19th Expert Committee on The Selection and Use of Essential Medicines

April 8-12 2013

Expert peer review on application for Adding Risperidone

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      NO


   This is a recent meta analysis (Dec 2012) comparing the efficacy and safety of first generation and individual second generation antipsychotics in schizophrenia spectrum disorders. Risperidone and quetiapine showed superior efficacy, greater treatment persistence and less extrapyramidal symptoms (EPS) than first generation antipsychotics (FGAs).


   In this meta-analysis of 21533 patients from 150 randomized controlled trials (RCTs), Risperidone showed better overall efficacy than FGAs (p = 0.002)

   b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      Risperidone has been shown in metanalyses to be superior to haloperidol for improvement in symptoms of schizophrenia (PANSS scores), and long term improvement of schizophrenia. Fewer patients on Risperidone dropped out and one study showed lower one year relapse rates. A Cochrane review has shown similar efficacy of Risperidone and Haloperidol for treatment of acute mania.

   c. Please provide any additional relevant information with reference

2. Assessment of safety
   a. Have all relevant studies on safety been included
      NO, References 1 and 2 above are not included

      They show safety results similar to other metanalyses. EPS is less with Risperidone than other with FGAs but Risperidone causes more weight gain.

   b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

      Patients on Risperidone have less extra pyramidal symptoms than those on haloperidol. In the 2003 Cochrane review, the number needed to treat (NNT) with Risperidone to prevent one case of EPS was just 3. Risperidone does cause more weight gain than conventional antipsychotics.

   c. Please provide any additional relevant information with reference
3. Assessment of cost and availability

a. Have all relevant data on cost efficacy been provided
   Yes

b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)

   The cost of Risperidone has come down significantly. Unpublished data from India report that treatment with Risperidone is as cheap as or cheaper than treatment with Haloperidol. Recent studies from Spain and Brazil have shown that Risperidone is as cost effective as Haloperidol in terms of DALYs/QALYs.

c. Please provide any additional relevant information with reference

d. Is the product available in several low and middle income countries?
   Yes

4. Assessment of public health need

a. Please provide the public health need for this product (1-2 sentences)

   Schizophrenia and bipolar affective disorder account for 5% of DALYs in the 15 – 44 year age group. Hence the public health need is large.

b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable YES

   WHO mhGAP Intervention guide

   American Psychiatric Association’s Practice Guideline for Treatment of Psychiatric Disorders

5. Are there special requirements for use or training needed for safe/effective use?

   If yes, please provide details in 1-2 sentences

   NO

6. Is the proposed product registered by a stringent regulatory authority?
   YES

7. Any other comments

8. What is your recommendation to the committee (please provide the rationale)

   I recommend that Risperidone be included in the WHO EML for the following reasons.

   Schizophrenia and bipolar affective disorder are diseases of public health importance.

   Several metaanalyses have shown that risperidone has superior efficacy to haloperidol for treatment of schizophrenia. A Cochrane review has demonstrated that the efficacy of Risperidone is comparable to that of Haloperidol in treatment of manic symptoms of bipolar affective disorder.
Risperidone has significantly less EPS and better long term tolerability as compared to Haloperidol though there is more weight gain and metabolic abnormalities (less so than Olanzapine)

Risperidone is off patent, is widely available around the world and many generics are available. The cost has been steadily decreasing. Studies have shown that Risperidone is as cost effective as Haloperidol in terms of QALY/DALY

REFERENCES


