

MEMORANDUM


From: Director, MSD



To: Dr Suzanne Hill,
Secretary, Expert
Committee on the
Selection and Use of
Essential Medicines

Date: 16 February 2009

Our ref: MSD

Attention:

Your ref: E19/81/17

Through: Dr T. Yasamy, MER 
Dr S. Saxena, MER 

Originator: Dr T. Dua,
 MSD/MER

Subject: WHO MODEL LIST OF ESSENTIAL
MEDICINES

With reference to your memorandum of 14 January 2009 on the subject, we have reviewed the applications for the categories of psychotherapeutic medicines, anticonvulsants/antiepileptics and antimigraine medicines mentioned therein, and we are enclosing the comments of the Department of Mental Health and Substance Abuse.

We will be pleased to provide further information, should this be required.


Dr Benedetto Saraceno

ENCL. As mentioned.

17th Expert Committee on the Selection and Use of Essential Medicines (2009)

Application on inclusion of antipsychotic and antidepressive medicines

It is proposed to include 6 antipsychotic and 3 antidepressive medicines in the application. The proposed antipsychotic medications are clozapine, olanzapine, risperidone, quetiapine, aripiprazole and ziprasidone. The proposed antidepressive medications are fluoxetine, paroxetine and sertraline.

The application provides some information on the comparative effectiveness and side-effects but the evidence is neither comprehensive nor systematically reviewed and presented. The benefit-risk profile for the medications is also not presented.

We would therefore propose that a comprehensive systematic review on the comparative effectiveness and adverse effects is conducted before considering these medications for inclusion in the essential medicines list. Also please note that fluoxetine, one of the antidepressive medications proposed is already included in the essential medicines list. Amongst the antipsychotic medications, clozapine is an important antipsychotic medications for treatment resistant schizophrenia with evidence available on its comparative effectiveness. However it has unique safety issues which need be kept in mind as they require monitoring. MSD would like to suggest commissioning a review for the inclusion of clozapine in the essential medicines list.

Application on inclusion of a Selective-Serotonin Reuptake Inhibitor (SSRI), for generalized anxiety disorder

This application summarises the evidence for SSRIs for inclusion into WHO essential medicines list for treatment of adult individuals with generalised anxiety disorder. It reviews evidence related to escitalopram, paroxetine and sertraline. The evidence has been comprehensively and systematically reviewed for these SSRIs.

Fluoxetine is an SSRI already included in the WHO essential medicines list. However the application does not systematically present the evidence on comparative effectiveness of fluoxetine versus the SSRIs being proposed for generalized anxiety disorder. The application does present the adverse effect profile for fluoxetine versus the above SSRIs. We therefore suggest that the above information is reviewed and presented before these SSRIs are considered for inclusion.

We would also suggest to the Expert Committee to consider separation of generalized anxiety disorder and sleep disorder as two different conditions rather than one as currently considered. In addition to epidemiological and clinical considerations, the pharmacological and non-pharmacological interventions for these two conditions are different. The application also provides detailed discussion on this topic.

Application on inclusion of a) sumatriptan b) ibuprofen for children and adolescents for acute migraine

This application proposes inclusion of sumatriptan as a second line medication for acute migraine. The application provides detailed information on the effectiveness of sumatriptan but the evidence is not systematically reviewed and presented. The benefit-risk profile for the medication is also not presented.

We therefore propose that comparative effectiveness and adverse effects of sumatriptan versus other triptans and aspirin is systematically reviewed and presented.

Ibuprofen is an important medication for acute migraine in children since use of aspirin is contraindicated because of risk of Reye syndrome. However the evidence is not systematically reviewed for ibuprofen versus other acute migraine medications as well as other NSAIDs. We would therefore suggest systematic review of evidence in this case also.

Application on inclusion of lamotrigine for epilepsy

This application proposes inclusion of lamotrigine as a monotherapy for treatment of new onset partial epilepsy in patients not tolerating carbamazepine and for the treatment of new onset generalized epilepsy in women who are contemplating pregnancy.

The application provides a comprehensive and systematic review of lamotrigine as an antiepileptic medication. We would suggest not to consider addition of lamotrigine for the following reasons. The category of epilepsy is not currently organized by type of epilepsy such as generalized or partial. There are already four first line antiepileptic medications included in the essential medicines list for the "new onset" epilepsy which are less expensive than lamotrigine. The evidence for use of lamotrigine in pregnant women is insufficient. There is a need to include a second-line or newer antiepileptic medicine in the essential medicine list for drug resistant epilepsy but this review does not demonstrate the comparative effectiveness of lamotrigine for drug resistant epilepsy.

Application on inclusion of lorazepam and midazolam as anticonvulsants

This application proposes inclusion of parenteral lorazepam for status epilepticus and parenteral midazolam for buccal administration for acute convulsive seizures and prolonged convulsive seizures where intravenous access is not available.

The application provides a comprehensive and systematic review on comparative effectiveness of lorazepam for management of convulsive status epilepticus. It is more or at least as effective than diazepam and has less adverse effects when used for management for convulsive status epilepticus. We would therefore support inclusion of parenteral lorazepam.

The application provides a comprehensive and systematic review on comparative effectiveness of buccal midazolam for management of acute convulsive seizures and prolonged convulsive seizures when intravenous access is not available. It is socially

more acceptable and more effective than rectal diazepam which is the most appropriate comparator in this case. However the evidence from use in community settings is insufficient as discussed in the application. Moreover the buccal preparation of midazolam is not available in most of the countries again emphasized in the application. Buccal route of administration also requires that health care providers are appropriately trained in delivering medication by this route. In case of both lorazepam and midazolam, the abuse potential has also to be kept in mind.