

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

April 8-12 2013

Expert peer review on application for Fixed dose combination therapy for secondary prevention of cardiovascular disease

1. Assessment of efficacy

a. Have all relevant studies on efficacy been included

Yes, but some not published or available

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

The combinations have not been tested for efficacy. 4 published trials of different combinations

TIPS1 and 2 trials assessed risk factors for Polycap REFS 21 and 22

New Zealand trial in PLoS One – lipid reduction lower, adverse events higher than “expected” (not a direct comparison, comparator was placebo)

Trinomia/Sincronium data are unpublished

Data in comparative data shows only small, statistical differences in lipids, blood pressure... no differences in discontinuations

c. Please provide any additional relevant information with reference

Statement about improving adherence by 33% from UMPIRE trial (86% FD vs 65% usual care), not published in full (meeting abstract)

Pharmacokinetic interaction of specific components have been measured

2. Assessment of safety

a. Have all relevant studies on safety been included

Yes, from the available trials

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

No major differences in the ADE reported, although NZ trial notes greater than would be anticipated from individual products

c. Please provide any additional relevant information with reference

3. Assessment of cost and availability

a. Have all relevant data on safety 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)

FDC have been deemed a “best buy” by WHO (REF 6 – not clear what this document is, not a guideline? Dated 2002), 2 cost-effectiveness analyses cited

c. Please provide any additional relevant information with reference

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

One manufacturer each for Indian Polycap and Trinomia/Sincronium, need new manufacturer for

4. Assessment of public health need

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

Cardiovascular diseases are leading causes of death worldwide, growing problem

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

WHO recommends as “best buy” (not a guideline), society guidelines recommend reducing pill burden

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

If yes, please provide details in 1-2 sentences

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

Yes No

Availability varies depending on pill

India: Indian Polycap (low dose: aspirin 100 mg, simvastatin 20 mg, ramipril 5 mg, atenolol 50 mg, hydrochlorothiazide 12.5 mg; high-dose: aspirin 200 mg, simvastatin 40 mg, ramipril 10 mg, atenolol 100 mg, and hydrochlorothiazide 25 mg)

Central / South America: Trinomia/Sincronium (aspirin 100 mg, simvastatin 40 mg, and ramipril (2.5 mg, 5 mg, or 10 mg))

Not registered: Red Heart pill

7. Any other comments

45 letters of support

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

Do not add to list, data insufficient and cannot differentiate between products

