Reviewer’s report

Title: Direct Acting Antivirals in Hepatitis C: A Systematic Review of Neuropsychiatric Risks and Psychiatric Drug Interactions

Version: 3 Date: 9 April 2013

Reviewer: peter hauser

Reviewer’s report:

Major Compulsory Revisions
1. none

Minor Essential Revisions
1. it is important to clarify that the neuropsychiatric side effects of antiviral therapy including daa addition to interferon alpha is very likely an underestimate as pharma has sponsored these studies and subjects with psychiatric illness are generally excluded (even given that there is a comparision group of subjects on interferon and not receiving DAAs). similarly the lifetime prevalence of psychiatric illness in people with HCV is very likely an underestimate as it is based on chart/clinical diagnosis and subject were not interviewed with psychiatric diagnostic instruments.

2. the assumption that ‘poorly controlled psychiatric illness may compromise adherence....’ is not supported in the literature and perpetuates a myth that psychiatrically ill people are not compliant with medications and therefore should not be offered antiviral therapy. also a large US Veteran Affairs study found no significant decrease among mild and moderate alcohol drinkers (but did in heavy drinkers) in SVR. Similarly Sylvestre found no significant decrease in SVR for intermittent IV drug users.

3. there are certain references that have not been included- Pariate studies- see Lancet 1999 among others, the Sylvestre study, the first prospective study of interferon induced depression by Hauser in the journal molecular psychiatry (2002), the US Veteran Affairs study that examined the effects of alcohol use on SVR in Veterans with HCV, studies of people with stable psychiatric illness who received antiviral therapy among others.

4. there is an implication that escitalopram is the antidepressant of choice for treatment of interferon-induced depression, which may be an artifact of phrama sponsored trials. generally SSRIs as a class and one could extrapolate that most antidepressants are efficacious in treating interferon-induced depression and that selection of an antidepressant may be guided by side effects profiles and DDI with DAA.

Discretionary Revisions-
1. consider another word for 'backbone' of HCV therapy.
2. expand on DDI between DAA and lamotrigine as severe rash is a side effect of DAAs and lamotrigine is associated with rash and in particular Steven’s Johnson syndrome

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests