

National Institute for Health and Clinical Excellence

071a – Allogeneic pancreatic islet cell transplantation for type 1 diabetes mellitus

Consultation Comments table

IPAC date: 14 February 2008

Comment no.	Consultee name and organisation	Section no.	Comments	Response
1	UK Islet Transplant Consortium	1	Overall the UK Islet Transplant Consortium is very supportive of this useful and appropriately balanced guidance.	Please respond to all comments Thank you for your comment

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2	UK Islet Transplant Consortium psychosocial outcome measures research team	1	<p>Recommendation 1.4 has been formulated from a very narrow conceptualisation of quality of life (QoL). NICE identified only one study assessing QoL. A recent systematic review using targeted search terms (in preparation) identified an additional six studies that assessed QoL as an outcome in islet transplantation. To identify whether outcomes of importance to the patient are impacted by, or benefit from, a particular treatment approach it is important to evaluate the treatment using a reliable, sensitive and valid standardised instrument that assesses the treatment as well as the disease. Existing research has suggested that the full QoL benefits of islet transplantation are not currently known. This is most likely to be a consequence of confounding factors (e.g. small samples) and inappropriate conceptualisation and measurement of QoL. Given the importance of clinically relevant QoL assessment in islet transplantation, it is important that NICE expand their recommendations to suggest that “Further audit and research should address the effect of the procedure on QoL(using appropriate, valid, sensitive and reliable transplant-specific questionnaires) and its long term efficacy ...</p>	<p>Thank you for your comment.</p> <p>Further published evidence is always welcomed.</p> <p>The post consultation literature identified the Toso study (2007) which includes published data on quality of life. This has been added to both the overview and the efficacy section of the guidance.</p>

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3	Diabetes UK	1.1	The provisional recommendations need to include the quality of life and clinical benefits of the procedure for people with Type 1 diabetes to present a fair balance in terms of the efficacy and benefits of the procedure. For example the procedure can improve the likelihood that hypoglycaemia and / or hypoglycaemic unawareness will be resolved, resulting in quality of life benefits including the ability to take on responsibilities that may previously have been avoided and increased freedom and flexibility in lifestyle as an individual may no longer require the presence of a full time carer. In addition clinical benefits include improvements in glycaemic control which in the long term can result in reducing the likelihood of an individual developing the long term complications associated with diabetes.	Thank you for your comment. The recommendations in NICE Interventional Procedures Guidance are not presented in this level of detail. The available evidence on glycaemic control is described in section 2.3, and is available in more detail in the overview
4	Diabetes UK	1.2	This recommendation would benefit from stating that people with diabetes should be given clear, high quality, objective information about the potential risks and benefits of this procedure, in a format they understand in order to make an informed decision in partnership with their healthcare professional team regarding the undertaking of this procedure.	Section 1.2 states that ‘clinicians should ensure that patients understand the potential complications of the procedure and the uncertainty about its efficacy in the long term’. In addition to the guidance, NICE will publish patient information (called ‘Understanding NICE guidance’) that explains the contents of this piece of guidance in lay terms.

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5	Individual Clinician	1.3	Transplant patients cannot be the sole responsibility of primary care or of diabetologists who have no experience in managing immunosuppression. This is because of the risks that immunosuppression entails.	Thank you for your comment. The procedure will only be carried out in specialist centres recognised by the National Commissioning Group in England (Wales, Scotland and Northern Ireland have also made arrangements for the specialist care of their patients, referred to in section 2.5.2 of the guidance.)
6	Diabetes UK	1.4	Diabetes UK has recently funded further research to explore optimised biomedical and psychosocial measures to determine overall outcomes in islet cell transplant recipients. It is important that quality of life considerations include the specific impact of the procedure, what bearing this will have on those undergoing the procedure and treatment satisfaction. Indicators and measures specific to this intervention would be beneficial and are currently under investigation as part of this research	Thank you for your comment. Further published evidence is always welcomed (see section 1.4 of the guidance).
7	Diabetes UK	2.1	2.1.1 More explicit recognition of the procedure's indication in people with intractable hypoglycaemic unawareness is needed to complete the statement.	Thank you for your comment. The Committee noted this comment but did not change the guidance as a result of it
8	Individual Clinician	2.2	Immunosuppressive therapy may be instituted at the time of the procedure, rather than before it in the case of hypoglycaemic unawareness. There is no proven benefit of starting pre-transplant.	Section 2.2.1 now states that immunosuppressive therapy is initiated and continues for the long-term.

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9	Diabetes UK	2.2	2.2.1 The last sentence “insulin therapy may be reduced or stopped” needs to be altered for accuracy to state “insulin therapy may be reduced” as currently people with diabetes having the procedure are kept on a maintenance dose to lengthen the working life of the transplanted islets.	Consider changing section 2.2.1 to ‘nsulin therapy may be reduced’
10	UK Islet Transplant Consortium	2.3	To further reflect the priority of outcome measures recommended by the Specialist Advisers, we suggest minor rewording of 2.3.3 to state: The Specialist Advisers considered key efficacy outcomes to include reduction in hypoglycaemic episodes, improved glycaemic control, maintained C-peptide levels (indicating ongoing graft function) and insulin independence.	Thank you for your comment. Section 2.3 has been amended accordingly..

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11	Diabetes UK	2.3	<p>There are quality of life benefits that have not been considered within the consultation document. These include the benefits that arise from reducing episodes of hypoglycaemia and of restoring hypoglycaemic awareness. The risks posed by hypoglycaemic unawareness and the fear of hypoglycaemia that can arise can have a significant impact on quality of life, restricting the activities an individual may choose to undertake, including activities such as work, driving or physical activity. Some individuals may require a 24 hour carer and activities such as holidays and trips can require significant planning removing opportunities for spontaneity for both the individual and their carer. In addition people with diabetes more generally have spoken about the judgement they have felt from others such as members of the public as a result of having a hypo in public and people not understanding what this is. With the return of hypoglycaemic awareness and reduced hypos individuals are able to enjoy greater freedom and flexibility in their lifestyle. They may undertake activities previously avoided, take on carer responsibilities, previously avoided, and may no longer require a carer. This can increase the individual's sense of independence. Where admission to hospital due to hypoglycaemic events has been an issue for an individual, there is the potential that this will also be reduced.</p>	<p>The post consultation literature identified the Toso study (2007) which includes published data on quality of life. This has been added to both the overview and the efficacy section of the guidance.</p>

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12	Diabetes UK	2.4	The immunosuppressive side-effects could include mouth ulcers and ankle swelling. Individuals will also be at greater risk of opportunistic infections and potentially at increased risk of developing certain types of cancer. This could lead to an increase in the number of medications an individual has to take, and possibly to further contacts with their healthcare professional team or admittance to hospital with more serious infections. This may increase disruption to daily life, although for some the benefits of reduced/ no hypos and the impact on this for other aspects of quality of life may outweigh the costs outlined above. It is important to note some of the side effects will be transient and manageable for some individuals. This will vary from individual to individual, as will which of the side effects are experienced.	Thank you for your comment. The safety outcomes reported are those which are described in the available literature. Side effects relating to immunosuppression fall outside the remit of Interventional Procedures guidance.
13	Individual Clinician	2.4.4	One complication you have not mentioned, but which is increasingly recognised, is sensitisation to human MHC antigens, something that will prejudice future transplants	Thank you for your comment. The Committee noted this comment but did not change the guidance as a result of it

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14	UK Islet Transplant Consortium psychosocial outcome measures research team	2.5	<p>In general, we consider the provisional guidance recommendations presented by NICE to be sufficiently detailed and, largely, an adequate update on the previous NICE guidance. It is encouraging that NICE is eager to understand the benefits/demands of islet cell transplantation from the patients' perspective and we commend NICE for recommending further evaluation of quality of life in islet transplantation. However, the recommendations provide little detail on the assessment of quality of life. In addition, satisfaction with treatment is also an important outcome in its own right as well as a useful proxy measure of adherence to treatment. Satisfaction has not been measured in existing studies. We recommend its systematic evaluation to be included in the recommendations. Both quality of life and treatment satisfaction measures informed by the literature and by patients who have undergone the procedure are under development, thanks to funding from a Diabetes UK grant Establishment of optimised biomedical and psychosocial measures to determine overall outcomes in islet transplant recipients.</p>	<p>Thank you for your comment. The Committee noted the importance of quality of life measures. The post consultation literature identified the Toso study (2007) which includes published data on quality of life. This has been added to both the overview and the efficacy section of the guidance.</p>

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15	Diabetes UK	General	<p>Opening paragraph on the NICE website before the recommendations:</p> <p>Please describe insulin as a substance that helps the control of blood glucose levels and not sugar levels.</p> <p>Type 1 diabetes is not just treatable with insulin injections as Continuous Subcutaneous Insulin Infusion (Insulin Pumps) is used which does not involve insulin injections.</p>	<p>Thank you for your comment.</p> <p>NICE will amend the description of the condition on the website.</p>