

NICE HTA: Oseltamivir Amantadine and Zanamivir for the prophylaxis of influenza



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Diabetes UK is one of Europe's largest patient organisations. Our mission is to improve the lives of people with diabetes and to work towards a future without diabetes through care, research and campaigning. With a membership of 175,000, including 6,000 health care professionals, Diabetes UK is an active and representative voice of people living with diabetes in the UK.

Facts about diabetes

- Prevalence of diabetes is 2.2 million in the UK.¹
- Diabetes affects the young and old, and has particularly poor outcomes in those of lower socio-economic status and in those from black and minority ethnic groups.^{2,3}
- Evidence is available supporting the need for improved education of people with diabetes and their carers if better control and improved outcomes are to be achieved.^{4,5,6}
- Diabetes, if undetected or not well managed, can lead to many complications and have a devastating impact on quality of life.

Executive Summary

- **All people with diabetes including people treated with diet and lifestyle interventions alone, should be considered as part of a high risk group and should have access to these technologies as part of flu prophylaxis provided it is safe to do so.**
- **The technologies are not a replacement for the flu vaccination but can be considered as an additional option for prophylaxis, particularly where the flu vaccination is contraindicated/inappropriate.**
- **Decisions about which technology to make available to an individual should be reached in partnership with the individual and should include informed patient choice. People with diabetes should have access to information about the risks, benefits, administration method and frequency, side effects, and contraindications to inform their choice.**
- **People with diabetes should be screened for complications to inform the decision making process about which technology to make available. If Amantadine is to be available as a technology for prophylaxis then this should include screening for psychological appropriateness by a competent professional owing to the side effects of depression, anxiety and anorexia noted in the Cochrane Review and eMC.**

Detailed Response

Access to the technologies for the prophylaxis of influenza

It is vital that all people with diabetes, including those who are treated with diet and lifestyle interventions alone, are considered as a high risk group and have access to these technologies as part of prophylaxis for influenza, provided it is safe to do so. Whereas the technologies in question are not a substitute for vaccination, they need to be made available to people with diabetes as another line of prophylaxis, particularly where vaccination is contraindicated in an individual. The Quality Outcome Framework figures for 2006/7 show there is vast variability in the number of people with diabetes recorded as having their flu vaccination, with a range stretching from 15.4 per cent of people with diabetes in one practice to 100 in another⁷. Decisions regarding which

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technology to use should be made in partnership with the individual and be based on the factors discussed below.

Patient Choice

Decisions about which technology to give to a person with diabetes should not be based on cost effectiveness alone. People with diabetes must have access to high quality, objective, information about the technologies, their risks, benefits, administration, side effects and contraindications in order to support them in making a decision in partnership with their healthcare professional about which technology is most appropriate. The importance of access to information about medications has been highlighted by people with diabetes in a report of their views on patient choice⁸. The themes of choice and control, and individuals receiving care tailored to their needs are strongly emphasised in the government health agenda, particularly for people with long term conditions⁹, and decisions about influenza prophylaxis should be incorporated as part of the care planning process and reviewed as appropriate with the individual.

Side effects

Amantadine

Some of the side effects as listed in the eMC¹⁰ and Cochrane Review¹¹ can directly impact on a person with diabetes. The nausea, vomiting, and disturbed sleep (nightmares) can all have an adverse effect on blood glucose control as a result of the malabsorption of food, and stress. Blood glucose control is central to diabetes management and the prevention of diabetes related complications¹². Cardiovascular complications have also been identified, and people with diabetes are at increased risk of developing or having CVD¹².

Amantadine has been associated with side effects that include anxiety, depression and anorexia^{10,11}. People with diabetes are three times more likely to have depression than the general population¹³ and anxiety and eating disorders are also associated with diabetes. At present we are aware that screening for and the treatment of psychological needs in people with diabetes is incredibly variable throughout England and Wales.¹⁴ Diabetes UK recommends that people with diabetes need to have been recently screened for psychological appropriateness by a competent professional before this technology is considered as an option, if it is to be made available for prophylaxis. A decision about suitability of this technology can then be made based on the side effects identified in the eMC for people with an underlying psychiatric disorder, or in light of the fact that anxiety, depression and anorexia can be brought on through use of amantadine in certain circumstances, which could potentially risk exacerbating these conditions where they already exist in an individual.

There is also a quality of life consideration in relation to side effects that prevent an individual from driving. This is of particular consideration where driving is a necessary part of daily life such as for work.¹⁰

Diabetes UK also notes the comments of the recent Cochrane review regarding the use of Amantadine¹¹.

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Oseltamivir

The concerns regarding renal impairment are highlighted in the use of oseltamivir and as dose adjustment is recommended for adults with severe renal insufficiency it is important that the relevant screening and risk assessment for renal complications in people with diabetes is undertaken¹⁰. The use of Oseltamivir is not recommended in people with severe renal impairment and those on dialysis. “There is insufficient clinical data available in children with renal impairment to be able to make any dosing recommendation”.¹⁰

Effects such as nausea, vomiting, particularly noted in young people¹⁵ and the subsequent malabsorption of food or stress, can have negative effects on blood glucose control which is vital for diabetes management and is needed to reduce the risk of developing complications. One Cochrane Review also noted aggravation of diabetes.¹⁶

Arrhythmia has also been noted by Cochrane Review in post marketing surveillance of oseltamivir.¹⁶ This must be considered as people with diabetes are at an increased risk of having or developing CVD.¹²

Convulsions and psychiatric events have also been identified, particularly in young people and children, although these have not been identified as specifically related to depression, anxiety or eating disorders^{10, 15}. The convulsions and psychiatric events have also been noted in those not taking oseltamivir.¹⁰

Zanamivir

Nothing contained within the eMC identifies side effects that relate specifically to people with diabetes, however the Cochrane Review relating to healthy adults did note the possibility of diarrhoea as a side effect of Zanamivir¹⁷. The same issues regarding malabsorption of food apply in relation to the negative effect this can have on blood glucose control and diabetes management.

One Cochrane review also identified oedema and arrhythmia as a side effect¹⁶ and as such again consideration must be given to the fact that people with diabetes are at increased risk of having or developing CVD.

Care should also be taken in relation to existing co-morbidities such as asthma and COPD following the potential side effects affecting these populations.

Method of administration

The technologies contained within this appraisal have various methods and frequency of administration, and the impact of these should also be considered when deciding upon which technology to make available. For example respiratory problems or difficulties swallowing tablets will have a bearing on the technology chosen. In addition the frequency and duration that a person is required to take the medication may impact on health related quality of life considerations, which in turn could impact on work, school, or travel commitments. The issue of how many

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tablets the person is already taking and how well they are managing their medications is also a factor for consideration.

Health related contraindications

The risk to the individual must be evaluated. Pregnancy, lactation and childhood^{10, 15, 16} are three states that will immediately exclude some of the technologies from consideration. People with diabetes are already at increased risk of renal complications and as such kidney function and creatinine clearance are particularly important for the diabetes population. People will need to be screened for complications that could be further aggravated by the technologies, and the results used to inform the decision making process. People with diabetes are at increased risk of micro and macro vascular complications including nephropathy, neuropathy, CVD and retinopathy.

General Comment

It is noted that there is still much debate in the literature regarding the effectiveness and suitability of the technologies in questions, with some reviews and meta analyses questioning the effectiveness of the technologies and others supporting their use. The efficacy of some of the technologies remain unproven in the over 65 population. The incidence of diabetes rises steeply with age with one in 20 people over the age of 65 in the UK having diabetes, and one in five over the age of 85.¹⁸ In light of all this it is relevant to re-emphasise the importance of the flu vaccination as the main form of prophylaxis.

Conclusion

Diabetes UK recommends these technologies are made available to all people with diabetes as a method of influenza prophylaxis within their licensed indications, provided they are a safe and effective method of prophylaxis. They should not detract from the importance of having a flu vaccination, but are recognised as another means of prophylaxis where vaccination is inappropriate. Decisions about which technology is made available to an individual should be based on an informed choice that is made by the individual in partnership with their healthcare professional and considers issues of health related contraindications, administration methods, safety and side effects.

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