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*HTA Decisions Review for Products  
Indicated in the Treatment of Systemic  
Lupus Erythematosus (SLE) and Lupus  
Nephritis in EU5 countries, Canada and  
Turkey*




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# Objective and Scope


## **OBJECTIVE and SCOPE**

- To conduct a HTA review of decisions for products indicated in the treatment of Systemic Lupus Erythematosus (SLE) and Lupus Nephritis

# Methods

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- Considering to the clinical guidelines of American College of Rheumatology and the British Society for Rheumatology, medicines used outside of standard treatment were determined for systemic lupus erythematosus and lupus nephritis.

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- HTA reports on these drugs were reviewed and examined on the websites of HTA institutions of these 7 countries: United Kingdom (NICE, NIHR), GERMANY (IQWiG, G-BA), FRANCE (HAS), ITALY (AIFA), SPAIN (AguAS, OSTEBA), CANADA (CADTH), TURKEY (HTA institution not available in Turkey, the reports of reimbursement agency (SGK) were examined).

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- As a result of the investigations, the suggested indications of institutions, ICER values and prices were reported.

# Selected HTA Institutions

NICE: National Institute for Health and Care Excellence

AquAS: Agència de Qualitat i Avaluació Sanitàries de Catalunya

G-BA: The Federal Joint Committee

IQWiG: Institute for Quality and Efficiency in Health Care

NIHR: National Institute for Health Research

HAS: Haute Autorité de Santé

CADTH: Canadian Agency for Drugs and Technologies in Health

OSTEBA: Basque Office For Health Technology Assessment

AIFA: The Italian Medicines Agency

SGK: Social Security Agency of Turkey\*

\* Turkey has not any official HTA agency. SGK, the reimbursement agency, published decisions about the products depending on evaluation of cost-effectiveness and budget impact analysis.

# Background of SLE

## Systemic Lupus Erythematosus (SLE)

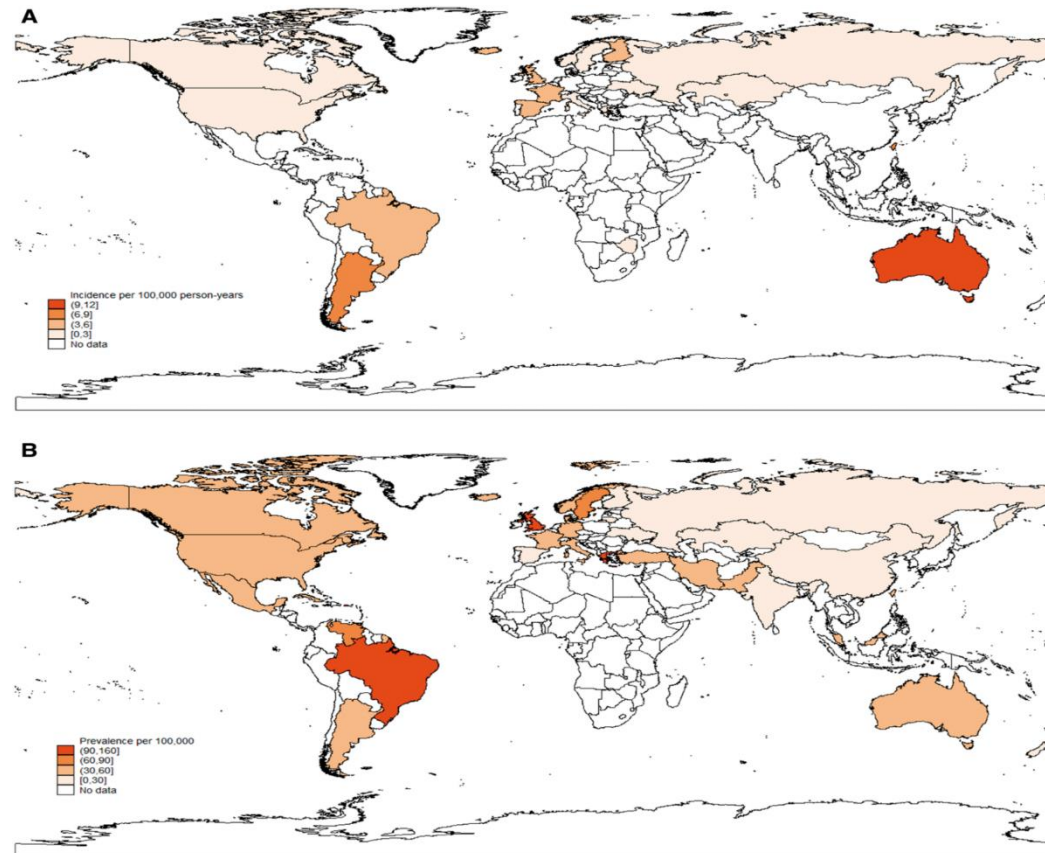
*Multisystem, complex, autoimmune disease, can present at any age*

*Lupus can cause damage to the skin, joints, kidneys, brain and lung.*

*It's not fully understood what causes lupus.*

*Standard Treatment:  
Anti-inflammatories and over-the-counter pain relievers,  
Corticosteroids, Antimalarials, Immunosuppressives  
(Immune Modulators), Anticoagulants*

# Epidemiology of SLE



Rheumatology, Volume 56, Issue 11, 09 August 2017, Pages 1945–1961, <https://doi.org/10.1093/rheumatology/kex260>.

# Recommendations of Clinical Guidelines

Depending on the guidelines the medicines used outside the standard treatment were Belimumab(GSK), Mycophenolate Mofetil(ROCHE) and Rituximab(ROCHE).

**American College of Rheumatology**: American College of Rheumatology Guidelines for Screening, Treatment, and Management of Lupus Nephritis (Arthritis Care & Research Vol. 64, No. 6, June 2012, pp 797–808)

**British Society for Rheumatology**: The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults (Rheumatology 2018;57:e1e45 doi:10.1093/rheumatology/kex286 Advance Access publication 6 October 2017)



# Indications of Drugs Approved by EMA



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

Drug	Therapeutic Indications
Belimumab	Belimumab is indicated as add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g., positive anti-dsDNA and low complement) despite standard therapy.
Mycophenolate Mofetil	Mycophenolate mofetil is indicated in combination with ciclosporin and corticosteroids for the prophylaxis of acute transplant rejection in patients receiving allogeneic renal, cardiac or hepatic transplants.
Rituximab	Rituximab is used to treat follicular lymphoma and diffuse large B cell non-Hodgkin's lymphoma, chronic lymphocytic leukaemia, severe rheumatoid arthritis, two inflammatory conditions of blood vessels known as granulomatosis with polyangiitis and microscopic polyangiitis (MPA). Depending on the condition it is used to treat, Rituximab may be given on its own, or with chemotherapy, methotrexate or a corticosteroid.



# HTA Reports from United Kingdom



Drug	HTA Institution	Recommendations	Price	ICER
Belimumab	NICE	Belimumab is recommended as an option as add-on treatment for active autoantibody-positive systemic lupus erythematosus with evidence for serological disease activity (low complement, positive anti-dsDNA) and SELENA-SLEDAI $\geq 10$ in adults. (22.06.2016)	120-mg-vial-£ 121,50 400-mg-vial-£ 405	£ 27,807 - £ 85,893 per QALY
Belimumab	NIHR	Belimumab is recommended as an option as add-on treatment for active autoantibody-positive systemic lupus erythematosus with evidence for serological disease activity (low complement, positive anti-dsDNA) and SELENA-SLEDAI $\geq 10$ in adults. (26.06.2011)	120-mg-vial-£ 114 400-mg-vial-£ 381	£ 54,518 - £ 85,893 per QALY

# HTA Reports from Germany



Drug	HTA Institution	Recommendations	Price	ICER
Belimumab	IQWiG - G-BA	Belimumab is indicated as an add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g. positive anti dsDNA and low complement) despite standard therapy. (02.08.2012)	400-mg-vial- 948,30 €	-
Mycophenolate Mofetil	G-BA	MMF for induction or maintenance therapy in patients with lupus nephritis.(Off-label use) (21.09.2017)	-	-

# HTA Report from France



Drug	HTA Institution	Recommendations	Price	ICER
Belimumab	HAS	HAS recommends continued inclusion on the list of medicinal products approved for hospital use for treatment of adult patients with active, autoantibody-positive systemic lupus erythematosus with a high degree of disease activity (e.g positive anti-dsDNA and low complement) as an add-on to standard treatment, after failing or being intolerant to properly conducted treatment with synthetic antimalarials, NSAIDs, corticosteroids and possibly immunosuppressants, depending on the specific organ involvement and at the dosages in the marketing authorisation. (ASMR IV) (25.06.2014)	-	-

# HTA Report from Italy



Drug	HTA Institution	Recommendations	Price	ICER
Belimumab	AIFA	Belimumab is recommended as an option as add-on treatment for active autoantibody-positive systemic lupus erythematosus with evidence for serological disease activity (low complement, positive anti-dsDNA) and SELENA-SLEDAI $\geq 10$ in adults. (22.11.2017)	120-mg-vial-241,32 € 400-mg-vial-804,41 € 200-mg-4pen- 1.608,81 €	-

# HTA Reports from Spain



Drug	HTA Institution	Recommendations	Price	ICER
Belimumab	OSTEBA	Belimumab is indicated as an add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g. positive anti dsDNA and low complement) despite standard therapy. (24.06.2013)	120-mg-vial-145,59 € 400-mg-vial-484,38 €	51,584 € - 760,864 € per QALY
Belimumab	AQuAS	Belimumab is indicated as an add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g. positive anti dsDNA and low complement) despite standard therapy. (04.2013)	120-mg-vial-151,35 € 400-mg-vial-503,51 €	£ 27,807 - £ 85,893 per QALY
Rituximab	AQuAS	Rituximab has been proposed for the treatment of refractory lupus nephritis.(Off-label use) (15.12.2015)	100-mg-vial-257,49 € 500-mg-vial-1.283,91 €	-

# Reimbursement Decisions from Turkey



Drug	HTA Institution	Recommendations	Price	ICER
Belimumab	SGK	Not Recommended / Reimbursed	400 mg – vial – 1750.43 ₺	-
Mikofenolat Mofetil	SGK	<p>Mycophenolate mofetil is indicated in combination with ciclosporin and corticosteroids for the prophylaxis of acute transplant rejection in patients receiving allogeneic renal, cardiac or hepatic transplants.</p> <p>If no response to steroid therapy, it is used in the treatment of treatment-resistant lupus erythematosus and lupus nephritis without additional confirmation.</p>	<p>500 mg-50tablets-153.01 ₺</p> <p>500 mg-150tablets-330.64 ₺</p> <p>250mg-100capsules-158.95 ₺</p>	-
Rituximab	SGK	<p>Rituximab is used to treat follicular lymphoma and diffuse large B cell non-Hodgkin's lymphoma , chronic lymphocytic leukaemia, severe rheumatoid arthritis, two inflammatory conditions of blood vessels known as granulomatosis with polyangiitis and microscopic polyangiitis (MPA).</p>	500-mg-vial-4001.34 ₺	-

# HTA Reports from Canada



Drug	HTA Institution	Recommendations	Price	ICER
Belimumab	CADTH (2012)	The Canadian Drug Expert Committee (CDEC) recommends that belimumab not to be listed. (25.04.2012)	-	-
Belimumab	CADTH (2014)	Based on available evidence, the potential impact of belimumab may be positive but is uncertain in both clinical and cost-effectiveness, so it is not recommended. (23.05.2018)	-	-



# Summary of HTA/Reimbursement Reports

Drugs	Countries						
	United Kingdom	Germany	France	Italy	Spain	Turkey	Canada
Belimumab	+	+	+	+	+	-	-
Mycophenolate Mofetil	N/A	+	N/A	N/A	N/A	+	N/A
Rituximab	N/A	N/A	N/A	N/A	+	+	N/A

+: Recommended

- : Not recommended

N/A: Not available any HTA report

# References

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- (2) [http://www.english.g-ba.de/downloads/91-1028-7/Belimumab\\_ENG.pdf](http://www.english.g-ba.de/downloads/91-1028-7/Belimumab_ENG.pdf) / [https://www.g-ba.de/downloads/40-268-2102/2012-08-02\\_AM-RL-XII\\_Belimumab\\_ZD.pdf](https://www.g-ba.de/downloads/40-268-2102/2012-08-02_AM-RL-XII_Belimumab_ZD.pdf)
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- (4) <https://www.cadth.ca/belimumab-6> / <https://www.cadth.ca/belimumab-treatment-adults-systemic-lupus-erythematosus-review-clinical-effectiveness-cost-0>
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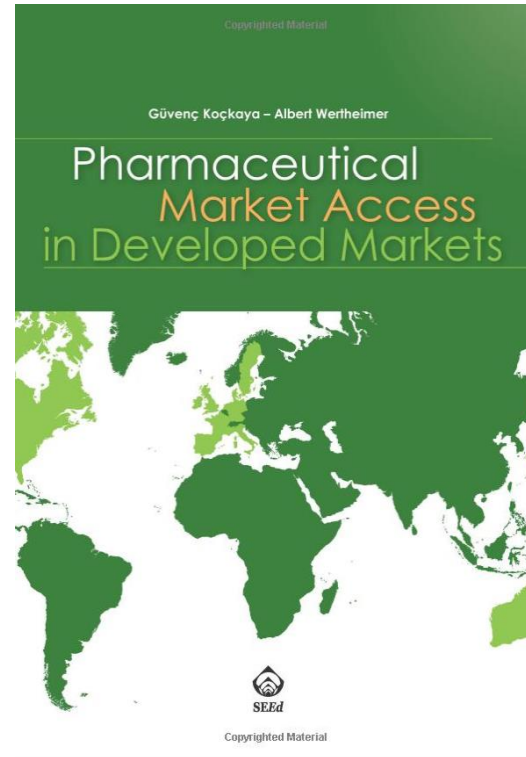
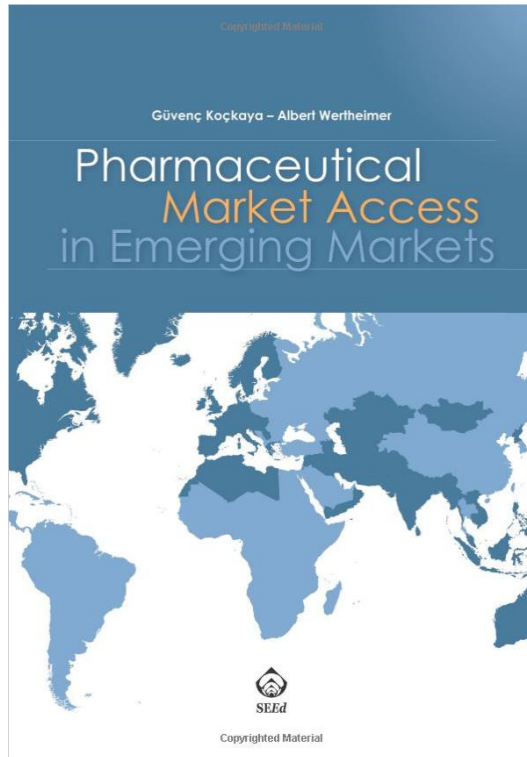
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# ECONiX References



\*References are belong to consultancy services of ECONiX or individual experiences of ECONiX Management Troika Team.

# Have a look market access with Amazon Best Sellers!!!



«In spite of many similarities between healthcare products and other goods in a free market economy, the healthcare market challenges the traditional economic paradigm. There are four features that clearly differentiate the healthcare market from other markets:

- ✓ The price is not determined by supply and demand
- ✓ Payers are committed to purchasing health for the society
- ✓ Health is specific to each individual
- ✓ Externality of health»

Toumi et al. Chapter I : Introduction to Market Access, Kockaya & Wertheimer, Pharmaceutical Market Access in Developed Markets, SEEd, Milano, 2017

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“Depending on the needs for market access, it could be said that marketing means being in love with the products, but market access means the marriage.”

Kockaya et al. 2017

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