Medicine RITUXIMAB (infusion)

Status: Off-label, listed on WHO EML for other indications
☐ Square box grouping with on-label OCRELIZUMAB

Problem MULTIPLE SCLEROSIS

2.8 million

2/3 women

Onset commonly: 20-40 years

Disability and unemployment

Benefits

LARGE benefit (RMS)
MODERATE benefit (PMS)

Relapsing forms of MS: large benefit
(RCT, vs no DMT, switching from another DMT)
Relapse 12 months: 198 fewer per 1000 (⊕⊕OO)

Relapsing forms of MS: large benefit
(NRCS, vs other DMTs, treatment-naïve)
Relapse 24 months: 84 to 227 fewer per 1000 (⊕⊕OO)

Progressive forms of MS (RCT, vs no DMT): moderate benefit
Disability 24 months: 85 fewer per 1000 (⊕OOO)
Relapse 24 months: 14 fewer per 1000 (⊕⊕⊕O)

Harms

SMALL harm (RMS)
SMALL - TRIVIAL harm (PMS)

Progressive and relapsing MS pooled: small harm
(RCT, vs no DMT, switching from another DMT)
Mortality: 6 fewer per 1000 (⊕OOO)
Serious Adverse Events (SAE): 21 more per 1000 (⊕OOO)
Long-term - cancer 24 months: 3 fewer per 1000 (⊕OOO)
Long-term - infections 12- 24 months: 19 more per 1000 (⊕OOO)

Progressive forms of MS (RCT, vs no DMT): trivial harm
Mortality: 8 fewer per 1000 (⊕⊕⊖⊖)
Serious Adverse Events (SAE): 6 more per 1000 (⊕OOO)
Discontinuation due to AE: 30 more per 1000 (⊕⊕⊕O)

Guideline

MSIF Essential Medicines and MSIF Off-Label guidelines

Balance

Probably favours RITUXIMAB (⊕OOO)

Pregnancy/breastfeeding

Safer to avoid, but can be managed with careful timing

Resources

Large costs

Person/year:
USD 120 - 8 813
Consistently lower cost than other DMTs, including ocrelizumab USD 1 200 - 66 681.
Large variability demonstrates pathways to affordability.

Cost-effectiveness

No studies

No systematic studies found. Norwegian HTA found rituximab to be cost-effective compared to ocrelizumab and fingolimod in treatment-naïve RMS.

Equity

Probably increased

Low cost compared to other DMTs, already listed on the WHO EML and many national EMLs, high feasibility to improve health equity.
Low monitoring costs, but need access to infusion facilities.

Acceptability

Probably yes

Infusion at healthcare facility but infrequent (every 6 months), with few monitoring requirements. Off-label but familiarity of use from other conditions.

Feasibility

Probably yes

Off-label but widely used, available and listed on WHO and national EMLs.
Product patent expired, several follow-on products available. WHO pre-qualification product.

Availability

Available

Used in 70 out of 107 countries surveyed, including 70% lower-middle income countries, listed on 41 national EMLs.
Listing on WHO EML allows focused efforts to further improve availability

Medicine CLADRIBINE (oral)

Status: On-label, not listed on EML

Problem MULTIPLE SCLEROSIS 2.8 million 2/3 women

Onset commonly: 20-40 years Disability and unemployment

Benefits LARGE benefit (RMS)

Relapsing forms of MS (RCT, vs no DMT):
Relapse 24 months: 240 fewer per 1000 (⊕⊕⊕⊕)
Disability 24 months: 53 fewer per 1000 (⊕⊕OO)
QoL (EQ-5D VAS): SMD 0.19 SD higher (⊕⊕⊕O)
QoL (EQ-5D index): SMD 0.24 SD higher (⊕⊕⊕O)

Harms TRIVIAL harm (RMS)

Relapsing forms of MS (RCTs, vs no DMT):
Mortality: 0 fewer per 1000 (⊕⊕⊕O)
Serious Adverse Events (SAE): 27 more per 1000 (⊕OOO)
Discontinuation due to AE: 18 more per 1000 (⊕⊕OO)

Guideline

MSIF Essential Medicines guidelines

Balance Favours CLADRIBINE (⊕⊕OO)

Pregnancy/breastfeeding Contraindicated, pregnancy can be planned outside treatment period

Resources

Large costs

Person/year:
USD 6 602 - 62 628
2 years treatment only
Large variability demonstrates pathways to affordability through voluntary licencing, pooled negotiation and procurement if listed on WHO EML.

Cost-effectiveness

Probably favours

Cost-effective compared to ocrelizumab, alemtuzumab, natalizumab and fingolimod.

Equity

Probably reduced

Increased health equity but decreased financial equity. Low monitoring costs, oral mode of administration.

Listing on WHO EML would reduce costs and increase health equity.

Acceptability

Yes

On-label, oral medication with few monitoring requirements. Short treatment period, although further treatment for some people may be necessary.

Feasibility

Probably yes

On-label, oral medication that can be used at home, with few monitoring requirements. No cold-chain required. Large costs, with secondary patents expiring 2024-25.

Availability

Probably not

Used in 52 out of 107 countries surveyed but more common in HICs. Approved recently in 2017.

Listing on WHO EML allows focused efforts to improve availability.

Medicine
GLATIRAMER ACETATE (injection)

Status: On-label, not listed on EML

Problem
MULTIPLE SCLEROSIS 2.8 million 2/3 women

Onset commonly: 20-40 years Disability and unemployment

Benefits
LARGE benefit (RMS)
MODERATE benefit (PMS)

Relapsing forms of MS (RCT, vs no DMT):
Relapse 24 months: 82 fewer per 1000 (⊕⊕⊕O)
Disability 24 months: 49 fewer per 1000 (⊕OOO)
New GAD+ T1 MRI 24 months: 135 fewer per 1000 (⊕OOO)

Progressive forms of MS (RCT, vs no DMT):
Disability 24 months: 68 fewer per 1000 (⊕OOO)

Harms
TRIVIAL harm (RMS, PMS)

Relapsing forms of MS (RCTs, vs no DMT):
Mortality: 1 fewer per 1000 (⊕⊕OO)
Serious Adverse Events (SAE): 4 fewer per 1000 (⊕⊕OO)
Discontinuation due to AE: 22 more per 1000 (⊕⊕⊕O)

Progressive forms of MS (RCTs, vs no DMT):
Mortality: 16 fewer per 1000 (⊕⊕⊕O)
Serious Adverse Events (SAE): 9 more per 1000 (⊕⊕OO)
Discontinuation due to AE: 36 more per 1000 (⊕⊕⊕O)

Guideline
MSIF Essential Medicines guidelines

Balance
Probably favours GLATIRAMER ACETATE (⊕OOO)

Pregnancy/breastfeeding
Can be used during pregnancy and breastfeeding

Resources
Large costs

Person/year:
USD 960 - 12 566
Large variability demonstrates pathways to affordability through voluntary licencing, pooled negotiation and procurement if listed on WHO EML.

Cost-effectiveness
Varies

Cost-effective compared to fingolimod, interferon beta 1b, but not dimethyl fumarate, peg-interferon beta 1a or teriflunomide. Indeterminate compared to interferon beta 1a.

Equity
Probably no impact

Increased health equity but decrease financial equity. Low monitoring costs, safe to use in pregnancy.

Listing on WHO EML would reduce costs and increase equity.

Acceptability
Probably yes

On-label with very few monitoring requirements. Frequent injections requiring cold-chain, but which can be done at home.

Feasibility
Probably yes

On-label with very few monitoring requirements. Can be useed in pregnancy and breastfeeding. Product patent expired, several follow-on products available.

Availability
Varies

Used in 65 out of 107 countries surveyed and listed on 19 national EMLs, but more common in HICs.

Listing on WHO EML allows focused efforts to improve availability.