

A.29 Triple fixed-dose combinations of antihypertensive medicines

MSF supports the proposal to include triple fixed-dose combinations (FDCs) of antihypertensive medicines on the WHO Model List of Essential Medicines (EML) for the treatment of hypertension in adult patients.

Currently, four dual FDCs of hypertensives medicines are included in the EML, with a square box symbol (□). The square box symbol ensures that the pharmacological class therapeutic equivalence is endorsed to provide choice for national protocols.

In 2019, MSF strongly supported the inclusion of these four dual fixed-dose antihypertensives in the EML.

The WHO HEARTS package and 2021 WHO hypertension treatment guidelines recommend the following combinations of antihypertensive medicines: Angiotensin Converting Enzyme Inhibitor (ACEi) or Angiotensin II Receptor Blocker (ARB) + long-acting dihydropyridine Calcium Channel Blocker (CCB) + Thiazide or Thiazide-like Diuretic.

The proposed combinations are Amlodipine + Valsartan + Hydrochlorothiazide, Amlodipine + Olmesartan + Hydrochlorothiazide, Amlodipine + Telmisartan + Indapamide and Amlodipine + Perindopril + Indapamide. The applicant highlights that the first three combinations (CCB +ARB + thiazide or thiazide-like diuretic) would be included in the same square box listing.

As clearly outlined in the application and substantiated by current guidelines and evidence, the use of triple FDCs presents a practical and evidence-based approach to improving hypertension control, especially in low- and middle-income countries (LMICs), where the burden of uncontrolled hypertension is highest.

Triple FDCs are ideal for patients whose blood pressure remains uncontrolled despite dual therapy. Evidence from randomized controlled trials have demonstrated that triple therapy improves blood pressure control over dual therapy; such improvements in blood pressure control are critical for reducing cardiovascular events and mortality. MSF especially notes the important evidence from trials carried out in LMICs' populations - from Sri Lanka (TRIUMPH) and Nigeria (VERONICA) - which confirmed efficacy and safety of triple FDCs in primary care settings in LMICs. We further note that these trials showed that FDCs-based treatment improved speed of control and reduced the number of visits required: both are crucial factors in the under-resourced health systems in many LMICs.

The application also highlights the alignment of the triple FDC approach with WHO HEARTS protocols (1), which include triple therapy as part of simplified treatment algorithms and MSF's own HTN treatment algorithms. MSF notes the triple FDC would also align with the Package of Essential Noncommunicable Disease Interventions-Plus (PEN-Plus) model for integrated care of people with stage 3 - 4 hypertension and hypertensive cardiomyopathy (1).

The move toward FDCs is particularly aligned with some of MSF's operational priorities, including simplified procurement and supply (as FDCs reduce the complexity of stocking and dispensing multiple / separate pills), improved adherence, and task-shifting (simplified protocols and reduced

pill burden are important for implementation in decentralized, integrated, and nurse-managed patient care, such as those MSF operates in a number of humanitarian and low-resource settings). These practical advantages were also emphasized in MSF's support for dual FDC inclusion in the 2019 EML.

MSF's Access Campaign worked with Resolve to Save Lives on the Under Pressure (2) report, which identified affordability, registration bottlenecks, and procurement inefficiencies as major barriers to hypertension treatment access. MSF thus aligns with the application's framing that inclusion in the EML can help catalyze affordability for governments. As noted in the Under Pressure report, especially in countries with strong local manufacturing (such as India and Brazil), single pill combinations (SPCs) were often priced lower than the equivalent treatments offered as individual medicines.

MSF recommends that WHO ensures price transparency for the triple FDCs to best support procurement and negotiation efforts as well as robust WHO Prequalification to support expanded generic manufacturing and countries' registrations, with a view to increased competition and lower prices.

MSF recommends prioritization of quality-assured generic manufacturing, along with WHO support for prequalification. WHO should also offer implementation guidance to support Member States' uptake of triple FDCs within national protocols and should include the recommended triple FDCs in any updates to the WHO hypertension treatment algorithm, particularly within differentiated service delivery models suitable for decentralized / integrated care in LMICs.

MSF urges the Expert Committee on the Selection and Use of Essential Medicines to include the triple antihypertensive fixed-dose combinations on the WHO Model List of Essential Medicines for adults, with square box listings to reflect interchangeable medicine classes (ARB or ACEi + CCB + thiazide/thiazide-like diuretic).



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