Health Technology Appraisal – Naltrexone

The second draft of the *Naltrexone for the Management of Opioid Dependence* evaluation report has taken on board most of the comments from the expert panel. I am in broad agreement with the findings of the report.

Comments on Appraisal Consultation document:

2.5, line 6 – it is not correct to say most people in treatment are there because of the availability of substitute medications. It would be more accurate to say that psychosocial treatments are poorly developed and delivered for illicit substances but contrast this to services for people who misuse alcohol where there are huge numbers in treatment but no substitution therapy.

2.6 – can we have dependence throughout the document – a *dependency* is a small country.

What is meant by 'medical' interventions – I think this is referring to pharmacotherapies which would be a better term.

2.8 – it is OK to compare methadone maintenance with buprenorphine maintenance but there should be caveats. While there is some overlap between the use of methadone and buprenorphine the two drugs are also targeted at different populations.

Because methadone is generally more effective at a higher dose, that is a dose that achieves some receptor blockade, initiation of methadone is also a commitment to prescribing up to say 80mg. This may be a higher dose of opiate than the substance user was originally taking, moreover, reducing and come off 80mg of methadone is likely to be protracted and difficult. It follows that methadone is a less desirable drug for individuals with lower levels of dependence and usage, notably young people.

Buprenorphine has the advantage of that it can be used for maintenance, it is now first line treatment for detoxification, and it is always possible to switch to methadone which will be preferred by service users looking for an opiate effect. So, it is reasonable to compare the two drugs but it should also be made clear that they have some separate indications for their use.

3.2 – is it confusing to say that naltrexone has a half life of 4.5 hours when the previous paragraph states that it is possible to use a 3 times a week dosing schedule. Presumably the discrepancy arises because of the very high receptor affinity of naltrexone.
It might be helpful to clarify this point.

3.3, line 5 – I am not aware of any evidence, nor does it make clinical sense, that naltrexone increases the risk of death. Certainly a high dose of heroin is required to overcome the naltrexone blockade but there would still be a significant amount of blockade.

The loss of tolerance is due to stopping opiates rather than taking naltrexone and this is a problem that needs to be addressed whenever people achieve abstinence from opiates. Surely this cannot be used as a reason against prescribing naltrexone.

6.1 – given that the review has identified a very poor quality of research I would have thought it reasonable to recommend a large multi centre trial of naltrexone with prospective economic evaluation.

Comments on main document overview:

pg1, para 1 – It is not correct to say that opiate dependence causes spread of blood borne viruses or overdose – better to say 'may be associated with'.

pg3, para 3 – can we use dependence throughout the document – *dependency* is a small country.

pg5, para 3 – see 3.2 above.

pg5, para 4 – see 3.3 above.

pg8, para 1 – retention is not particularly a good outcome measure for naltrexone. As far as the service user is concerned naltrexone may have a similar effect to placebo, namely nothing at all, unless the service user relapses into opiate use. This is really judging the quality of the relapse prevention work which should be a structured psychosocial therapy.

Comments on main document text:

pg15, para 1 – comment already made on the appropriateness of retention as an outcome measure.

pg20, para 4 – see comment 3.3 above – this statement is commonly made and it would be helpful to clarify the evidence.

pg21, para 1 – detoxified service users have not necessarily reduced their dependence on opiates from a psychological point of view – this is the point of naltrexone. Suggest removing 'formerly opioid dependent'.