





Impetigo: antimicrobial prescribing

NICE guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

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Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should <u>assess and reduce the environmental impact of implementing NICE recommendations</u> wherever possible.

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Overview

This guideline sets out an antimicrobial prescribing strategy for adults, young people and children aged 72 hours and over with impetigo. It aims to optimise antibiotic use and reduce antibiotic resistance.

For managing other skin and soft tissue infections, see the <u>NICE topic pages on skin</u> conditions and infections.

We have also produced guidelines on antimicrobial prescribing for cellulitis and erysipelas and antimicrobial stewardship: systems and processes for effective antimicrobial medicine use.

Who is it for?

- Healthcare professionals
- · People with impetigo, their families and carers

Recommendations

1.1 Managing impetigo

Advice to reduce the spread of impetigo

1.1.1 Advise people with impetigo, and their parents or carers if appropriate, about good hygiene measures to reduce the spread of impetigo to other areas of the body and to other people.

For a short explanation of why the committee made the recommendation, see the rationale section on advice to reduce the spread of impetigo.

Full details of the evidence and the committee's discussion are in evidence review.

Initial treatment

Localised non-bullous impetigo

- 1.1.2 Consider hydrogen peroxide 1% cream for people with localised <u>non-bullous</u> impetigo who are not systemically unwell or at high risk of complications (see recommendations on choice of antimicrobial). Although other topical antiseptics are available for treating superficial skin infections, no evidence was found for using them to treat impetigo.
- 1.1.3 If hydrogen peroxide 1% cream is unsuitable, offer a short course of a topical antibiotic for people with localised non-bullous impetigo who are not systemically unwell or at high risk of complications (see recommendations on choice of antimicrobial).

Widespread non-bullous impetigo

- 1.1.4 Offer a short course of a topical or oral antibiotic for people with widespread non-bullous impetigo who are not systemically unwell or at high risk of complications (see <u>recommendations on choice of antimicrobial</u>). Take into account:
 - that topical and oral antibiotics are both effective at treating impetigo
 - the preferences of the person and, if appropriate, their parents or carers, including the practicalities of administration (particularly to large areas) and possible adverse effects
 - previous use of topical antibiotics because antimicrobial resistance can develop rapidly with extended or repeated use.

Bullous impetigo or impetigo in people who are systemically unwell or at high risk of complications

- 1.1.5 Offer a short course of an oral antibiotic for:
 - all people with bullous impetigo
 - people with non-bullous impetigo who are systemically unwell or at high risk of complications.

See recommendations on choice of antimicrobial.

Combination treatment

1.1.6 Do not offer combination treatment with a topical and oral antibiotic to treat impetigo.

For a short explanation of why the committee made these recommendations, see the rationale section on initial treatment.

Full details of the evidence and the committee's discussion are in evidence review.

Advice on treatment

1.1.7 Advise people with impetigo, and their parents or carers if appropriate, to seek medical help if symptoms worsen rapidly or significantly at any time, or have not improved after completing a course of treatment.

Reassessment and further treatment

- 1.1.8 Reassess people with impetigo if their symptoms worsen rapidly or significantly at any time or have not improved after completing a course of treatment.
- 1.1.9 When reassessing people with impetigo, take account of:
 - other possible diagnoses, such as herpes simplex
 - any symptoms or signs suggesting a more serious illness or condition, such as cellulitis
 - previous antibiotic use, which may have led to resistant bacteria.
- 1.1.10 For people with impetigo that is worsening or has not improved after treatment with hydrogen peroxide 1% cream, offer:
 - a short course of a topical antibiotic if the impetigo remains localised or
 - a short course of a topical or oral antibiotic if the impetigo has become widespread (see the <u>recommendation on widespread non-bullous impetigo</u>).
- 1.1.11 For people with impetigo that is worsening or has not improved after completing a course of topical antibiotics:
 - offer a short course of an oral antibiotic (see the <u>recommendations on choice</u> of <u>antimicrobial</u>) and
 - consider sending a skin swab for microbiological testing.
- 1.1.12 For people with impetigo that is worsening or has not improved after completing a course of oral antibiotics, consider sending a skin swab for microbiological testing.

- 1.1.13 For people with impetigo that recurs frequently:
 - send a skin swab for microbiological testing and
 - consider taking a nasal swab and starting treatment for <u>decolonisation</u>.
- 1.1.14 If a skin swab has been sent for microbiological testing:
 - review the choice of antibiotic when results are available and
 - change the antibiotic according to results if symptoms are not improving, using a narrow-spectrum antibiotic if possible.

For a short explanation of why the committee made these recommendations, see the rationale section on reassessment and further treatment for impetigo.

Full details of the evidence and the committee's discussion are in evidence review.

Referral and seeking specialist advice

- 1.1.15 Refer to hospital:
 - people with impetigo and any symptoms or signs suggesting a more serious illness or condition (for example, cellulitis)
 - people with widespread impetigo who are immunocompromised.
- 1.1.16 Consider referral or seeking specialist advice for people with impetigo if they:
 - have bullous impetigo, particularly in babies (aged 1 year and under)
 - have impetigo that recurs frequently
 - are systemically unwell
 - are at high risk of complications.

For a short explanation of why the committee made these recommendations, see the rationale section on referral and seeking specialist advice for impetigo.

Full details of the evidence and the committee's discussion are in evidence review.

1.2 Choice of antimicrobial

- 1.2.1 When prescribing an antimicrobial for impetigo, take account of local antimicrobial resistance data when available and follow:
 - Table 1 for adults aged 18 years and over
 - Table 2 for children and young people under 18 years.

Table 1 Antimicrobials for adults aged 18 years and over

Treatment	Antimicrobial, dosage and course length
Topical antiseptic	Hydrogen peroxide 1%: Apply two or three times a day for 5 days
First-choice topical antibiotic if hydrogen peroxide is unsuitable (for example, if impetigo is around eyes) or ineffective	Fusidic acid 2%: Apply three times a day for 5 days
Alternative topical antibiotic if fusidic acid resistance is suspected or confirmed	Mupirocin 2%: Apply three times a day for 5 days
First-choice oral antibiotic	Flucloxacillin: 500 mg four times a day for 5 days

Treatment	Antimicrobial, dosage and course length
Alternative oral antibiotic for penicillin allergy or if flucloxacillin is unsuitable (for people who are not pregnant)	Clarithromycin: 250 mg twice a day for 5 days (the dosage can be increased to 500 mg twice a day, if needed for severe infections)
Alternative oral antibiotic for penicillin allergy in pregnancy	Erythromycin: 250 mg to 500 mg four times a day for 5 days Erythromycin is preferred if a macrolide is needed in pregnancy, for example, if there is true penicillin allergy and the benefits of antibiotic treatment outweigh the harms. See the Medicines and Healthcare products Regulatory Agency (MHRA) Public Assessment Report on the safety of macrolide antibiotics in pregnancy.
If meticillin-resistant Staphylococcus aureus is suspected or confirmed	Consult a local microbiologist

See the <u>BNF</u> for appropriate use and dosing in specific populations, for example, in people with hepatic or renal impairment, and in pregnancy and breastfeeding.

A 5-day course is usually appropriate but can be increased to 7 days based on clinical judgement, depending on the severity and number of lesions.

Other topical antiseptics besides hydrogen peroxide are available for superficial skin infections, but no evidence was found for these in impetigo

As with all antibiotics, extended or recurrent use of topical fusidic acid or mupirocin may increase the risk of developing antimicrobial resistance. See the <u>BNF</u> for more information.

Table 2 Antimicrobials for children and young people under 18 years

Treatment	Antimicrobial, dosage and course length
Tanical anticontic	Hydrogen peroxide 1%:
Topical antiseptic	Apply two or three times a day for 5 days

Treatment	Antimicrobial, dosage and course length
First-choice topical antibiotic if hydrogen peroxide is unsuitable (for example, if impetigo is around eyes) or ineffective	Fusidic acid 2%: Apply three times a day for 5 days
Alternative topical antibiotic if fusidic acid resistance is suspected or confirmed	Mupirocin 2%: Apply three times a day for 5 days
	Flucloxacillin (oral solution or capsules):
First-choice oral antibiotic	1 month to 1 year, 62.5 mg to 125 mg four times a day for 5 days
	2 years to 9 years, 125 mg to 250 mg four times a day for 5 days
	10 years to 17 years, 250 mg to 500 mg four times a day for 5 days
	Clarithromycin:
	1 month to 11 years:
Alternative oral antibiotic for	under 8 kg, 7.5 mg/kg twice a day for 5 days
penicillin allergy or if flucloxacillin is unsuitable (for people who are not pregnant; for example, if an oral solution is unpalatable and the child is unable to swallow capsules)	8 kg to 11 kg, 62.5 mg twice a day for 5 days
	12 kg to 19 kg, 125 mg twice a day for 5 days
	20 kg to 29 kg, 187.5 mg twice a day for 5 days
	30 kg to 40 kg, 250 mg twice a day for 5 days
	12 years to 17 years, 250 mg twice a day for 5 days (the dosage can be increased to 500 mg twice a day, if needed for severe infections)

Treatment	Antimicrobial, dosage and course length
	Erythromycin:
	8 years to 17 years, 250 mg to 500 mg four times a day for 5 days
Alternative oral antibiotic for penicillin allergy in pregnancy	Erythromycin is preferred if a macrolide is needed in pregnancy, for example, if there is true penicillin allergy and the benefits of antibiotic treatment outweigh the harms. See the Medicines and Healthcare products Regulatory Agency (MHRA) Public Assessment Report on the safety of macrolide antibiotics in pregnancy.
If meticillin-resistant Staphylococcus aureus is suspected or confirmed	Consult a local microbiologist

See the <u>BNF for Children</u> for appropriate use and dosing in specific populations, for example, in people with hepatic or renal impairment, and in pregnancy and breastfeeding. Dosing in some age groups may be <u>off-label</u>.

The age bands apply to children of average size and, in practice, the prescriber will use the age bands with other factors such as the severity of the condition being treated and the child's size in relation to the average size of children of the same age.

A 5-day course is usually appropriate but can be increased to 7 days based on clinical judgement, depending on the severity and number of lesions.

Other topical antiseptics besides hydrogen peroxide are available for superficial skin infections, but no evidence was found for these in impetigo.

Licenses for mupirocin use in infants vary between products. See individual summaries of product characteristics for details.

As with all antibiotics, extended or recurrent use of topical fusidic acid or mupirocin may increase the risk of developing antimicrobial resistance. See the <u>BNF for Children</u> for more information.

If flucloxacillin oral solution is not tolerated because of poor palatability, consider capsules

(see the Medicines for Children leaflet on helping your child to swallow tablets).

For a short explanation of why the committee made this recommendation, see the rationale section on choice of antimicrobial for impetigo.

Full details of the evidence and the committee's discussion are in evidence review.

Terms used in the guideline

Non-bullous impetigo

Impetigo characterised by thin-walled vesicles or pustules that rupture quickly, forming a golden-brown crust.

Bullous impetigo

Impetigo characterised by the presence of fluid-filled vesicles and blisters often with a diameter of over 1 cm that rupture, leaving a thin, flat, yellow-brown crust.

Decolonisation

Use of topical treatments (antiseptic body wash, nasal ointment or a combination of both) and personal hygiene measures to remove the bacteria causing the infection from the body.

Recommendation for research

The guideline committee has made the following recommendation for research.

1 Antiseptics compared with antibiotics for impetigo

For which people with impetigo are antiseptics as effective as antibiotics?

For a short explanation of why the committee made the recommendation for research, see the rationales.

Full details of the evidence and the committee's discussion are in the evidence review.

Rationales

The recommendations in this guideline are based on the evidence identified and the experience of the committee.

Advice to reduce the spread of impetigo

Why the committee made the recommendation

Recommendation 1.1.1

The committee agreed, based on its experience, that good hygiene measures help reduce the spread of impetigo, both to other areas of the body and to other people. The committee noted that resources are available with further information (see the management of impetigo in NICE's clinical knowledge summary on impetigo).

Return to the recommendations

Initial treatment

Why the committee made the recommendations

Recommendations 1.1.2 to 1.1.6

The evidence showed that impetigo was cured or improved with a placebo in some people. However, impetigo is highly infectious, and the committee agreed that treatment is important to limit the spread of infection and the worsening of symptoms, and to hasten recovery. A faster recovery is also likely to mean less time off school, nursery or work.

It was not clear in the evidence reviewed if impetigo was localised or widespread. The committee agreed that different treatment options are appropriate for impetigo based on the type and extent of the infection. It agreed that clinical judgement should be used to determine whether impetigo is localised or widespread.

Localised non-bullous impetigo

The evidence suggested that hydrogen peroxide 1% cream (a topical antiseptic) is as effective as a topical antibiotic for treating impetigo. Impetigo was cured or improved in a large proportion of people using hydrogen peroxide. The committee noted this evidence came from 1 randomised controlled trial. Based on its experience, the committee agreed that the risk of adverse effects from hydrogen peroxide at 1% concentration, such as irritation and skin bleaching, are minimal. They also agreed that the significance of this is especially low when compared with the risk of adverse effects associated with topical antibiotics, such as rapid development of antimicrobial resistance.

The committee was aware that the use of hydrogen peroxide 1% cream for impetigo is a change in practice and health professionals may not be familiar with its use. It noted that some other topical antiseptics are licensed for superficial skin infections, which may be cheaper and more widely available. However, no evidence was identified for treating impetigo with other topical antiseptics, so the committee could not make a recommendation for their use. Based on the available evidence, the committee agreed that the long-term benefits of good antimicrobial stewardship, in combination with the low risk of adverse events compared with using a topical antibiotic, outweighed the additional cost of hydrogen peroxide 1% cream.

Overall, the evidence showed that a topical antibiotic was as effective as an oral antibiotic for curing or improving impetigo. Based on the evidence and its experience, the committee agreed that topical antibiotics would cause fewer adverse effects than oral antibiotics, and that applying a topical antibiotic is usually straightforward for localised impetigo. The committee discussed its experience of antimicrobial resistance with topical antibiotics compared with oral antibiotics. It agreed that the likely increased risk of resistance with topical antibiotics applied to a localised area of impetigo for a short duration was outweighed by the increased risk of adverse events with oral antibiotics. The committee therefore agreed that if hydrogen peroxide 1% cream is unsuitable, for example, because impetigo is around the eyes, a topical antibiotic should be offered for people who are not systemically unwell or at high risk of complications.

Widespread non-bullous impetigo

Based on its experience, the committee agreed that people with widespread non-bullous impetigo should be offered a short course of either a topical or an oral antibiotic. They discussed that the choice of topical or oral use would be an individualised clinical decision, taking local antimicrobial resistance data into account alongside patient preference,

practicalities of administration, possible adverse effects and previous use.

The committee discussed that effectively applying a cream may be difficult over larger skin areas. It agreed that an oral antibiotic may be a better option for some people with widespread non-bullous impetigo, despite the higher risk of adverse events, and that the decision should be based on a discussion of the person's preferences and the balance of risks and benefits. Antimicrobial resistance can develop rapidly with the use of topical antibiotics, and the committee agreed that repeated doses or extended use of the same topical antibiotic should be avoided.

Bullous impetigo or impetigo in people who are systemically unwell or at high risk of complications

The evidence on treating bullous impetigo was limited to a small study in newborn babies. From its experience, the committee discussed that the presence of bullae may mean that a topical antibiotic is unable to reach the infected area. Therefore, it agreed that an oral antibiotic is needed to target the infection adequately.

No evidence was identified for treating people who are systemically unwell or at higher risk of complications. Based on its experience of current practice, and because of the high risk of harm if topical application of antibiotic is inadequate, the committee agreed that this population should be offered an oral antibiotic. People at higher risk of complications can include, for example, people who are immunocompromised or have coexisting skin conditions.

Combination treatment

The evidence suggested that combination treatment with an oral and topical antibiotic was no more effective than a topical antibiotic alone. The committee agreed that combination treatment should be discouraged because of the increased risk of adverse events and antimicrobial resistance.

Recommendation for research

The committee agreed that further research is needed to more clearly show which populations would benefit from antiseptic treatment. In order to encourage more research in this area, a <u>recommendation for research on antiseptics compared with antibiotics for impetigo was developed, which may contribute to future antibiotic-sparing</u>

recommendations and help reduce the risk of resistance and adverse events with antibiotics.

For more detail see the summary of the evidence on antimicrobials.

Return to the recommendations

Reassessment and further treatment

Why the committee made the recommendations

Recommendations 1.1.8 to 1.1.14

No evidence was identified for reassessing people with impetigo if initial treatment is unsuccessful. Therefore, the committee agreed on good practice points for this population based on consensus.

Based on its experience and the evidence for initial treatment, the committee agreed that a short course of a topical antibiotic should be offered for localised non-bullous impetigo if hydrogen peroxide 1% cream is ineffective. If impetigo becomes widespread after treatment, a short course of a topical or oral antibiotic should be offered, in line with the recommendation for initial treatment for widespread non-bullous impetigo. Although there is no evidence that oral antibiotics are more effective than topical antibiotics, the committee agreed that an oral antibiotic is more likely to target all areas of infection and that there is a risk of inadequate application of topical antibiotics. Based on its experience, the committee decided that an oral antibiotic should be an option if a topical antibiotic is unsuccessful. It also agreed that microbiological testing of an area of infected skin may help to guide antimicrobial prescribing.

For people with impetigo that recurs frequently, the committee agreed that a skin swab should be sent for microbiological testing to determine antimicrobial susceptibility. A nasal swab should also be considered if nasal carriage of Staphylococcus aureus is suspected. A nasal or skin (or combination) decolonisation regimen should be considered, based on clinical judgement and microbiological test results, in order to remove the bacteria causing recurrence of infection. The committee recognised that family decolonisation may be appropriate in some cases but did not make a recommendation because this decision should be based on specialist advice.

The committee agreed on good practice for antimicrobial stewardship when reviewing the results of microbiological tests. This includes changing to a narrow-spectrum antibiotic or continuing with a narrow-spectrum antibiotic that has shown resistance in microbiological tests if symptoms are already improving.

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Referral and seeking specialist advice

Why the committee made the recommendations

Recommendations 1.1.15 to 1.1.16

Based on its experience, the committee agreed that people who may have a more serious illness or condition or are immunocompromised with widespread impetigo need further assessment and treatment in hospital. Sometimes impetigo is difficult to treat (for example, bullous impetigo or impetigo that recurs frequently) and the committee agreed that referral or specialist advice should be an option.

Return to the recommendations

Choice of antimicrobial

Why the committee made the recommendation

Recommendation 1.2.1

Choice of antiseptic

The evidence suggested that hydrogen peroxide 1% cream is effective and based on its experience, the committee agreed that a short course of treatment is associated with a low risk of adverse events. There was no evidence identified for other topical antiseptics.

Choice of antibiotic

The evidence showed that fusidic acid is as effective as other topical antibiotics and is

associated with fewer adverse events. Based on this evidence, current practice and its experience, the committee agreed that the **first-choice topical antibiotic** in adults, young people and children with non-bullous impetigo when hydrogen peroxide 1% cream is unsuitable (including when impetigo is widespread) is **fusidic acid 2**% (either as a cream or an ointment). Based on its experience, the committee agreed that fusidic acid resistance rates are higher than for some other antibiotics. However, the evidence showed fewer skin reactions with fusidic acid compared with mupirocin. The committee agreed that the risk of antimicrobial resistance should be considered when offering an antibiotic, but that this risk is likely to be low in people with a first episode of impetigo.

The alternative topical antibiotic in adults, young people and children with non-bullous impetigo (when a topical antiseptic is unsuitable or has been ineffective) and fusidic acid resistance is suspected or confirmed is mupirocin 2% (either as a cream or an ointment). The committee based this on its experience and knowledge of current practice, evidence that mupirocin is as effective as other topical antibiotics for treatment of impetigo and its experience that mupirocin resistance rates are low.

National antimicrobial resistance data from Public Health England's voluntary surveillance reports on Staphylococcus aureus showed resistance rates for meticillin-susceptible Staphylococcus aureus (MSSA) bloodstream infection of 13% for fusidic acid and less than 1% for mupirocin in 2018. The equivalent rates for meticillin-resistant Staphylococcus aureus (MRSA) bloodstream infection were 25% and 3%. However, the committee discussed that resistance rates in blood isolates may not be a good indicator of resistance rates in skin isolates, which can vary greatly from person to person, based on their history of antibiotic use, and between localities.

There was some evidence showing that topical ozenoxacin is more effective than placebo for treating impetigo. However, because the evidence did not compare topical ozenoxacin with another antibiotic, the committee could not make recommendations for its use. It was also noted that topical ozenoxacin is not currently available in the UK.

Based on its experience and knowledge of current practice, the committee agreed that the **first-choice oral antibiotic** in adults, young people and children is **flucloxacillin**. This is a relatively narrow-spectrum penicillin that is effective against Staphylococcus aureus and Streptococcus pyogenes. The committee recognised that some children may not be able to tolerate flucloxacillin solution or swallow capsules. For these children, the alternative oral antibiotic is suitable.

The **alternative oral antibiotic** in adults, young people and children with penicillin allergy or if flucloxacillin is unsuitable is **clarithromycin**. In pregnancy, **erythromycin** was recommended if there is true penicillin allergy. The committee agreed that these antibiotics are effective against the common pathogens that cause impetigo, and the evidence indicated that macrolides are as effective as penicillins for treating impetigo.

The committee discussed the MHRA Public Assessment Report on the safety of macrolide antibiotics in pregnancy. This found that the available evidence is insufficient to confirm with certainty whether there is a small increased risk of birth defects or miscarriage when macrolides are taken in early pregnancy. They agreed with the UK Teratology Information Service monograph on the use of macrolides in pregnancy. They decided that there should be an informed discussion of the potential benefits and harms of treatment. Then, after such a discussion, macrolides can be used if there is a compelling clinical need and there are no suitable alternatives with adequate pregnancy safety data. Erythromycin is the preferred choice if a macrolide is needed during pregnancy, for example, if there is true penicillin allergy and the benefits of antibiotic treatment outweigh the harms. This is because there is more documented experience of its use than for other macrolides.

The committee discussed that in its experience, MRSA infection in impetigo is rare and that appropriate antibiotic choice may depend on local antimicrobial resistance rates. Therefore, the committee agreed that for people with suspected or confirmed MRSA, a local microbiologist should be consulted.

Course length and dosage

There was very little evidence on dosage and course length. Therefore, the recommendations were based on committee experience of current practice and the BNF. The committee also agreed that the shortest course that is likely to be effective should be prescribed to reduce the risk of antimicrobial resistance and adverse effects. All doses are given as in the BNF. Based on its experience that lower doses are not clinically effective due to poor oral bioavailability, the committee agreed that the higher dose for flucloxacillin recommended in the BNF is appropriate for treating impetigo in adults. The committee agreed that dose ranges are appropriate for children as the appropriate dose may vary depending on the age and weight of the child.

From its experience, the committee agreed that 5 days of treatment would be sufficient for treating most people with impetigo, and this is consistent with current practice. However, the committee was aware that some people may need a longer course because of the

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severity or number of lesions, so agreed that this could be up to 7 days, based on clinical judgement. The committee noted current BNF advice that topical fusidic acid and mupirocin should not be used for longer than 10 days.

For more details see the <u>summary of the evidence on choice of antibiotic</u>.

Return to the recommendations

Context

Impetigo is a contagious, bacterial infection of the superficial layers of the skin. The most common bacterial pathogen is Staphylococcus aureus, although infection with Streptococcus pyogenes or a combination of both pathogens is also seen. Impetigo affects all age groups; however it is most common in young children.

Summary of the evidence

This is a summary of the evidence, for full details see the evidence review.

Antimicrobials

Efficacy of topical antibiotics

The following topical antibiotics were shown to be more effective than placebo for the outcome of cure or improvement:

- · mupirocin in adults, young people and children
- fusidic acid in children
- · ozenoxacin in children.

Efficacy of oral antibiotics

Phenoxymethylpenicillin was not statistically significantly different compared with placebo in children for the outcome of cure or improvement.

Topical antibiotics compared with antiseptics, steroids or antifungals

There were no statistically significant differences in clinical effectiveness of the following comparisons for the outcome of cure or improvement:

- topical antibiotic (fusidic acid) compared with a topical antiseptic (hydrogen peroxide
 1%) in children
- topical antibiotic (gentamicin) compared with a topical steroid (betamethasone valerate; age not reported)
- topical antibiotic (gentamicin) plus a topical steroid (betamethasone valerate)
 compared with a topical steroid (betamethasone valerate; age not reported)

 topical antibiotic (mupirocin) compared with a topical antifungal (terbinafine) in children.

Safety of antibiotics

There were no statistically significant differences in adverse effects for the following comparisons:

- topical mupirocin and placebo in adults, young people and children
- topical fusidic acid and disinfectants in children
- topical mupirocin and antifungals in children.

No safety or tolerability data were reported for the other comparisons.

The evidence for the efficacy and safety of antimicrobials is based on 1 systematic review and meta-analysis of randomised controlled trials (RCTs; Koning et al. 2012) and 1 pooled-analysis of 2 RCTs (Hebert et al. 2018).

Choice of antibiotics

Topical antibiotics

There were no statistically significant differences in the clinical effectiveness of the following topical antibiotic comparisons for the outcome of cure or improvement:

- topical mupirocin compared with topical fusidic acid in adults, young people and children
- topical mupirocin compared with topical neomycin in children and young people
- topical mupirocin compared with topical polymyxin B plus neomycin (population not reported).

Some differences were seen for cure or improvement for other topical antibiotic comparisons:

topical fusidic acid was more effective than topical neomycin plus bacitracin in

children

• topical gentamicin was more effective than topical neomycin in adults, young people and children.

There were no statistically significant differences in adverse effects between topical mupirocin compared with topical polymyxin B plus neomycin (age not reported).

The incidence of skin rash was increased with topical mupirocin compared with topical fusidic acid in adults, young people and children.

No safety or tolerability data were reported for the other comparisons.

Oral antibiotics

There were no statistically significant differences in the clinical effectiveness of the following oral antibiotic comparisons for the outcome of cure or improvement:

- oral macrolides compared with oral penicillins in adults, young people and children
- oral erythromycin compared with oral amoxicillin in children
- oral azithromycin compared with oral erythromycin in adults, young people and children
- oral cefalexin compared with oral cefadroxil in children and young people
- oral cefalexin compared with oral erythromycin in children or oral azithromycin in adults
- oral cefaclor compared with oral azithromycin or oral co-amoxiclav in children
- oral cefadroxil compared with oral flucloxacillin in adults, young people and children.

Some differences were seen for cure or improvement for other antibiotic comparisons:

- oral erythromycin was more effective than phenoxymethylpenicillin in children
- oral co-amoxiclav was more effective than oral amoxicillin in children and young people
- oral cefalexin was more effective than oral phenoxymethylpenicillin in children.

There were no statistically significant differences in adverse effects for the following oral antibiotic comparisons:

- oral co-amoxiclav compared with oral amoxicillin in children and young people
- oral cefalexin compared with oral azithromycin in adults
- oral cefaclor compared with oral azithromycin in children
- oral cefaclor compared with co-amoxiclav in children.

Some differences were seen in adverse effects for other oral antibiotic comparisons:

- there were more incidences of diarrhoea in children taking oral erythromycin compared with oral amoxicillin
- there were more incidences of stomach ache, rash, fever or vomiting but fewer incidents of diarrhoea in adults, young people and children taking oral cefadroxil compared with oral flucloxacillin.

No safety or tolerability data were reported for the other comparisons.

Dual antibiotics

Oral plus topical antibiotics compared with topical antibiotics

There were no statistically significant differences in the clinical effectiveness of the following antibiotic comparisons in children for the outcome of cure or improvement:

- oral cefdinir plus topical tetracycline compared with topical tetracycline
- oral minomycin plus topical tetracycline compared with topical tetracycline
- oral fosfomycin plus topical tetracycline compared with topical tetracycline.

The evidence for choice of antibiotics is based on 1 systematic review and meta-analysis of RCTs (Koning et al. 2012).

Course length

Shorter course antibiotics compared with longer course antibiotics

A 3-day course of oral co-trimoxazole was not statistically significantly different compared with a 5-day course of oral co-trimoxazole for treatment success in children.

The evidence for course length of antibiotics is based on 1 non-inferiority RCT (Bowen et al. 2014).

Route of administration

Topical antibiotics compared with oral antibiotics

There were no statistically significant differences in the clinical effectiveness of the following antibiotic comparisons for the outcome of cure or improvement:

- topical mupirocin compared with oral erythromycin in adults, young people and children
- topical mupirocin compared with oral cefalexin in children with impetigo, or in adults, young people and children with secondary impetigo
- topical mupirocin compared with oral ampicillin (age not reported)
- topical fusidic acid compared with oral erythromycin in newborn babies (aged 3 days to 14 days) with bullous impetigo
- topical chloramphenicol compared with oral erythromycin in newborn babies (aged 3 days to 14 days) with bullous impetigo.

Oral erythromycin was more effective than topical neomycin plus bacitracin for the outcome of cure or improvement in newborn babies (aged 3 days to 14 days) with bullous impetigo.

Topical mupirocin was not statistically significantly different compared with oral cefalexin for adverse effects in children.

Topical mupirocin was associated with fewer gastrointestinal adverse events than oral erythromycin in adults, young people and children.

No safety or tolerability data were reported for the other comparisons.

Intramuscular antibiotics compared with oral antibiotics

Intramuscular ceftriaxone was not statistically significantly different compared with oral cefadroxil for cure in children.

Oral co-amoxiclav was non-inferior to intramuscular benzylpenicillin for treatment success in children.

Intramuscular benzylpenicillin was associated with more adverse events than cotrimoxazole in children.

The evidence for route of administration of antibiotics is based on 1 systematic review and meta-analysis of RCTs (Koning et al. 2012), and 2 RCTs (Al-Samman et al. 2014 and Bowen et al. 2014).

Other considerations

Medicines safety

As with all antibiotics, extended or recurrent use of topical fusidic acid or mupirocin may increase the risk of developing antimicrobial resistance. See the BNF for more information.

About 10% of the general population claim to have a penicillin allergy; this is often because of a skin rash that occurred while taking a course of penicillin as a child. Fewer than 10% of people who think they are allergic to penicillin are truly allergic. See the NICE guideline on drug allergy: diagnosis and management for more information.

People with a history of immediate hypersensitivity to penicillins may also react to cephalosporins and other beta-lactam antibiotics (BNF, November 2019).

Macrolides should be used with caution in people with a predisposition to QT interval prolongation (BNF, November 2019).

See the <u>summaries of product characteristics</u> for information on contraindications, cautions, drug interactions and adverse effects of individual medicines.

Medicines adherence

Medicines adherence may be a problem for some people taking antibiotics that need frequent dosing or longer treatment duration (see the <u>NICE guideline on medicines</u> adherence).

Resource implications

- Recommended antibiotics are available as generic formulations. See the <u>Drug Tariff</u> for costs.
- The incremental cost of hydrogen peroxide 1% cream is estimated to be around £3.50 more per person, when compared with current treatment options for people with localised non-bullous impetigo who are not systemically unwell or at risk of

complications. We expect the population that will be eligible for this treatment will not be greater than around 125,000 people per year, with the biggest incidence occurring in children.

See the <u>evidence review</u> for more information.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the <u>NICE</u> topic pages on skin conditions, infections and antimicrobial stewardship.

For full details of the evidence and the guideline committee's discussions, see the <u>evidence review</u>. You can also find information about <u>how the guideline was</u> developed, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting our guidelines into practice, see <u>resources</u> to help you put NICE guidance into practice.

Update information

Minor changes since publication

January 2022: We made minor wording changes to reflect updated advice on the use of macrolides in pregnancy.

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