NICE Update Bulletin October 2017

Hyperlinks to the relevant NICE web page are included.

Details are also available from the NICE website (**http://www.nice.org.uk**)

Type	Guidance title and reference number
Technology Appraisals (TAs)	**Immunosuppressive therapy for kidney transplant in children and young people TA482** **Recommendations** 1.1 Basiliximab, when used as part of an immunosuppressive regimen that includes a calcineurin inhibitor, is recommended as an initial option to prevent organ rejection in children and young people having a kidney transplant. 1.2 Immediate-release tacrolimus, when used as part of an immunosuppressive regimen, is recommended as an initial option to prevent organ rejection in children and young people having a kidney transplant. Treatment should normally be started with the least expensive product. However, treatment can be started with an alternative dosage form if the least expensive product is not suitable (for example, if the child or young person is not able to swallow capsules or they are unable to have a particular ingredient because of allergy or religious reasons). Tacrolimus granules for oral suspension (Modigraf) should be used only if the company provides it at the same price or lower than that agreed with the Commercial Medicines Unit. 1.3 Mycophenolate mofetil, when used as part of an immunosuppressive regimen, is recommended as an initial option to prevent organ rejection in children and young people having a kidney transplant. Treatment should normally be started with the least expensive product. However, treatment can be started with an alternative dosage form if the least expensive product is not suitable (for example, if the child or young person is not able to swallow capsules or they are unable to have a particular ingredient because of allergy or religious reasons). 1.4 Rabbit anti-human thymocyte immunoglobulin, prolonged-release tacrolimus, mycophenolate sodium, sirolimus, everolimus and belatacept are not recommended as initial treatments to prevent organ rejection in children and young people having a kidney transplant. 1.5 The committee was unable to make recommendations on any of the technologies considered in this appraisal as options for preventing organ rejection in children or young people who are, or become, unable to have the technologies recommended in sections 1.1 to 1.3 or azathioprine and corticosteroids (for example, because of treatment failure, contraindications, or intolerance such as nephrotoxicity associated with calcineurin inhibitors, or thrombotic microangiopathy). This includes children and young people who: • are unable to continue having their initial therapy and need to switch to another therapy during the life of their graft or • have a second or subsequent transplant, having previously found that 1 or more of the recommended initial treatments or standard treatments are clinically unsuitable, for example because of treatment failure, contraindications or intolerance.

1.6 These recommendations are not intended to affect treatment with any of the technologies in this appraisal that was started in the NHS before this guidance was published. Children and young people having treatment outside these recommendations, or for whom the committee were unable to make a recommendation, may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop. This decision should be made jointly by the clinician and the child or young person or their parents or carers.

The technologies

Basiliximab is a monoclonal antibody that acts as an interleukin-2 receptor antagonist. It has a marketing authorisation in the UK for the prophylaxis of acute organ rejection in people having a kidney transplant. The indication includes children and young people aged 1 to 17 years.

Rabbit anti-human thymocyte immunoglobulin is made by injecting human thymus cells into rabbits. The drug contains immunoglobulins (antibodies) that attach to and destroy some of the cells of the immune system. It has a marketing authorisation in the UK for the prevention of graft rejection in kidney transplant. The summary of product characteristics states that it is usually used with other immunosuppressive drugs, but does not state whether the indication includes children and young people.

Some drugs in this appraisal contain the same active ingredient but in different formulations. Tacrolimus is a calcineurin inhibitor and is available in an immediate-release formulation and a prolonged-release formulation. Mycophenolic acid is an antiproliferative agent. It is available as a prodrug called mycophenolate mofetil and a sodium salt called mycophenolate sodium.

Belatacept is a soluble fusion protein designed to selectively inhibit CD28-mediated co-stimulation of T-cells. Belatacept, in combination with corticosteroids and a mycophenolic acid, has a marketing authorisation in the UK for prophylaxis of graft rejection in adults having a kidney transplant. The summary of product characteristics recommends that an interleukin-2 receptor antagonist is added to this belatacept-based regimen. It also states that the safety and efficacy of belatacept in children and adolescents under 18 years have not yet been established and that no data are available.

Sirolimus is an antiproliferative that blocks a protein called mammalian target of rapamycin (mTOR). It has a marketing authorisation in the UK for the prophylaxis of organ rejection in adults having a kidney transplant, who are at low to moderate immunological risk. It is recommended to be used initially with ciclosporin and corticosteroids for 2 to 3 months, and may be continued only if ciclosporin can be progressively discontinued. The summary of product characteristics states that the safety and efficacy of sirolimus in children and adolescents under 18 years have not been established.

Everolimus is an antiproliferative that blocks mTOR. It has a marketing authorisation for the prophylaxis of organ rejection in adults having a kidney transplant, who are at low to moderate immunological risk. The summary of product characteristics states that everolimus should be used with ciclosporin and corticosteroids. Everolimus is administered orally as a tablet. The recommended initial dose for adults is 1.5 mg/day. The summary of product characteristics states that there is insufficient experience to recommend the use of everolimus in children and adolescents.

Financial factors

These technologies are commissioned by NHS England.

NICE does not expect this guidance to have a significant impact on resources; that is, it will be less than £5m per year in England (or £9,100 per 100,000 population). This is because they do not anticipate a significant change in practice as a result of the guidance. The recommended immunosuppressive therapy treatments are already available in the NHS for children and young people having a kidney transplant.

Immunosuppressive therapy for kidney transplant in adults TA481

Recommendations

1.1 Basiliximab, when used as part of an immunosuppressive regimen that includes a calcineurin inhibitor, is recommended as an initial option to prevent organ rejection in adults having a kidney transplant.

1.2 Immediate-release tacrolimus, when used as part of an immunosuppressive regimen, is recommended as an initial option to prevent organ rejection in adults having a kidney transplant. Treatment should normally be started with the least expensive product. However, treatment can be started with an alternative dosage form if the least expensive product is not suitable (for example, if the person is not able to swallow capsules as a result of a disability or they are unable to have a particular ingredient because of allergy or religious reasons). Tacrolimus granules for oral suspension (Modigraf) should be used only if the company provides it at the same price or lower than that agreed with the Commercial Medicines Unit.

1.3 Mycophenolate mofetil, when used as part of an immunosuppressive regimen, is recommended as an initial option to prevent organ rejection in adults having a kidney transplant. Treatment should normally be started with the least expensive product. However, treatment can be started with an alternative dosage form if the least expensive product is not suitable (for example, if the person is not able to swallow capsules as a result of a disability or they are unable to have a particular ingredient because of allergy or religious reasons).

1.4 Rabbit anti-human thymocyte immunoglobulin, prolonged-release tacrolimus, mycophenolate sodium, sirolimus, everolimus and belatacept are not recommended as initial treatments to prevent organ rejection in adults having a kidney transplant.

1.5 The committee was unable to make recommendations on any of the technologies considered in this appraisal as options for preventing organ rejection in adults who are, or become, unable to have the technologies recommended in sections 1.1 to 1.3 or standard triple therapy with ciclosporin, azathioprine and a corticosteroid (for example, because of treatment failure, contraindications, or intolerance such as nephrotoxicity associated with calcineurin inhibitors, or thrombotic microangiopathy). This includes adults who:

- are unable to continue having their initial therapy and need to switch to another therapy during the life of their graft or
- have a second or subsequent transplant, having previously found that 1 or more of the recommended initial treatments or standard treatments are clinically unsuitable for example, because of treatment failure, contraindications or intolerance.

1.6 These recommendations are not intended to affect treatment with any of the technologies in this appraisal that was started in the NHS before this guidance was published. Adults having treatment outside these recommendations, or for whom the committee were unable to make a recommendation, may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

The technologies

Basiliximab is a monoclonal antibody that acts as an interleukin-2 receptor antagonist. It has a marketing authorisation in the UK for the prophylaxis of acute organ rejection in adults having a kidney transplant.

Rabbit anti-human thymocyte immunoglobulin is made by injecting human thymus cells into rabbits. The drug contains immunoglobulins (antibodies) that attach to and destroy some of the cells of the immune system. It has a marketing authorisation in the UK for the prevention of graft rejection in kidney transplant.

Some drugs in this appraisal contain the same active ingredient but in different formulations. Tacrolimus is a calcineurin inhibitor and is available in an immediate-release formulation and a prolonged-release formulation. Mycophenolic acid is an antiproliferative agent. It is available as a prodrug called mycophenolate mofetil and a sodium salt called mycophenolate sodium.

Belatacept is a soluble fusion protein designed to selectively inhibit CD28-mediated co-stimulation of T-cells. Belatacept, in combination with corticosteroids and a mycophenolic acid, has a marketing authorisation in the UK for prophylaxis of graft rejection in adults having a kidney transplant.

Sirolimus is an antiproliferative that blocks a protein called mammalian target of rapamycin (mTOR). It has a marketing authorisation in the UK for the prophylaxis of organ rejection in adults having a kidney transplant, who are at low to moderate immunological risk.

Everolimus is an antiproliferative that blocks mTOR. It has a marketing authorisation for the prophylaxis of organ rejection in adults having a kidney transplant, who are at low to moderate immunological risk.

Financial factors

These technologies are commissioned by NHS England.

NICE does not expect this guidance to have a significant impact on resources; that is, it will be less than £5m per year in England (or £9,100 per 100,000 population). This is because they do not anticipate a significant change in practice as a result of the guidance. The recommended immunosuppressive therapy treatments are already available on the NHS for adults having a kidney transplant.

Tofacitinib for moderate to severe rheumatoid arthritis TA480

Recommendations

1.1 Tofacitinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to intensive therapy with a combination of conventional disease-modifying anti-rheumatic drugs (DMARDs), only if:

- disease is severe (a disease activity score [DAS28] of more than 5.1) and
- the company provides tofacitinib with the discount agreed in the patient access scheme.

1.2 Tofacitinib, with methotrexate, is recommended as an option for treating active rheumatoid arthritis in adults whose disease has responded inadequately to, or who cannot have, other DMARDs, including at least 1 biological DMARD, only if:

- disease is severe (a DAS28 of more than 5.1) and
- they cannot have rituximab and
- the company provides tofacitinib with the discount agreed in the patient access scheme.

1.3 Tofacitinib can be used as monotherapy for adults who cannot take methotrexate because it is contraindicated or because of intolerance, when the criteria in sections 1.1 and 1.2 are met.

1.4 Continue treatment only if there is a moderate response measured using European League Against Rheumatism (EULAR) criteria at 6 months after starting therapy. After an initial response within 6 months, withdraw treatment if at least a moderate EULAR response is not maintained.

1.5 These recommendations are not intended to affect treatment with tofacitinib that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

The technology

Tofacitinib in combination with methotrexate has a marketing authorisation in the UK for the 'treatment of moderate to severe active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs'. Tofacitinib can be given as monotherapy in patients who are intolerant to methotrexate or when treatment with methotrexate is inappropriate.

Financial factors

This technology is commissioned by CCGs.

NICE does not expect this guidance to have a significant impact on resources; that is, it will be less than £5 million per year in England (or £9,100 per 100,000 population). This is because the technology is an option alongside current standard treatment options.

Reslizumab for treating severe eosinophilic asthma TA479

Recommendations

1.1 Reslizumab, as an add-on therapy, is recommended as an option for the treatment of severe eosinophilic asthma that is inadequately controlled in adults despite maintenance therapy with high-dose inhaled corticosteroids plus another drug, only if:

- the blood eosinophil count has been recorded as 400 cells per microlitre or more
- the person has had 3 or more severe asthma exacerbations needing systemic corticosteroids in the past 12 months and
- the company provides reslizumab with the discount agreed in the patient access scheme.

1.2 At 12 months:

- stop reslizumab if the asthma has not responded adequately or
- continue reslizumab if the asthma has responded adequately and assess response each year.

An adequate response is defined as:

- a clinically meaningful reduction in the number of severe exacerbations needing systemic corticosteroids or
- a clinically significant reduction in continuous oral corticosteroid use while maintaining or improving asthma control.

1.3 These recommendations are not intended to affect treatment with reslizumab that was started in the NHS before this guidance was published. Adults having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

The technology

Reslizumab is an interleukin-5 inhibitor that reduces eosinophil numbers and activity.

Financial factors

This technology is commissioned by NHS England.

The list price is £499.99 per 100 mg vial and £124.99 per 25 mg vial (excluding VAT). The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of reslizumab, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. Dose is given intravenously every four weeks at 3mg/kg. The default annual cost for a 78kg patient is £15,248.78 per annum (no VAT or discount applied).

Brentuximab vedotin for treating relapsed or refractory systemic anaplastic large cell lymphoma TA478

Recommendations

1.1 Brentuximab vedotin is recommended as an option for treating relapsed or refractory systemic anaplastic large cell lymphoma in adults, only if:

- they have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 and
- the company provides brentuximab vedotin according to the commercial access agreement with NHS England.

1.2 When using ECOG performance status, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect ECOG performance status and make any adjustments they consider appropriate.

1.3 These recommendations are not intended to affect treatment with brentuximab vedotin that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

The technology

Brentuximab vedotin is indicated for 'the treatment of adult patients with relapsed or refractory systemic anaplastic large cell lymphoma'.

Brentuximab vedotin has been available to patients in England through the Cancer Drugs Fund (CDF) since April 2013 for relapsed or refractory systemic anaplastic large cell lymphoma.

Financial factors

This technology is commissioned by NHS England.

NICE does not expect this guidance to have a significant impact on resources; that is, it will be less than £5 million per year in England (or £9,100 per 100,000 population). This is because the population size is small (around 160 people per year in England are estimated to be eligible and less than 50 people are anticipated to have brentuximab vedotin, based on the current usage in the CDF).

	Autologous chondrocyte implantation for treating symptomatic articular cartilage defects of the knee TA477 This guidance replaces NICE technology appraisal guidance 89 on the use of autologous chondrocyte implantation for the treatment of cartilage defects in the knee joints. **Recommendations** 1.1 Autologous chondrocyte implantation (ACI) is recommended as an option for treating symptomatic articular cartilage defects of the knee, only if: • the person has not had previous surgery to repair articular cartilage defects • there is minimal osteoarthritic damage to the knee (as assessed by clinicians experienced in investigating knee cartilage damage using a validated measure for knee osteoarthritis) • the defect is over 2 cm^2 and • the procedure is done at a tertiary referral centre. **The technologies** The OsCell John Charnley Laboratory has approval from the Medicines and Healthcare products Regulatory Agency to provide **traditional ACI services** under a hospital exemption from the advanced therapy medicinal products regulation for products prepared on a non-routine basis. It also has approval from the Human Tissues Authority for procuring, testing, storing and importing human tissues and cells for human application, and storing relevant material that has come from a human body for use for a scheduled purpose. The indication for use of traditional ACI in the knee is for the repair of single or multiple symptomatic, full-thickness cartilage defects of the joint with or without bone involvement in adults. Traditional ACI involves implanting a cell suspension under either a periosteal- or collagen-based membrane. Traditional ACI can be considered when the Oswestry Risk of Knee Arthroplasty (ORKA) score is 3 or 4, but only when other factors can be corrected, for example, using meniscal allograft or realignment osteotomy. **Matrix-associated chondrocyte implantation** (MACI) had a European marketing authorisation for the repair of symptomatic, full-thickness cartilage defects of the knee (grades III and IV of the Modified Outerbridge Scale) between 3 cm2 and 20 cm2. The marketing authorisation is currently suspended while Vericel validates a new site for culturing cells. **ChondroCelect** had a European marketing authorisation for repair of symptomatic cartilage defects of the femoral condyle of the knee (International Cartilage Repair Society grades III or IV), which was withdrawn by TiGenix during the course of this appraisal for commercial reasons. **Financial factors** This technology is commissioned by NHS England. NICE estimates that nationally 500 people with symptomatic articular cartilage defects of the knee are eligible for ACI each year at a unit cost of £20,717.
Highly specialised technology guidance (HSTs)	None published so far this month.
NICE Guidelines (NGs)	**Sinusitis (acute): antimicrobial prescribing NG79** This guideline sets out an antimicrobial prescribing strategy for acute sinusitis. It aims to limit antibiotic use and reduce antimicrobial resistance. Acute sinusitis is

usually caused by a virus, lasts for about 2 to 3 weeks, and most people get better without antibiotics. Withholding antibiotics rarely leads to complications.

The guideline includes recommendations on:

- managing symptoms, including advice when an antibiotic is not needed and the use of corticosteroids and nasal sprays
- choice of antibiotic when a back-up or immediate prescription is needed
- self-care

Cystic fibrosis: diagnosis and management NG78

This guideline covers diagnosing and managing cystic fibrosis. It specifies how to monitor the condition and manage the symptoms to improve quality of life. There are also detailed recommendations on treating the most common infections in people with cystic fibrosis.

The guideline includes recommendations on:

- diagnosis
- service delivery, including how to organise services and multidisciplinary teams
- annual and routine reviews
- monitoring, assessment and management, including for lung disease, pulmonary infection, distal intestinal obstruction syndrome, liver disease and cystic-fibrosis-related diabetes
- preventing cross-infection

Cataracts in adults: management NG77

This guideline covers managing cataracts in adults aged 18 and over. It aims to improve care before, during and after cataract surgery by optimising service organisation, referral and surgical management, and reducing complications. It further aims to improve the availability of information for people with cataracts before, during and after cataract surgery.

The guideline includes recommendations on:

- patient information
- referral for cataract surgery
- preoperative assessment and biometry
- preventing wrong lens implant errors
- surgical timing and technique
- preventing and managing complications
- postoperative assessment

Hepatitis B (chronic): diagnosis and management CG165 (update)

This guideline covers assessing and managing chronic hepatitis B in children, young people and adults. It aims to improve care for people with hepatitis B by specifying which tests and treatments to use for people of different ages and with different disease severities.

October 2017: NICE changed a footnote to update the information on UK marketing authorisations for entecavir.

Child abuse and neglect NG76

This guideline covers recognising and responding to abuse and neglect in children and young people aged under 18. It covers physical, sexual and emotional abuse, and neglect. The guideline aims to help anyone whose work brings them into contact with children and young people to spot signs of abuse and neglect and to know how to respond. It also supports practitioners who carry out assessments and

	provide early help and interventions to children, young people, parents and carers. The guideline includes recommendations on: • principles for working with children, young people, parents and carers • factors that increase vulnerability to child abuse and neglect • recognising child abuse and neglect • assessing risk and need • early help for families showing possible signs of child abuse or neglect • multi-agency response to child abuse and neglect • therapeutic interventions for children, young people and families after child abuse and neglect • planning and delivering services **Child maltreatment: when to suspect maltreatment in under 18s CG89 (update)** This guideline covers the signs of possible child maltreatment in children and young people aged under 18 years. It aims to raise awareness and help health professionals who are not child protection specialists to identify the features of physical, sexual and emotional abuse, neglect and fabricated or induced illness. **October 2017:** NICE published a guideline on child abuse and neglect. Recommendations relevant to both health and social care practitioners appear in this guideline and the child abuse and neglect guideline. Clinical features (including physical injuries) are covered in this guideline. Minor edits were made to a number of to recommendations in line with NICE's child abuse and neglect guideline. They also added a link to recommendation 1.3.6 to the NICE guideline on faltering growth. Recommendation 1.4.8 was also updated with information on Prader–Willi syndrome.
NICE Public Health Guidelines	None published so far this month.
NICE Medicines Practice Guidelines (MPGs)	None published so far this month.
Interventional Procedures Guidance (IPGs)	None published so far this month.
Medical Technologies Guidance	None published so far this month.
Diagnostics Guidance	None published so far this month.
NICE Quality Standards	**Cerebral palsy in children and young people QS162** This quality standard covers diagnosing, assessing and managing cerebral palsy in children and young people under 25. It describes high-quality care in priority areas for improvement.

Current NICE consultations with links and end dates for stakeholders to contribute

Title / link	End date of consultation
Lyme disease	06/11/2017
Social and emotional wellbeing: early years	06/11/2017
Nivolumab for treating metastatic or unresectable urothelial cancer after platinum-based chemotherapy [ID995]	09/11/2017
Memokath-051 stent for the treatment of ureteric obstruction	09/11/2017
Lenvatinib and sorafenib for treating differentiated thyroid cancer after radioactive iodine [ID1059]	10/11/2017
Thyroid disease: assessment and management	13/11/2017
Strimvelis for treating severe combined immunodeficiency caused by adenosine deaminase deficiency [ID926]	13/11/2017
Thopaz+ portable digital system for managing chest drains	13/11/2017
Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism (Update)	15/11/2017
Postnatal care up to 8 weeks after birth (update)	15/11/2017
Adjunctive colposcopy technologies for assessing suspected cervical abnormalities (update of DG4)	16/11/2017
Learning disabilities and behaviour that challenges: service design and delivery	20/11/2017
Persistent pain: assessment and management	22/11/2017
Ab interno supraciliary microstent insertion with phacoemulsification for primary open-angle glaucoma	23/11/2017
MRI-guided focused ultrasound thalamotomy for treatment-resistant essential tremor	23/11/2017
MRI-guided focused ultrasound thalamotomy for moderate-to-severe tremor in Parkinson's disease	23/11/2017
Aortic valve reconstruction with processed bovine pericardium	23/11/2017
Venous thromboembolic diseases: diagnosis, management and thrombophilia testing (2019)	13/02/2018

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