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Drugs to prevent the rejection of kidney transplants in children and adolescents

Understanding NICE guidance – information for people undergoing kidney transplants, their families and carers, and the public

Information about NICE Technology Appraisal 99

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Ordering information

You can download the following documents from www.nice.org.uk/TA099

- This booklet.
- The full guidance on this appraisal.
- A short version for healthcare professionals – the quick reference guide.
- The assessment report – details of all the studies that were looked at.

For printed copies of the quick reference guide or information for the public, phone the NHS Response Line on 0870 1555 455 and quote:

- N1024 (quick reference guide)
- N1025 (information for the public).

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What is NICE guidance?

The National Institute for Health and Clinical Excellence (NICE) is the independent organisation responsible for providing national guidance on the promotion of good health and the prevention and treatment of ill health. One of NICE's roles is to produce guidance (recommendations) on the use of medicines, medical equipment, diagnostic tests and clinical and surgical procedures within the NHS.

To produce this guidance, NICE looks at how well the medicine, equipment or procedure works and also how well it works in relation to how much it costs. This process is called an appraisal. The appraisal process involves the manufacturer of the medicine or equipment for which guidance is being produced and the organisations that represent the healthcare professionals, patients and carers who will be affected by the guidance.

NICE was asked to look at the available evidence on the use, in children and adolescents, of drugs called basiliximab, daclizumab, tacrolimus, mycophenolate mofetil, mycophenolate sodium and sirolimus. These belong to a group of drugs known as immunosuppressives that are given to people who have had a kidney transplant to prevent rejection of the new kidney. NICE was asked to provide guidance that will help the NHS in England and Wales decide how to use these drugs in children and adolescents having a kidney transplant.

When is kidney transplantation needed?

The kidneys remove waste products and excess water from the blood. Kidney failure occurs when the kidneys are not working properly. When kidney failure is extremely severe (end-stage kidney failure), the work of the kidneys must be done either by dialysis, or by giving the person a replacement kidney. Replacing a kidney with one from someone who has recently died or from a relative (the donor) is known as kidney transplantation.

What are immunosuppressive drugs?

One problem with kidney transplantation is that the person's immune system (which protects the body from infection) attacks the transplanted kidney. This attack is known as rejection, and it prevents the kidney from working properly. Rejection can be prevented by taking medicines known as immunosuppressive drugs (also called immunosuppressive therapy or immunosuppressants). These drugs weaken the body's immune system, making it less likely to attack the new kidney.

Most people who have a kidney transplant need to take at least one immunosuppressive drug for the rest of their lives.

Immunosuppressive drugs often have side effects, which are more severe for some people than for others. The side effects of the different drugs vary. Some immunosuppressive drugs may damage the transplanted kidney in some people.

Currently, in the UK there is no standard immunosuppressive treatment after kidney transplantation in children or adolescents, but the most common treatment used is a combination of three different drugs. This is called 'triple therapy'. The drugs most commonly used in the triple therapy are:

- ciclosporin – one of a type of drugs known as calcineurin inhibitors
- azathioprine – one of a type of drugs known as antiproliferative agents
- and one drug of a type known as corticosteroids.

There are different stages of immunosuppressive treatment after a kidney transplantation:

- induction therapy – treatment with very high doses of drugs for about 2 weeks after the transplantation (although it is sometimes started just before the operation)
- initial therapy – treatment with high doses of drugs in the first 3 months after transplantation
- maintenance therapy – long-term treatment at lower doses.

Basiliximab, daclizumab, tacrolimus, mycophenolate mofetil, mycophenolate sodium, and sirolimus are newer immunosuppressant drugs than ciclosporin and azathioprine. NICE looked at the evidence on them and considered how they should be used in relation to standard 'triple therapy' to help prevent the rejection of transplanted kidneys in children and adolescents.

What has NICE recommended?

During the appraisal, NICE's Appraisal Committee read and heard evidence from:

- studies of basiliximab, daclizumab, tacrolimus, mycophenolate mofetil, mycophenolate sodium and sirolimus
- doctors with specialist knowledge of immunosuppressive drugs to prevent the rejection of kidney transplants
- individuals with specialist knowledge of the issues affecting children and adolescents undergoing kidney transplantation
- organisations representing the views of people who will be affected by the guidance (because they have, or care for someone with, the condition or because they work in the NHS and are involved in providing care for children or adolescents undergoing a kidney transplant)
- the manufacturers of the immunosuppressive drugs.

The evidence is summarised in the full guidance and additional information about the studies can be found in the assessment report for this appraisal (see 'Further information' section for details).

NICE has made the following recommendations about the use of immunosuppressive drugs in children and adolescents receiving kidney transplants within the NHS in England and Wales.

Basiliximab and daclizumab. Doctors should consider using basiliximab or daclizumab for induction therapy. These drugs should only be used with a combination of other drugs that includes ciclosporin. The cheaper one of the two drugs (basiliximab or daclizumab) should be used, unless there is a medical reason why the patient cannot take the cheaper drug.

Tacrolimus. Tacrolimus is a calcineurin inhibitor and can be used instead of ciclosporin when a person needs a calcineurin inhibitor as part of their initial therapy or maintenance therapy. The choice of tacrolimus or ciclosporin should be made after considering their side effects and how they are likely to affect individual patients. (For example, if a side effect of one drug was likely to lead to a patient not taking their treatment, it might be better to choose the other drug.)

Mycophenolate mofetil. Doctors should consider using mycophenolate mofetil as part of immunosuppressive treatment after kidney transplantation only when a person has to stop taking a calcineurin inhibitor, or has to take a lower dose. This could happen because the calcineurin inhibitor has already damaged the transplanted kidney. It might also be needed for a few weeks or months when there is a high risk that the calcineurin inhibitor would damage the kidney.

NICE considered the use of mycophenolate mofetil with ciclosporin to reduce the amount of corticosteroid needed in the immunosuppressive treatment. (Corticosteroids can contribute to effects such as poor growth and so a doctor might want to try to cut down on the amount of corticosteroid a child or adolescent is taking.)

NICE concluded that mycophenolate mofetil should be used in treatment aimed to cut down on or stop the use of corticosteroids only if the treatment was being carried out as part of a research study known as a 'randomised clinical trial'.

Mycophenolate sodium. NICE does not recommend the use of mycophenolate sodium as part of immunosuppressive regimens for children or adolescents undergoing kidney transplantation.

Sirolimus. NICE does not recommend the use of sirolimus as part of immunosuppressive regimens for children or adolescents undergoing kidney transplantation, except when a patient has had to stop taking calcineurin inhibitors because of their side effects.

By following these recommendations, doctors may sometimes be using drugs in ways that are not covered by their licences[1]. NICE has reminded doctors that, when this happens, they should explain this to the child or adolescent and/or to their parent or guardian, and make sure that they get their consent to the use of the drug in this way.

What should I do next?

If you or someone you care for is about to have or has had a kidney transplant, you should discuss this guidance with your specialist.

Will NICE review its guidance?

Yes. NICE will consider whether to review this guidance in March 2009.

[1] Doctors can legally prescribe unlicensed medicines where there are no suitable alternatives and where use is justified by a responsible body of professional opinion (Royal College of Paediatrics and Child Health, 2000; see www.rcpch.ac.uk)

Further information

The NICE website (www.nice.org.uk) has further information about NICE and the full guidance on immunosuppressive therapy for renal transplantation in children and adolescents that has been issued to the NHS. The assessment report, which contains details of the studies that were looked at, is also available from the NICE website. A short version of the guidance (a 'quick reference guide') is available on the website and from the NHS Response Line (phone 0870 1555 455 and quote reference number N1024).

NICE issued guidance on immunosuppressive drugs for adults undergoing renal transplantation in September 2004. You can find details on the NICE website (www.nice.org.uk/TA085) or order a copy of the information for the public from the NHS Response Line (quote reference number N0543).

If you have access to the Internet, you can find more information about kidney failure and kidney transplants on the NHS Direct website (www.nhsdirect.nhs.uk). You can also phone NHS Direct on 0845 46 47.

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