

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Baloxavir marboxil for treating influenza

Draft scope (pre-referral)

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of baloxavir marboxil within its marketing authorisation for treating influenza.

**Background**

Influenza is an acute respiratory illness caused by infection with influenza A and B viruses. It causes significant morbidity and increased mortality. Typical symptoms for uncomplicated influenza are cough, malaise, fever, chills, headache, nasal congestion, sore throat and aching muscles. However, symptoms can range from asymptomatic infection through respiratory illness (particularly bronchitis and pneumonia) to multi-system complications affecting the heart, lungs, brain, liver, kidneys and muscles. Influenza infection is usually self-limiting and lasts for 3-4 days, with some symptoms persisting for 1-2 weeks.

Older people, infants, people who might be immunosuppressed and people with chronic illnesses are more at risk of severe influenza, complications and hospitalisation associated with influenza. People living or working in residential care are at greater risk of infection. Influenza occurs in a seasonal pattern with outbreaks in the winter months, typically between December and March, however the overall burden is difficult to measure because many people do not access healthcare, and virological confirmation is very rarely performed.<sup>1</sup> Influenza-like illness peaked at 17.4 per 100,000 people in England during weeks 5 and 6 in 2019.<sup>2</sup> If this prevalence is applied to the mid-2018 population in England, this equates to a peak weekly flu prevalence of around 9,740. In the UK Severe Influenza Surveillance System (USISS) sentinel hospital surveillance scheme, a total of 5,505 hospitalised confirmed influenza cases were reported across England during week 40 in 2018 to week 15 in 2019. There were 273 deaths from influenza in intensive care units in the same time period.<sup>2</sup>

The treatment of influenza is mainly supportive, consisting of alleviation of symptoms and managing complications that may arise. [NICE technology appraisal 168](#) recommends oseltamivir and zanamivir for the treatment of influenza in adults and children if: national surveillance schemes indicate that influenza virus A or B is circulating; the person is in an 'at-risk' group\*, and; the person has a 'flu-like illness' and can start treatment within 48 hours (or within 36 hours for zanamivir treatment in children) of the first sign of symptoms.

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\* 'At risk' group – people who have one or more of the following: chronic respiratory disease (including asthma and chronic obstructive pulmonary disease), chronic heart disease, chronic renal disease, chronic liver disease, chronic neurological conditions, or diabetes mellitus. People aged 65 years+ and people who might be immunosuppressed are also defined as 'at risk'

### The technology

Baloxavir marboxil (Xofluza, Roche) inhibits cap-dependent endonuclease and transcription of the influenza virus genome, preventing viral replication early in the influenza viral life cycle. It is administered orally.

Baloxavir marboxil does not currently have a marketing authorisation in the UK for treating influenza. It has been studied in clinical trials compared with placebo or oseltamivir in people aged 12 to 64 years with symptomatic influenza.

- One trial included people who were otherwise healthy
- One trial included people who were at high-risk of complications (for example people with asthma, diabetes or comprised immune system)

<b>Intervention</b>	Baloxavir marboxil
<b>Population</b>	People aged 12 years and older with influenza
<b>Comparators</b>	<p>People in an 'at risk' group</p> <ul style="list-style-type: none"> <li>• oseltamivir</li> <li>• zanamivir</li> </ul> <p>People not in an 'at risk' group</p> <ul style="list-style-type: none"> <li>• no anti-viral treatment</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• time to clinical resolution of influenza</li> <li>• length of influenza illness</li> <li>• time to return to normal activities</li> <li>• incidence of influenza-related complications</li> <li>• duration of hospitalisation</li> <li>• incidence of antibiotic treated complications</li> <li>• mortality</li> <li>• virological outcomes</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life</li> </ul>

<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out.</p> <p>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
<b>Other considerations</b>	<p>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<b>Related NICE recommendations and NICE Pathways</b>	<p><b>Related Technology Appraisals:</b></p> <p><a href="#">‘Amantadine, oseltamivir and zanamivir for the treatment of influenza’</a> (2009). NICE Technology Appraisal TA168. Static list.</p> <p><a href="#">‘Oseltamivir, amantadine (review) and zanamivir for the prophylaxis of influenza’</a> (2008). NICE Technology Appraisal 158. Static list.</p> <p><b>Appraisals in development:</b></p> <p><a href="#">‘Peramivir for treating influenza’</a> NICE technology appraisals guidance [ID828]. Suspended.</p> <p><a href="#">‘Intravenous zanamivir for treating influenza in hospital’</a> NICE technology appraisals guidance [ID1196]. Publication date to be confirmed.</p> <p><b>Related NICE Pathways:</b></p> <p>Influenza (2009) NICE pathway  <a href="http://pathways.nice.org.uk/influenza">http://pathways.nice.org.uk/influenza</a></p>
<b>Related National Policy</b>	<p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2018/2019) Chapter 130 Specialist services for children with infectious diseases <a href="#">NHS manual for prescribed specialist services (2018/2019)</a></p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 3.  <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a></p>

### Questions for consultation

Have all relevant comparators for baloxavir marboxil been included in the scope?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom baloxavir marboxil is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which baloxavir marboxil will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider baloxavir marboxil to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of baloxavir marboxil can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at <http://www.nice.org.uk/article/pmg19/chapter/1-Introduction>).

NICE has published an addendum to its guide to the methods of technology appraisal (available at <https://www.nice.org.uk/Media/Default/About/what-we->

[do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf](#)), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

### References

1 Adler et al. '[Incidence and risk factors for influenza-like-illness in the UK: online surveillance using Flusurvey](#)' BMC Infectious Diseases 2014, 14:232. Accessed September 2019

2 Public Health England (2019) '[Flu annual report: winter 2018 to 2019](#)'. Accessed September 2019.