Towards equitable access to treatment for multiple sclerosis

Access to treatments for neurological disorders is egregiously insufficient, particularly in low-income and middle-income countries (LMICs). The inclusion of therapeutic agents on the WHO Model List of Essential Medicines (referred to as the essential medicines list [EML]) is an initial step to potentially increase their availability worldwide, as the list serves as a guide for the development of national and institutional EMLs. The *Intersectoral Global Action Plan On Epilepsy and Other Neurological Disorders* promotes the inclusion and updating of essential and affordable medicines and health products for neurological disorders in national EMLs, as guided by the WHO list. However, neurological conditions remain poorly represented on the WHO EML, and multiple sclerosis is a case in point, as there are no treatments listed for the disease. Neurology organisations are working hard to tackle this situation and, on Dec 11, 2022, the Multiple Sclerosis International Federation (MSIF) applied to WHO for the addition of disease-modifying treatments for multiple sclerosis to their EML.

MSIF, an alliance of national multiple sclerosis organisations, first applied (in 2018) for three disease-modifying treatments—glatiramer acetate, fingolimod, and ocrelizumab—to be added to the WHO EML. The WHO Expert Committee on Selection and Use of Essential Medicines did not recommend adding any of the three therapies to the 2019 WHO EML, noting that there was no clear evidence that glatiramer acetate, fingolimod, or ocrelizumab were superior to other multiple sclerosis drugs in terms of safety, efficacy, and affordability, and that the application had excluded commonly used drugs and off-label medications.

In response to this feedback, the MSIF, in collaboration with the Cochrane multiple sclerosis group, has systematically assessed all on-label and off-label disease-modifying therapies for multiple sclerosis—ie, 30 therapies in total—before submitting a revised application. An MSIF international panel (comprising multiple stakeholders, including patient representatives from LMICs) used recommendations from two guidelines, produced by the MSIF Off-Label Treatment panel (MOLT) and the MSIF Essential Medicines Panel (MEMP), and systematically collected evidence for three special populations (ie, children and adolescents, pregnant women, and breastfeeding women) to identify essential medicines. Treatments were short-listed, using the GRADE evidence-to-decision framework, on the basis of the associated balance of benefits and harms; the certainty of the evidence; cost and cost-effectiveness in LMICs; health outcomes valued by patients, potential to reduce health inequities, acceptability, feasibility, and availability in LMICs; the availability of generic and biosimilar versions; and the needs of the special populations. Consideration was also given to whether a drug is or could be used to treat other conditions. Three disease-modifying approaches (rituximab [or ocrelizumab as an alternative given that off-label prescribing can be complex or prohibited in some countries], cladribine, and glatiramer acetate) were selected for inclusion in the application to the WHO EML.

The WHO Expert Committee will meet on April 24–28, 2023, to discuss all EML applications. If successful, the MSIF application, which is comprehensive, rigorous, and has the endorsement of international organisations, could serve as a blueprint for EML applications for other neurological disorders. However, addition of a drug to the EML is still the first hurdle to achieving access to therapies. How access to these medications is implemented in LMICs will be the next challenge. For example, levodopa is on the WHO EML for the treatment of Parkinson's disease, but it is not accessible or affordable in many LMICs.

As some of the disease-modifying treatments for multiple sclerosis that have been proposed by MSIF are still under patent (ie, ocrelizumab and oral cladribine), some are biologicals (ie, ocrelizumab and rituximab), and one is a complex drug (ie, glatiramer acetate), they will remain costly. Therefore, additional schemes must be considered to make these drugs affordable globally, such as patent pooling, which requires that patent owners license their patents to third parties to allow them to manufacture and sell these products at an affordable price. In parallel, a lot needs to be done to improve neurological services in LMICs to improve the diagnosis and management of patients with multiple sclerosis. Suitable infrastructure and training need to be in place to use these therapies safely and effectively. Nevertheless, approval by WHO of the MSIF application will be a crucial first step to ensure that people with multiple sclerosis will be able to access appropriate treatment options in LMICs.

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For more on the **Intersectoral global action plan on epilepsy and other neurological disorders** see https://www.who.int/news/item/28-04-2022-draft-intersectoral-global-action-plan-on-epilepsy-and-other-neurological-disorders-2022-2031

For more on the **Multiple Sclerosis International Federation** see https://www.msif.org/

For more on the **MSIF application** see https://www.who.int/groups/expert-committee-on-selection-and-use-of-essential-medicines/24th-eml-expert-committee

For more on the **WHO Expert Committee recommendation in 2018** see **Editorial** *Lancet Neurol* 2019; **18:** 1067

For the **MOLT recommendations** see https://www.msif.org/molt-guidelines-azathioprine-rituximab/

For the **MEMP recommendations** see https://www.msif.org/improving-access/essential-medicines-for-ms/public-consultation-guidelines-essential-medicines/

For more on **GRADE evidence to framework methodology** see *BMJ* 2016; **353:** i2016

For more on **levodopa and the WHO EML** see Parkinson disease: a public health approach. Technical brief. Geneva: World Health Organization; 2022

For more on **patent pooling** see *Iran J Public Health* 2018; **47:** 1493–1503 and https://medicinespatentpool.org/