

Allogeneic pancreatic islet cell transplantation for type 1 diabetes mellitus

Interventional procedures guidance

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www.nice.org.uk/guidance/ipg257

This guidance partially replaces IPG13.

1 Guidance

This document together with the guidance published on [autologous pancreatic islet cell transplantation for improved glycaemic control after pancreatectomy \(IPG274\)](#) replaces previous guidance IPG013 on pancreatic islet cell transplantation.

- 1.1 The evidence on allogeneic pancreatic islet cell transplantation for type 1 diabetes mellitus shows short-term efficacy with some evidence of long-term efficacy. The evidence on safety shows that serious complications may occur as a result of the procedure. The long-term immunosuppression required is also associated with a risk of adverse events. In units with established experience in allogeneic pancreatic islet cell transplantation, the procedure may be used with normal

arrangements for clinical governance (see also section 2.5.2).

- 1.2 During consent, clinicians should ensure that patients understand the potential complications of the procedure and the uncertainty about its efficacy in the long term. They should provide patients with clear, written information. In addition, use of the Institute's [information for patients](#) ('Understanding NICE guidance') is recommended.
- 1.3 Patient selection for this procedure should involve a multidisciplinary team. Selection criteria should take into account that the procedure is particularly indicated for patients with hypoglycaemia unawareness and/or those already on immunosuppressive therapy because of renal transplantation.
- 1.4 Further audit and research should address the effect of the procedure on quality of life and its long-term efficacy, particularly in relation to the complications of diabetes (see section 3.1).

2 The procedure

2.1 Indications and current treatments

- 2.1.1 Type 1 diabetes mellitus is caused by insufficient insulin secretion and is treated with exogenous insulin. This may result in hypoglycaemic episodes, which are usually easily recognised and treated. In a few people, hypoglycaemia occurs without warning ('hypoglycaemia unawareness'), with life-threatening consequences.

2.2 Outline of the procedure

- 2.2.1 Islet cells are obtained from pancreata of brain-dead donors (two are often required). The patient is started on immunosuppressive therapy, which continues for the long term. Under local anaesthesia (sometimes with sedation) and using imaging guidance, a catheter is inserted percutaneously into the portal vein and the grafted islet cells infused into the liver. More than one infusion may be required.

Sections 2.3 and 2.4 describe efficacy and safety outcomes which were available in the published literature and which the Committee considered as part of the evidence about this procedure. For more details, refer to the Sources of evidence.

2.3 Efficacy

- 2.3.1 A registry study of 112 patients reported that a severe hypoglycaemic episode was experienced by 5% in the year following transplantation compared with 82% in the year prior to transplantation (numbers not reported). In a case series of 36 patients, there were no hypoglycaemic episodes among patients with residual graft function during follow-ups of 1–12 months. A case series of 65 patients reported significantly reduced hypoglycaemia unawareness and improved diabetic control compared with baseline for up to 4 years after transplantation (numbers not reported).
- 2.3.2 In the registry study of 112 patients, 67% and 58% were insulin independent at 6 months and 1 year after transplantation, respectively (numbers not reported). For patients who remained insulin dependent, insulin requirements were reduced by a mean of 57% from baseline at 6 months and 69% at 1 year. In this study, 13% (15/112) of patients had complete graft failure. In the case series of 36 patients, 58% (21/36) achieved insulin independence during a median follow-up of 41 months. However, 76% (16/21) were insulin dependent again after 2 years.
- 2.3.3 A non-randomised controlled trial of 99 patients who had the procedure reported that fear of hypoglycaemic episodes as measured by the 'Hypoglycaemia fear survey' improved significantly following the first infusion of islet cells ($p < 0.00001$).
- 2.3.4 The Specialist Advisers considered key efficacy outcomes to include reduction in hypoglycaemic episodes, improved glycaemic control, normalised C-peptide levels (indicating graft function) and insulin independence.

2.4 Safety

- 2.4.1 Two case series of 65 and 51 patients reported procedure-related intraperitoneal bleeding in 23% (15/65), and 8% (4/51; 7 haemorrhage episodes) of patients. A case series of 36 patients reported intraperitoneal bleeding during 9% (7/77) of infusions. Portal (or branch) vein thrombosis was reported in 8% (5/65), 4% (2/51) and 3% (2/36) of patients, and gall bladder puncture requiring laparotomy in 3% (2/65 and 1/36) of patients.
- 2.4.2 In the registry study of 112 patients, 77 serious adverse events were reported; 22% (17/77) were life-threatening and 58% (45/77) required hospitalisation. Overall, 95% (73/77) of adverse events resolved without residual effects. The authors judged that 17% of all adverse events were related to the infusion procedure and 27% to immunosuppression (numbers not reported).
- 2.4.3 A case report described a patient who died of West Nile virus encephalitis – a potential infection in immunosuppressed patients.
- 2.4.4 The Specialist Advisers considered theoretical adverse events to include haemorrhage, portal vein thrombosis, portal hypertension, immunosuppression-related complications and transmission of donor material containing infectious agents or neoplastic cells.

2.5 Other comments

- 2.5.1 The Committee noted that immunosuppressive regimens and technology for harvesting islet cells continue to evolve.
- 2.5.2 The Committee noted that the National Commissioning Group (NCG), which has a remit to commission highly specialised national services for very rare conditions or treatments for the population of England, has developed service standards for pancreatic islet cell transplantation that are used as the basis for designation and commissioning of these services. Scottish residents also have access to the service under an agreement between the NCG and the National Services Division, Scotland. Health Commission Wales has a separate agreement with the

provider for Welsh residents. The Regional Medical Services Consortium (RMSC) commissions specialist regional services for the population of Northern Ireland. The RMSC will commission outside the region, on an individual basis, in cases for which services are not available in Northern Ireland.

3 Further information

- 3.1 This guidance requires that clinicians or units undertaking the procedure for the first time make special arrangements for audit. NICE has identified relevant audit criteria and developed an [audit tool](#) (which is for use at local discretion).
- 3.2 NICE has issued a clinical guideline on [type 1 diabetes](#) and technology appraisals guidance on [insulin pump therapy for type 1 diabetes](#) and [long-acting insulin analogues for type 1 and 2 diabetes](#). NICE is developing interventional procedures guidance on autologous pancreatic islet cell transplantation for prevention of diabetes after pancreatectomy [Now published as '[Autologous pancreatic islet cell transplantation for improved glycaemic control after pancreatectomy](#)']].

Sources of evidence

The evidence considered by the Interventional Procedures Advisory Committee is described in the [overview](#).

Information for patients

NICE has produced [information on this procedure for patients and carers](#) ('Understanding NICE guidance'). It explains the nature of the procedure and the decision made, and has been written with patient consent in mind.

4 About this guidance

NICE interventional procedure guidance makes recommendations on the safety and efficacy of the procedure. It does not cover whether or not the NHS should fund a

procedure. Funding decisions are taken by local NHS bodies after considering the clinical effectiveness of the procedure and whether it represents value for money for the NHS. It is for healthcare professionals and people using the NHS in England, Wales, Scotland and Northern Ireland, and is endorsed by Healthcare Improvement Scotland for implementation by NHSScotland.

This guidance was developed using the NICE [interventional procedure guidance](#) process.

This guidance together with the guidance published on autologous pancreatic islet cell transplantation for improved glycaemic control after pancreatectomy (IPG274) updates and replaces NICE interventional procedure guidance 013.

It has been incorporated into the [NICE pathway on diabetes](#), along with other related guidance and products.

We have produced a [summary of this guidance for patients and carers](#). Tools to help you put the guidance into practice and information about the evidence it is based on are also [available](#).

Changes since publication

11 January 2012: minor maintenance.

Your responsibility

This guidance represents the views of NICE and was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

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Endorsing organisation

This guidance has been endorsed by [Healthcare Improvement Scotland](#).