

Medicine RITUXIMAB (infusion)

Status: Off-label, listed on WHO EML for other indications



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 ($\oplus \oplus OO$)

Relapsing forms of MS: large benefit

(NRCS, vs other DMTs, treatment-naïve) Relapse 24 months: 84 to 227 fewer per 1000 ($\oplus \oplus OO$)

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

Discontinuation due to AE: 30 more per 1000 ($\oplus \oplus \oplus O$) Safer to avoid, but can be Balance Probably favours RITUXIMAB 5 Pregnancy/breastfeeding managed with careful timing (⊕000) Å ITA K X Equity Acceptability Feasibility Availability Cost-effectiveness Resources Probably yes Probably yes Large costs Probably increased Available No studies Used in 70 out of 107 Low cost compared to Infusion at Off-label but widely Person/year: No systematic studies USD 120 - 8 813 other DMTs, already healthcare facility used, available and countries surveyed, found. Norwegian HTA Consistently lower including 70% lowerlisted on the WHO EML but infrequent (every listed on WHO and found rituximab to be costcost than other DMTs, 6 months), with few middle income and many national EMLs, national EMLs. effective compared to including ocrelizumab countries. listed on 41 high feasibility to improve monitoring Product patent ocrelizumab and USD 1 200 - 66 681. health equity. requirements. Offexpired, several national EMLs. fingolimod in treatment-Large variability Low monitoring costs, but label but familiarity of follow-on products Listing on WHO EML naïve RMS. demonstrates use from other allows focused efforts need access to infusion available. WHO prepathways to to further improve facilities. conditions. qualification product. affordability. availability

Problem MULTIPLE SCLEROSIS 2.8 million 👬 2/3 women

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 \bigcirc Onset commonly: 20-40 years \bigcirc Disability and unemployment



(RCT, vs no DMT, switching from another DMT)

Serious Adverse Events (SAE): 21 more per 1000 (⊕OOO)

Long-term - cancer 24 months: 3 fewer per 1000 (\oplus 000)

Progressive forms of MS (RCT, vs no DMT): trivial harm

Serious Adverse Events (SAE): 6 more per 1000 (⊕000)

Long-term - infections 12- 24 months: 19 more per 1000 (⊕000)

Mortality: 6 fewer per 1000 (\oplus 000)

Mortality: 8 fewer per 1000 ($\oplus \oplus \Theta \Theta$)

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

Progressive and relapsing MS pooled: small harm

Guideline

MSIF Essential Medicines and MSIF Off-Label guidelines



Status: On-label, not listed on EML



WHO EML.

Benefits LARGE benefit (RMS)

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





Onset commonly: 20-40 years

Disability and unemployment

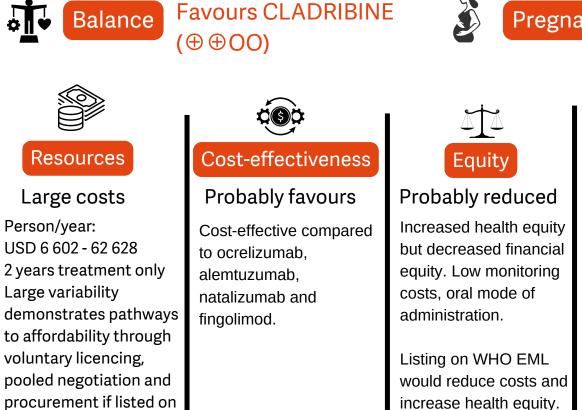
2.8 million 🛉 👗 2/3 women



TRIVIAL harm (RMS)

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

MSIF Essential Medicines guidelines



Pregnancy/breastfeeding

medication with few

requirements. Short

treatment period,

although further

people may be

necessary.

treatment for some

monitoring

Contraindicated, pregnancy can be planned outside treatment period



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.



GLATIRAMER ACETATE (injection)

Status: On-label, not listed on EML



LARGE benefit (RMS) MODERATE benefit (PMS)

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

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



Probably favours GLATIRAMER ACETATE (\oplus 000)



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.

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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.



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.

Problem MULTIPLE SCLEROSIS 2.8 million 👬 2/3 women



Onset commonly: 20-40 years Disability and unemployment



TRIVIAL harm (RMS, PMS)

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

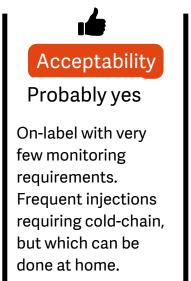
Progressive forms of MS (RCTs, vs no DMT): Mortality: 16 fewer per 1000 ($\oplus \oplus \oplus O$) Serious Adverse Events (SAE): 9 more per 1000 ($\oplus \oplus OO$) Discontinuation due to AE: 36 more per 1000 ($\oplus \oplus O$)

Pregnancy/breastfeeding



MSIF Essential Medicines guidelines

Can be used during pregnancy and breastfeeding



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. 2 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.