To: Paul Chrisp - Director, Centre for Guidelines, National Institute for Health and Care Excellence (NICE) **25.3.2021**

Dear Paul,

I hope you and yours are safe and well.

In this open letter, the International Institute for Psychiatric Drug Withdrawal, requests, for the second time, that NICE reverse its decision to exclude antipsychotic medications from the scope of the guidelines currently being written for 'Medicines Associated with Dependence or Withdrawal Symptoms: Safe Prescribing and Withdrawal Management for Adults'.

Our ten reasons are:

1. The first scientific paper[1] describing how patients can safely come off antipsychotic medication while minimising the risk of withdrawal effects, and risk of relapse, has just been published, this week.

   Professor David Taylor, the study's senior author and Professor of Psychopharmacology at King's College London, has said: '*Antipsychotics induce long-lasting changes to nerve cells in the brain and they need to be withdrawn very slowly (and in a particular way) to allow time for the brain to re-set*.' [2]

   Co-author, Professor Sir Robin Murray, Professor of Psychiatric Research at the Institute of Psychiatry, Psychology and Neuroscience, has commented: '*Patients suddenly stop the medication by themselves with the result that they relapse. Much better that psychiatrists become expert in when and how to advise their patients to slowly reduce their antipsychotic*.' [2]

   If such esteemed psychiatrists recognise the urgent need for guidance, we believe that NICE should adjust its stance accordingly, in the interest of public safety.

2. Other research published since your original decision has revealed the true extent of the problem. The first systematic review and meta-analysis on the occurrence of withdrawal symptoms after antipsychotic discontinuation has found that 'A weighted average of 53% individuals showed withdrawal symptoms after abrupt antipsychotic discontinuation and placebo substitution'.[3]

   A survey of antipsychotic users (the largest to date - 832 from 30 countries) has found that 65% reported withdrawal effects when trying to stop, and that 51% of these described their withdrawal effects as 'severe'.[4] Participants' comments included: *"Withdrawal from the anti-psychotic was torturous and took a very long time" "Withdrawal symptoms were always blamed on relapse of my 'disease'* " [5]

Furthermore, as we have previously pointed out to NICE:

3. Other bodies that support inclusion of antipsychotic drugs include: all four groups participating in your own guideline scoping workshop, the All-Party Parliamentary Group for Prescribed Drug Dependence, and the mental health charity Mind. Even drug companies Grünenthal and Pfizer support inclusion.

4. NICE's position that 'these medicines are prescribed for very specific defined conditions' and therefore the issues are dealt with by NICE guidance for schizophrenia, is untenable. The current NICE guidance on schizophrenia (CG178) relating to safe stopping of antipsychotics only states "If withdrawing antipsychotic medication, undertake gradually and monitor regularly for signs and symptoms of relapse." This is clearly inadequate to guide prescribers on how to stop these medications safely. We trust NICE will urgently update this guidance also.

5. Furthermore, antipsychotic drugs are increasingly prescribed 'off label', e.g. for insomnia and anxiety, and for 'behavioural management' in prisons and care homes. Only around 50% of people prescribed antipsychotics in the UK have a psychotic condition.[6] The care of the other 50% will not be guided by the schizophrenia guidelines even after you have updated them.

6. Antipsychotic drugs are one of the fastest growing classes of drugs being prescribed in England, increasing from 9.4 million prescriptions in 2015/2016 to 11 million prescriptions in 2019/2020.

7. Antipsychotics are often prescribed against the person's will. This creates a particularly strong duty to carefully consider withdrawal effects when making treatment decisions.

8. Without formal guidelines for withdrawal, long-term prescription of antipsychotics is common and can cause severe, sometimes dangerous, adverse effects.

9. We are grateful that you discussed the issue of the inclusion of antipsychotics with the Royal College of Psychiatrists, but we are disappointed that it did not support inclusion. We believe that over reliance on the views of the College may have facilitated decades of denial and minimisation of the withdrawal effects of other psychiatric drugs, such as antidepressants. We greatly appreciate your recent update to NICE guidance regarding antidepressant withdrawal, given previous guidance did not represent the full scale of the problem, partly because of advice from the College.

10. We realise that this, our second appeal against your original decision, comes to NICE late in terms of your timeline. There are, however, already two sets of guidelines[7] that could, along with this week's Horowitz et al. paper[1] that prompted this second appeal, form the basis for the development of NICE guidelines for antipsychotic withdrawal. We hope these will be helpful to you in the coming months.

Antipsychotic withdrawal has been repeatedly described in the scientific literature since the 1970s. A range of rationales has been deployed, for nearly half a century now, to avoid taking action to safeguard the safety of the patients involved and to guide the doctors trying to help

them. Please now make a decision, based on the most recent research, to include antipsychotics in the 'Medicines Associated with Dependence or Withdrawal Symptoms' guidance.

Warm regards

Professor John Read
Chair, *International Institute for Psychiatric Drug Withdrawal* www.iipdw.org

1 Horowitz, M. et al. (2021). A Method for Tapering Antipsychotic Treatment That May Minimize the Risk of Relapse. *Schizophrenia Bulletin*, sbab017, https://doi.org/10.1093/schbul/sbab017

2 https://metro.co.uk/2021/03/23/new-paper-on-how-to-stop-antipsychotic-drugs-deemed-historic-breakthrough-14287804/?ito=cbshare

3 Brandt, L. et al. (2020). Antipsychotic withdrawal symptoms: a systematic review and meta-analysis. *Frontiers in Psychiatry*, https://doi.org/10.3389/fpsyt.2020.569912

4 Read, J., Williams, J. (2019). Positive and negative effects of antipsychotic medication: an international online survey of 832 recipients. *Current Drug Safety,* 14(March), 1–28.

5 Read, J., Sacia, A. (2020). Using open questions to understand 650 people's experiences with antipsychotic drugs. *Schizophrenia Bulletin, 46,* 896-604.

6 Marston, L. et al. (2014). Prescribing of antipsychotics in UK primary care: A cohort study. *BMJ Open*, *4*(12). http://doi.org/10.1136/bmjopen-2014-006135

7 The RADAR Study Reduction Manual (Research into Antipsychotic Discontinuation and Reduction, NIHR Programme Grant); and the recent German National Guidelines for Schizophrenia - Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde (2019b). S3-Leitlinie Schizophrenie. AWMF-Register Nr. 038-009. Abbreviated Version (English). Düsseldorf: DGPPN.