Baloxavir marboxil (Influenza, post-exposure prophylaxis, ≥ 12 years)

Resolution of: 5 August 2021 valid until: unlimited
Entry into force on: 5 August 2021
BAnz AT 27 08 2021 B7

Therapeutic indication (according to the marketing authorisation of 7 January 2021):

Treatment of influenza: Xofluza is indicated for the treatment of uncomplicated influenza in patients aged 12 years and above.

Post-exposure prophylaxis of influenza: Xofluza is indicated for post-exposure prophylaxis of influenza in individuals aged 12 years and above.

Xofluza should be used in accordance with official recommendations.

Therapeutic indication of the resolution (resolution of 5 August 2021):

Xofluza is indicated for post-exposure prophylaxis of influenza in individuals aged 12 years and above.

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

a) adults and adolescents aged 12 years and above with influenza exposure without risk of influenza-related complications

Appropriate comparator therapy for post-exposure prophylaxis:

monitoring wait-and-see approach

Extent and probability of the additional benefit of baloxavir marboxil compared to monitoring wait-and-see approach:

Indication of a considerable additional benefit

b) adults and adolescents 12 years of age and above with influenza exposure at risk for influenza-related complications:

Appropriate comparator therapy for post-exposure prophylaxis:

antiviral therapy (oseltamivir or zanamivir)

Extent and probability of the additional benefit of baloxavir marboxil compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) adults and adolescents aged 12 years and above with influenza exposure without risk of influenza-related complications[2]

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant difference for the benefit assessment
Morbidity	↑↑	Advantage for the endpoint "symptomatic influenza infection"
Health-related quality of life	∅	There are no data.
Side effects	↔	No relevant difference for the benefit assessment

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
↓: statistically significant and relevant negative effect with low/unclear reliability of data
↑↑: statistically significant and relevant positive effect with high reliability of data
↓↓: statistically significant and relevant negative effect with high reliability of data
↔: no statistically significant or relevant difference
∅: There are no usable data for the benefit assessment.
n.a.: not assessable

BLOCKSTONE study: RCT (baloxavir marboxil **vs** placebo); 14 days observation

Endpoint category Endpoint BLOCKSTONE study	**Baloxavir marboxil**		**Placebo**		**Baloxavir marboxil vs placebo**
	N	Subjects with event n (%)	N	Subjects with event n (%)	RR[a] [95% CI] p-value
Mortality					
There were no deaths in the BLOCKSTONE study.					
Morbidity					
symptomatic influenza infection[b,c]	275	10 (3.6)	274	59 (21.5)	0.17 [0.09; 0.32]; < 0.001
positive RT-PCR test for influenza independent of symptoms *(presented additionally)*	275	27 (9.8)	274	81 (29.6)	0.33 [0.22; 0.49]; < 0.001

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A21-22) unless otherwise indicated.
[2] Results for the evaluation-relevant sub-population aged ≥ 12 years and at no risk for influenza-related complications.

Health-related quality of life					
Quality of life was not recorded in the BLOCKSTONE study.					
Side effects					
AEs [d] *(presented additionally)*	275	54 (19.6)	274	49 (17.9)	-
SAEs	275	0 (0)	274	1 (0.4)	-[e]
Discontinuation because of AEs	275	0 (0)	274	1 (0.4)	-[e]

a. RR with CI and p-value: modified Poisson regression adjusted for the time from onset of influenza virus infection of index patient to informed consent, treatment of index patient (baloxavir marboxil, other medication) at start of the study
b. operationalised as fever ≥ 37.5 °C or at least 1 other influenza symptom (cough, sore throat, nasal discharge/nasal congestion, headache, chills, muscle or joint pain, or fatigue with a severity score of "2 (moderate)" or "3 (severe)"), plus positive RT-PCR test
c. No information is available on the frequency of the individual symptoms.
d. Inadequate efficacy (such as the occurrence of influenza virus infection) or a change in influenza symptoms following the occurrence of influenza virus infection have not been documented as AEs unless they were considered severe.
e. no presentation of effect estimate with CI and p-value, as not informative

Abbreviations used: CI: confidence interval; n: number of subjects with (at least 1) event; N: number of subjects evaluated; RCT: randomised controlled trial; RR: relative risk; RT-PCR: reverse transcriptase-polymerase chain reaction; SAE: serious adverse event; AE: adverse event

b) <u>adults and adolescents 12 years of age and above with influenza exposure at risk for influenza-related complications</u>

No adequate data are available to allow an assessment of the additional benefit.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	There are no data.
Morbidity	∅	There are no data.
Health-related quality of life	∅	There are no data.
Side effects	∅	There are no data.

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
↓: statistically significant and relevant negative effect with low/unclear reliability of data
↑↑: statistically significant and relevant positive effect with high reliability of data
↓↓: statistically significant and relevant negative effect with high reliability of data
↔: no statistically significant or relevant difference

∅: There are no usable data for the benefit assessment. n.a.: not assessable

2. Number of patients or demarcation of patient groups eligible for treatment

a) adults and adolescents aged 12 years and above with influenza exposure without risk of influenza-related complications

approx. 1,113,000 to 2,291,000 subjects

b) adults and adolescents 12 years of age and above with influenza exposure at risk for influenza-related complications

approx. 796,000 to 1,640,000 subjects

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Xofluza (active ingredient: baloxavir marboxil) at the following publicly accessible link (last access: 15 July 2021):
https://www.ema.europa.eu/en/documents/product-information/xofluza-epar-product-information_de.pdf

4. Treatment costs

a) adults and adolescents aged 12 years and above with influenza exposure without risk of influenza-related complications

Designation of the therapy	Treatment costs/ subject
Medicinal product to be assessed:	
Baloxavir marboxil[3]	€ 109.60 – € 209.92
Appropriate comparator therapy:	
Monitoring wait-and-see approach	incalculable

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 July 2021)

Costs for additionally required SHI services: not applicable

[3] The range of baloxavir marboxil is based on different doses depending on body weight (< 80 kg bw or ≥ 80 kg bw, respectively)

b) <u>adults and adolescents 12 years of age and above with influenza exposure at risk for influenza-related complications</u>

Designation of the therapy	Treatment costs/ subject
Medicinal product to be assessed:	
Baloxavir marboxil[3]	€ 109.60 – € 209.92
Appropriate comparator therapy:	
Oseltamivir	€ 28.40
Zanamivir	€ 32.21

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 July 2021)

Costs for additionally required SHI services: not applicable