Health Technology Appraisal – Naltrexone

The conclusions on page 94 should perhaps go so far as to say that the evidence base is so poor that it is not possible at this time to draw any reliable conclusions on the effectiveness or cost effectiveness of naltrexone.

An essential variable that will be taken into account by most clinicians is probably best described as 'motivation' or 'stage of change'. It follows that where naltrexone is prescribed for people committed to achieving abstinence from opiates retention is not necessarily a good outcome measure. It is known that much of the change that occurs in treatment, or at least that has been attributed to treatment, happens early on. What is called treatment is actually a longer process, involving changes in behaviour and thoughts, which occur in the setting of particular social circumstances. People come to treatment ready to change or having already made significant change. Once this change process has been set in train then the maintenance of abstinence (assuming an abstinence goal in a discussion of naltrexone) will be strongly influenced by an individual's social support network and the experience of positive life events that may follow from abstinence. In other words continued improvement does not necessarily depend upon compliance with a naltrexone prescription.

Some specific points:

1. p14 para 1 and p19 paras 3 and 4 The statement "detoxified formerly opioid dependenct individuals" is misleading. Dependence does not end at the point where individuals achieve abstinence. Dependence may or may not reduce over a long period of time.

2. p19, 3rd para To distinguish only between harm reduction and abstinence approaches is somewhat limited. Harm reduction might usefully be seen as reducing harm without changing substance use – thus it is different to treatment which may be abstinence orientated or involve opiate substitution.

3. p20, para 3 This is referring to an increased risk of death for individuals who are unaware that they may lose their tolerance to opiates after even a short period of abstinence. There is nothing specific to naltrexone, rather, it is important that individuals are given adequate information about loss of tolerance whenever this may occur.

4. p21, para 2 It is not necessary to wait as long as five days following discontinuation of a short acting opiate such as heroin or dihydrocodeine before giving naltrexone – experience has shown 2 days to be adequate. Naltrexone may also be prescribed 2 days after a buprenorphine detoxification regimen.

5. p23, 2.3.2 Genetics has very little, if anything, to do with opiate use in the general population. Probably best to put this section at the end or to delete.

6. p25, 2.3.4 This section, quite rightly, is about much more than health. It is probably worth pointing out that there are few health consequences of opiate use per se. Injecting any drug is, of course, a high risk behaviour for the transmission of blood borne viruses and DVTs.

7. p27 References 18 and 19 are important studies but both from the USA. There are three very good UK papers on comorbidity from the DH phase 1 R&D programme – Tim Weaver was principal investigator.

8. p27/28 This section mixes up both the effects of substance use and treatment. The evidence presented is uneven and it would be desirable to have a review paper – the Royal College of Psychiatrists review of comorbidity would be a starting point. The conclusions seem to be that mental illness and substance misuse should be treated in parallel – there is a consensus among clinicians on this approach.

9. p42, 4.2.2.3 Taking retention as the main outcome measure is not particularly appropriate for naltrexone. For the reasons given above much depends on motivational state – retention may well be important for those individuals coerced into treatment but for those who have a commitment to change naltrexone may be a safety net to see them through the first few weeks or months of abstinence and the social change process gathers momentum.

10. p67, 4.5.4 It is interesting that studies designed to improve compliance achieved a mean of 19% fewer patients dropping out of treatment. These are quite sophisticated additional interventions. Nothing has been said about naltrexone supervised by a significant other such as parent or partner – there is evidence that this is important to the effectiveness of disulfiram and it is reasonable to assume that the same applies to naltrexone.

11. p93, para 1 The comment that naltrexone is not widely used in the UK reflects the current harm reduction approach to the treatment of opiate use. This is not so much practitioner or evidence driven but an effect of central policy regarding the management of opiate users coming through criminal justice system.

12. Chapter 5 The economic analyses need careful scrutiny by a competent health economist. From a clinician's point of view what is most striking is that it is relatively easy to change cost effectiveness findings by manipulating assumptions made in the regression models. As the review points out inclusion or otherwise of criminal justice system costs makes a huge difference – this is problematic in itself but even more so because of the variability in individual criminal justice system costs. As noted earlier opiate use per se does not have a huge impact on health; injecting drugs will no doubt increase the cost significantly. Many of the impacts are general to misuse or dependence on any substance but are difficult to value – for example family break up, children in care, unemployment. Any commissioning recommendations that might be taken from these cost-effectiveness analyses need to be covered by ample caveats and cautions.

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