remains ongoing. There is unlikely to be any impact on recommendation 1.3.1.2 regarding lofexidine.

Public Health England	Yes	We would agree that, within its current scope, there is at present insufficient evidence on which to base an update to CG52. However, we would suggest that there is a need for NICE to consider a shorter-than-usual timetable for a further review and to look more broadly at drug misuse treatment than allowed for by this limited scope. It will only be acceptable not to update CG52 if there is other work in this area. Specifically, as we have discussed with NICE, in the context of constrained finance and local authorities reviewing the levels of drug misuse care they provide there is, or will be, a need for guidance in two areas of drug misuse treatment: 1. Injectable and depot formulations of buprenorphine. While these may rightly be the subject of technical appraisals (TAs) as they appear on the market, in the context of squeezed local authority funding, they have the potential to destabilise treatment systems and/or radically alter the nature of drug treatment delivery. A TA is important if it is the vehicle for cost-benefit analysis but a TA that recommended the use of expensive medicines could cause severe financial problems for a small system, with a severely-limited formulary, that is not protected by the NHS's size or its ability to save money in other areas of prescribing. There is also a risk that depot formulations will lead to disinvestment in the psychosocial components of drug treatment, because patients will not need to be seen as regularly in relation to pharmacological interventions. TAs would also not go far enough in considering the wider	Thank you for your comments. Broader management of drug misuse Although no new evidence impacts on the current guideline recommendations, we recognise a need to clarify the broader care pathway for the management of drug misuse. We are therefore engaging with system partners with the aim of developing NICE guidance that is comprehensive and accessible. Lofexidine Topic experts were not aware of the date of future availability of lofexidine or what its cost will be, but it is expected to become available again. There is unlikely to be any immediate impact on recommendation 1.3.1.2, since the licensing status and effectiveness of lofexidine as a treatment in detoxification remains unchanged. Safety of Methadone The study by Pierce et al. is included in the consultation document (reference 18). This evidence is relevant to recommendation 1.3.1.1 for suitability of methadone and recommendation 1.2.2.3 on special considerations for people who are opioid dependent and have comorbid health problems. Cross reference to the updated Department of Health and Social Care's Drug misuse and dependence: UK guidelines on clinical management misuse and dependence from NICE guideline CG52 will ensure alignment with national advice relating to older people who are dependent on opioids.

		ramifications for drug misuse treatment of injectable and depot formulations: a. Either freeing up clinician time from weekly/fortnightly prescription debates with patients, and patient time from frequent medicine pick-ups, to allow more creative, psychological and recovery-focused interventions. b. Or, again in the context of a financially-squeezed system, facilitating a retreat of treatment into pharmacological-only, with infrequent clinician-patient interactions, to save money. 2. Broader aspects of treatment not currently covered by NICE guidance. Specifically, while there are clinical guidelines for opioid detoxification and for psychosocial interventions, there is only a TA for the medicines used in opioid maintenance therapy – there is no NICE clinical guidance in this area and in the broader recovery interventions that, since 2007, have come to form a central part of the treatment offer. The severe impact of the increased buprenorphine price since April demonstrates the lack of resilience in the drug treatment system. The surveillance review refers repeatedly to an impact on TA114 but doesn't say what should be done about this.	### Department of Health guidance The proposed amendment to the reference to the updated Department of Health and Social Care's Drug misuse and dependence: UK guidelines on clinical management misuse and dependence will use the title from the recommended citation: Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group (2017) Drug misuse and dependence: UK guidelines on clinical management. London: Department of Health ### National Treatment Agency for Substance Misuse We will change the proposal to direct to the suggested link to Alcohol and drug misuse prevention and treatment guidance page, in place of the National Treatment Agency for Substance Misuse.

		There should perhaps be a clear proposal to review and update TA114. A few other comments on the surveillance review content: • Lofexidine may not come back on to the UK market at all and this will limit the detoxification options available to clinicians. • There is no reference to Pierce et al (2018)*, only to Marteau (ref 19). Pierce's findings more robustly suggest additional risks associated with methadone, especially as those on opioid substitution treatment get older. However, there is also further evidence of methadone's broader protective effect in Hickman et al (2018)**. This is one thing that should be considered further, perhaps in an update to TA114. • The references to the Orange Book confuse the author and title. They should be: Title: Drug misuse and dependence: UK guidelines on clinical management. Author: Clinical Guidelines on Drug Misuse and Dependence Update 2017 Independent Expert Working Group (2017).	

		• The logical successor to the National Treatment Agency for Substance Misuse weblink is to Public Health England's collection: https://www.gov.uk/government/collections/alcohol-and-drug-misuse-prevention-and-treatment-guidance, not the much broader GOV.UK drug misuse and dependence page. *Pierce, M., Millar, T., Robertson, J. R., & Bird, S. M. (2018). Ageing opioid users' increased risk of methadone-specific death in the UK. The International journal on drug policy, 55, 121-127. ** Hickman M1, Steer C1, Tilling K1, Lim AG1, Marsden J2, Millar T3, Strang J2, Telfer M4, Vickerman P1, Macleod J1. The impact of buprenorphine and methadone on mortality: a primary care cohort study in the United Kingdom. Addiction. 2018 Aug;113(8):1461-1476	
Napp Pharmaceuticals Limited	No	No comments provided	Thank you.
British Association for Psychopharmacology	No	**Introduction** – last paragraph: i) Change reference to Department of Health publication "Drug misuse and dependence: UK guidelines on clinical management" to 2017 update	Thank you for your comments. NICE Guideline introduction Amendments are proposed to update the reference to the updated (2017) Department of Health and Social Care's Drug misuse and dependence: UK guidelines on clinical management misuse and dependence, and to replace the reference to the National Treatment

		ii) National Treatment Agency for Substance Misuse (NTA) has closed, since becoming part of Public Health England in 2013. The reference for more information should be to Public Health England. **1.1 General Considerations** 1.1.1.6– this point needs updating regarding current support groups. **1.3 Pharmacological interventions** 1.3.1.2 Lofexidine – the guidance is still current and appropriate, but lofexidine is not currently available in the UK. I am not sure what position NICE is expected to take in this situation. **1.5.1 Contingency management** This section is not within the main remit of BAP as it concerns psychosocial elements of the detoxification process. However it is likely this section will need review in relation to more recent contingency management research and practice. Section 1.5.1.2 is potentially misleading in suggesting take-home methadone doses as a suitable incentive as this is in a point concerned with contingency management "during and after detoxification". The point has been made earlier in 1.3.2 that detoxification "should not be confused with … gradual dose reduction". The rationale for take-home methadone doses within a	Agency for Substance Misuse. Please refer to the editorial amendments section of the surveillance report for further details. ### 1.1 General Considerations The surveillance review did not identify any evidence or intelligence about new support groups to indicate a change is needed to recommendation 1.1.1.6 and therefore no impact is anticipated. ### 1.3 Pharmacological interventions Topic experts were not aware of the date of future availability of lofexidine or what its cost will be, but it is expected to become available again. The consultation document reflected this feedback, and no immediate impact is anticipated on the guideline. ### 1.5.1 Contingency management Section 1.5 of NICE guideline CG52 cross refers to NICE's guideline on drug misuse in over 16s: psychosocial interventions for contingency management in more detail, in addition to other components of psychosocial interventions. Both guidelines are also covered in the NICE Pathway on drug misuse. The guideline on drug misuse in over 16s: psychosocial interventions was reviewed in 2016 and no new evidence was found that affected the recommendations in the guideline. As mentioned above, NICE guideline CG52 will also link to the updated version of the Department of Health and Social Care guidance on drug misuse and dependence, thereby aligning with current national guidance on psychosocial interventions, including contingency management.

		detoxification process needs explanation. This section also makes reference to an NTA programme, so this needs updating. Length of detoxification should also be considered in light of evidence published after guidance - Nosyk et al. (2012) Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: Results from a population-based retrospective cohort study, Addiction, 107 (9); 1621 – 1629. This Canadian study of methadone treatment episodes suggested tapers of greater than 12 weeks were more likely to be successful	Section 1.5.1.2 is consistent with the Department of Health and Social Care guidance on drug misuse and dependence section 3.6.1 Psychosocial interventions in management of OST prescribing: A range of psychosocial interventions can be used alongside OST. Initially, core elements that support safe prescribing identify service user objectives, encourage engagement, develop the therapeutic alliance and provide motivational support. The evidence base on rewards and contingency management (CM) supports linking stabilisation on medication to positive feedback, and using encouragement and acknowledgement of incremental progress to reinforce improvements. Rewards, rather than punitive responses, are appropriate, although it is important to explain the constraints of safe prescribing and what evidence of progress will be needed to enable changes to be made to prescribing arrangements. As individuals demonstrate progress, arrangements for supervision of consumption, prescribing regimens and the availability of take-home doses can all be adjusted to incentivise and support recovery. A clear and consistent approach should be used for this to be effective so that the individual is clear about how their behaviour will affect their progress in treatment. An editorial amendment will be proposed to replace the reference to the NTA programme in recommendation 1.5.2.2, with a reference to the phased approach set out in Department of Health and Social Care guidance on drug misuse and dependence section 3.7.

			### Length of detoxification Tapering of methadone maintenance treatment is covered by NICE technology appraisal Methadone and buprenorphine for the management of opioid dependence and new evidence, including the submitted study, will be considered in the review process for this guidance. Although methadone maintenance treatment is outside the remit of NICE guideline CG52, we recognise a need to clarify the broader care pathway for the management of drug misuse. We are therefore engaging with system partners with the aim of developing NICE guidance that is comprehensive and accessible.
Indivior UK Ltd	Yes	1. Indivior agrees with the decision of not updating CG52. 2. Indivior conclusively agrees with NICE's decision to not assess the benefits of RBP-6000 through an update of CG52. The NICE surveillance report states, at page 4, that this is because a separate NICE programme (NICE medicines and technology appraisal team) is reviewing evidence on "the benefits of the depot route for buprenorphine", with expected publication in January 2019.	Thank you for your comments. ### Broader management of drug misuse The evidence summary being produced by the NICE medicines team on depot buprenorphine, including RBP-6000, will not be reviewed regularly because it does not constitute NICE guidance that would be subject to a review cycle. However, we recognise a need to clarify the broader care pathway for the management of drug misuse. We are therefore engaging with system partners with the aim of developing NICE guidance that is comprehensive and accessible. NICE will be holding a workshop in the near future to discuss the development of this guidance, and how to integrate the guideline, technology appraisals TA114 and TA115, and the evidence summary, which is due to be published in early 2019. Maintenance treatment, including evidence for RBP-6000, will be considered in this process.

		The NICE surveillance report should make it clear that what is expected to be published in January 2019 is an evidence summary for a new medicine. Indivior suggests that the evidence summary should be regularly reviewed by NICE in order to reflect the evolving evidence base for RBP-6000 that will include critical phase 3 studies. Most importantly, Indivior believes that CG52, with its main focus on detoxification, is not the correct perspective to review the range of benefits (for patients, the NHS and PSS and society at large) of RBP-6000 as an opioid-agonistic therapy in the maintenance treatment of patients with OUD (opioid use disorder). Indeed, pharmacological interventions are only assessed in the context of a detoxification goal within CG52, as reported in the "Notes on the scope of the guidance" section of CG52, page 22, where it is also stated that CG52 does not address pharmacological maintenance programmes for OUD. On the other hand, as recognised in TA114 (on "Methadone and buprenorphine for the management of opioid dependence"), maintenance treatments aim to provide stability to patients, by reducing craving and preventing withdrawal, eliminating the hazards of injecting and freeing the person from preoccupation with obtaining illicit opioids, and to enhance overall function.	

		3) The NICE Quality Standards 23 notes that: “Opioid misuse is often characterised as a chronic condition with periods of remission and relapse. Although abstinence may be one of the long-term goals of treatment, it is not always achieved.” Detoxification is a treatment option which is suitable for a specific cohort of patients but before deciding on a patient’s suitability for detoxification a full assessment should be conducted.	
Change Grow Live	No	1) The guidance document is over 10 years old and the field has changed considerably during this time. It needs updating in accordance with changes. 2) The guidance document needs to be updated in line with the Drug Misuse and Dependence : UK Guidelines on Clinical management published in 2017 (Orange Guidelines 2017). 3) Greater emphasis is required on assessing the impact of drug misuse, safety profile of medications used in the treatment of drug misuse when there are children and young persons in the family (1.2.1.1) 4) Lofexidine is listed as a medication option for pharmacological interventions in detoxification. This	Currency of the guideline The surveillance review did not identify any evidence or intelligence to indicate a change is needed to any of the guideline recommendations and therefore no impact is anticipated. However, we recognise a need to clarify the broader care pathway for the management of drug misuse. We are therefore engaging with system partners with the aim of developing NICE guidance that is comprehensive and accessible. NICE will be holding a workshop in the near future to discuss the development of this guidance, and how to integrate the guideline, technology appraisals TA114 and TA115, and the evidence summary being produced by the NICE medicines team on depot buprenorphine.

		medication is not available in the UK since early 2018 and it is not certain when it will return to the market.(1.3.1.2) Clonidine is being re-considered in the absence of Lofexidine and guidance is required on this.(1.3.1.3) 5) Adjunctive medications are being used more routinely and this needs to be reflected in the guidelines.(1.3.4.1) 6) There is no mention of Take Home Naloxone and Overdose Prevention & Management training during detoxification and post-detoxification. 7) Medications that assist with relapse prevention are not mentioned in Continued treatment and support after detoxification (1.4.2) Guidance on Naltrexone implants and whether this would be of benefit in certain treatment cohorts should be included. 8) 1.2.3 needs to include misuse of Novel Psychoactive Substances, Pregabalin and Gabapentin misuse which are presenting concerns in service users accessing treatment. 9) The role of contingency management as a psycho social intervention is detailed in the guidance document (1.5.1). However the role of efficacy of other psycho social interventions which support detoxification and relapse prevention should be detailed in the guidance. 10) It would be useful if more specific guidance could be given on the duration of a 'short' prison sentence or period in remand to minimize confusion and varying	The proposed editorial amendment to cross refer to the updated Department of Health and Social Care's Drug misuse and dependence: UK guidelines on clinical management misuse and dependence will also ensure alignment with current national guidance. This will include guidance on the areas highlighted as gaps in the guideline: • take home naloxone • overdose prevention and management training • novel psychoactive substances • adjunctive medications • relapse prevention medications. **Impact of drug misuse on child family members** The surveillance review did not identify any evidence or intelligence to indicate a change is needed to recommendation 1.2.1.1 and, in the absence of any submitted evidence, no impact is anticipated. **Lofexidine** Topic experts were not aware of the date of future availability of lofexidine or what its cost will be, but it is expected to become available again. There is unlikely to be any immediate impact on recommendation 1.3.1.2, since the licensing status and effectiveness of lofexidine as a treatment in detoxification remains unchanged. The surveillance review did not identify any evidence or intelligence to indicate a change is needed to recommendation 1.3.1.3 advising against the routine use of clonidine. This is also consistent with the above mentioned updated Department of Health and Social Care guidance in this area.

		interpretation by organizations making it dififcult to provide consistent care in custodial sentences (Section 1.2.2.1)	### Adjunctive and relapse prevention medications The surveillance review did not identify any evidence or intelligence to indicate a change is needed to recommendations 1.3.4.1 or 1.4.2 and, in the absence of any submitted evidence, no impact is anticipated. The proposed cross reference to the updated Department of Health and Social Care guidance will ensure alignment with current national guidance in these areas (see above). ### Psychosocial interventions Section 1.5 of NICE guideline CG52 cross refers to NICE's guideline on drug misuse in over 16s: psychosocial interventions for contingency management in more detail, in addition to other components of psychosocial interventions. Both guidelines are also covered in the NICE Pathway on drug misuse. The guideline on drug misuse in over 16s: psychosocial interventions was reviewed in 2016 and no new evidence was found that affected the recommendations in the guideline. Further evidence will be considered at the next review point for both guidelines. The proposed cross reference to the updated Department of Health and Social Care guidance will ensure alignment with current national guidance in these areas (see above). ### Duration of custodial sentences The surveillance review did not identify any evidence or intelligence to indicate a change is needed to recommendations 1.2.2.1 and, in the absence of any submitted evidence, no impact is anticipated. The proposed cross reference to the updated Department of Health and Social Care guidance (see above) will ensure alignment with current national guidance in the area of drug misuse management in

			police custody and prison environments, over both short and long-term durations.
RCN		The RCN have no comments to submit at this stage	Thank you.

Do you have any comments on areas excluded from the scope of the guideline?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Turning Point	No	No comments provided	Thank you.
Public Health England	Yes	See above	Thank you for your comments. Responses are included with the earlier comments.
Napp Pharmaceuticals Limited	Yes	The availability of Take Home Naloxone (THN) offers users, carers and emergency services an easily accessible rescue therapy. We believe that NICE should include THN in this guideline. We suggest that it would be appropriate for NICE to suggest that THN should be offered to all users when collecting detoxification medicines and / or at needle exchange centres. There is also an opportunity to provide THN to people who may have misused opioids while in prison.	Thank you for your comments. It is proposed that the guideline should cross refer to the Department of Health and Social Care's Drug misuse and dependence: UK guidelines on clinical management misuse and dependence which will align with current national advice in the area of take home naloxone.

		We suggest that THN can play a part in reducing deaths from poisoning by opioids and that it would be appropriate for NICE to include THN in all reviews and updates of its guidance and guidelines relating to substance misuse and dependency where appropriate.	
British Association for Psychopharmacology	Not answered	No comments provided	Thank you.
Indivior UK Ltd	No	No comments provided	Thank you.
Change Grow Live	No	No comments provided	Thank you.
RCN	Not answered	No comments provided	Thank you.

Do you have any comments on equalities issues?

Stakeholder	Overall response	Comments	NICE response
Turning Point	No	No comments provided	Thank you.
Public Health England	No	No comments provided	Thank you.
Napp Pharmaceuticals Limited	No	N/A	Thank you.
British Association for Psychopharmacology	Not answered	No comments provided	Thank you.

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

Indivior UK Ltd	No	No comments provided	Thank you.
Change Grow Live	YES	Issues that impact on a equality assessment including ethnicity, language, gender identity, sexual orientation, visual impairment, learning disability are not mentioned.	The surveillance review did not identify any evidence or intelligence to indicate inequalities in the highlighted areas and, in the absence of any submitted evidence, no impact is anticipated.
RCN	Not answered	No comments provided	Thank you.