



Title	Guideline for the use of off-label azathioprine and rituximab for the treatment of multiple sclerosis in low-resource settings.	Provide title of the document/guideline that will reflect its scope.
Purpose	Guidelines for the use off-label azathioprine and rituximab aim to improve appropriate treatment options for multiple sclerosis in low-resource settings where a range of on-label disease-modifying therapies are not available and affordable.	Specify health intents (i.e., prevention, diagnosis, treatment, etc.) and expected benefits or outcomes. E.g. preventing thromboembolic complications of patients undergoing elective orthopedic surgery.
Perspective	The guideline is aimed to support informed decision-making for the person with multiple sclerosis and treating clinician, and help health systems and payers consider reimbursement policies for off-label treatments in low-resource settings.	Specify the perspective that the panel will take when making recommendations: this of an individual patients, their families, providers caring for those patients, public health, health system, payer, population (the society), etc.
Target population	People with relapsing or progressive forms of multiple sclerosis.	Specify subjects to whom those recommendations apply (i.e. patients, society, etc.) E.g. adults undergoing elective orthopedic surgery, all women 40 years of age or older, etc.
Setting	These guidelines are aimed at MS providers and neurologists working in secondary or tertiary care in low-resource settings. Low-resource settings can refer to health systems in low- and middle-income countries or disadvantaged populations in high-income countries (e.g. uninsured people, refugees).	Specify level of health care (i.e. primary, high, etc.) where these recommendations are supposed to be implemented.
Key coexisting conditions	It is important to manage co-morbidities that co-exist with MS, as MS treatments for acute relapses and maintenance may have an impact on these conditions. These include, migraine, diabetes mellitus, hypertension, hypercholesterolemia, anxiety, depression, thyroid disease and osteoporosis.	Specify the key coexisting conditions (comorbidities) that might need to be considered when making recommendations. E.g. patients with COPD frequently have coexisting heart failure and diabetes that may influence the choice of the optimal management.

	There may also be other coexisting autoimmune conditions, such as rheumatoid arthritis, psoriasis, ankylosing spondylitis and Systemic Lupus Erythematosus.	
Types of interventions	Two disease-modifying therapies that are used off-label to treat multiple sclerosis in the largest number of countries; azathioprine (used in at least 68 countries) and rituximab (used in at least 70 countries).	Specify which preventive, therapeutic and diagnostic interventions will be covered and which will be not.
Key stakeholders and users	The direct users of this guideline are people with and affected by multiple sclerosis, MS providers and neurologists in low-resource settings. Other key stakeholders include ministries of health, payers, neurological associations and MS patient organisations.	Specify all relevant professional groups, institutions, patients, public, etc. who are target users or beneficiaries of these guidelines and/or whose views should be sought
Key resources to consider	Adequate infrastructure and diagnostic capabilities are needed for accurate differential diagnosis of multiple sclerosis and monitoring of disease activity. Rituximab requires access to infusion suites.	Specify resources needed for the implementation of guidelines (i.e. need for additional human resources, equipment, infrastructure, system changes, etc.) and potential barriers to implementation.
Key issues for implementation	The perception and associated practice and legislation of off-label treatments varies in different countries. This can make people with multiple sclerosis and treating clinicians reluctant to use off-label treatments. Health systems and payers do not always reimburse off-label treatments, even if considered safe, effective and cost-effective, solely based on the off-label status.	
Existing documents	MENACTRIMS treatment guidelines: https://menactrims.com/guidelines/ ECTRIMS/EAN multiple sclerosis treatment guidelines: https://www.ectrims.eu/guidelines/ AAN multiple sclerosis treatment guidelines: https://www.aan.com/Guidelines/home/GuidelineDetail/898	List all existing documents/guidelines on the same or similar topic that are likely to be currently used in practice (e.g. guidelines developed by other organizations).