National Institute for Health and Care Excellence

Neonatal infection: antibiotics for prevention and treatment

[R] Evidence review for switching from intravenous to oral antibiotics for suspected early-onset neonatal bacterial infection

NICE guideline NG195

Evidence underpinning recommendations 1.15.3, 1.22.1 to 1.22.6 and a recommendation for research

May 2026

Final

NICE National Institute for Health and Care Excellence®

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

Copyright

ISBN: 978-1-4731-9516-5

Contents

Switching from intravenous to oral antibiotics for suspected early-onset neonatal bacterial infection 4
1.1 Review question 4
1.1.1 Summary of the protocol 4
1.1.2 Methods and process 5
1.1.3 Effectiveness evidence 7
1.1.4 Summary of studies included in the effectiveness evidence 9
1.1.5 Summary of effectiveness evidence 12
1.1.6 Economic evidence 15
1.1.7 Economic model 15
1.1.8 Committee discussion and interpretation of the evidence 16
1.1.9 Recommendations supported by this evidence review 27
1.1.10 References 28

Switching from intravenous to oral antibiotics for suspected early-onset neonatal bacterial infection

1.1 Review question

This evidence review summarises the evidence for:

What is the impact of switching from intravenous to oral antibiotics for babies with suspected early-onset bacterial infection on morbidity and mortality, family outcomes, cost and resource use, and the views, experiences, and perceptions of healthcare professionals, parents or carers and families?

Further technical detail can be found in the separate technical appendices for this review.

1.1.1 Summary of the protocol

This evidence review used an existing systematic review from an external source. A summary of the existing review protocol is available in Table 1.

Table 1: Summary of the existing review protocol (PICOS)

Population	Clinically stable, term and late pre-term (>35 weeks gestation) babies with suspected early-onset sepsis (within the first 72 hours of life)
Interventions	Switch from intravenous to oral antibiotics Oral Antibiotic Therapy Oral antibiotics such as amoxicillin, ampicillin, augmentin, cefalexin, cefpodoxim, chloramphenicol, cloxacillin, co-amoxiclav, flucloxacillin, nafcillin, penicillin The existing review protocol did not specify any restrictions on the time frame.
Comparator	Remain on intravenous antibiotics
Outcomes	• Bacterial re-infection rate or late onset sepsis • Re-presentation at or readmission to the hospital for infection within 28 days of birth • Adverse events e.g. cannulation attempts, allergic reaction to antibiotics

	• Completion of antibiotic course • Impact on gut biome • Mortality • Breastfeeding rates • Sleep quality • Parental anxiety • Parent/child bonding • Quality of life • Parent perspectives/willingness to give antibiotics • Length of stay in hospital • Additional healthcare visits including GP, midwife, health visitor, 111, and emergency department • Drug and equipment costs • Costs to the family • Views, perceptions and experiences of healthcare professionals, parents and families
Study type	• Randomised studies • Non-randomised studies • Qualitative studies • Conference abstracts • Protocols • Ongoing trials
Key confounders	Not specified

The full protocol for the original systematic review has been published on PROSPERO (The International Prospective Register of Systematic Reviews). Registration number CRD420251044158.

1.1.2 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual for using an existing systematic review. The existing review was conducted by an external team at the University of Exeter and was published as a preprint, which had not been peer-reviewed at the time of guideline development. Methods for the existing review are described in the review protocol and preprint article. Methods

specific to this evidence review are described in **appendix J** in the technical appendices document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.2.1 Search methods

A search was not conducted for this evidence review because an existing systematic review from an external source was used. Details of the search methods used in the existing review are available in the preprint article.

1.1.2.2 Protocol deviations

The review included indirect outcomes that did not match those specified in the protocol. For the protocol outcome readmission to hospital for infection within 28 days of birth, the review reported outcomes at different follow-up points and some studies included readmissions that were not for infection, such as readmission within 28 days of treatment completion, readmission within 3 days of treatment completion, readmission due to infection within 60 days of treatment completion, and post-discharge admissions (timepoint not reported). For adverse events, the review included the indirect outcome of clinical deterioration within intervention (7 days). For treatment completion, the review reported protocol violation as an indirect outcome.

1.1.2.3 Methods specific to this review

This evidence review is based on the findings of a recent systematic review conducted by Whear 2025. The quality of the existing review was assessed using the ROBIS tool. Searches, included and excluded studies, quality assessments and raw data from the included studies were obtained from the review. However, additional analyses, including a GRADE assessment, were conducted by the NICE team as effect estimates for the outcomes had not been calculated in accordance with NICE methods. A meta-analysis was not conducted due to substantial heterogeneity in study designs and methodological approaches across the included studies; instead, the results

of individual studies have been presented. Subgroup analysis using the PROGRESS-Plus framework was planned in the protocol for the existing review but was not possible due to insufficient evidence.

Expert testimony was considered as part of the evidence base for this topic.

Further details are described **appendix J** in the technical appendices document.

1.1.3 Effectiveness evidence

1.1.3.1 Included studies

Study selection

The existing review authors conducted a systematic search to identify potentially relevant studies. Details of the search and number of records screened are available in the preprint article.

The existing review is summarised in Table 2. Four studies were included in the review: one randomised controlled trial (open-label, non-inferiority) and 3 non-randomised studies (one prospective cohort study, one case-control study, one pre-post study).

There was no evidence available for the following outcomes:

- Impact on gut biome
- Parental anxiety
- Parent/child bonding
- Quality of life
- Parent perspectives/willingness to give antibiotics
- Costs to the family

- Views, perceptions and experiences of healthcare professionals, parents and families.

1.1.3.2 Excluded studies

Details of studies excluded at full text from the existing review, along with the primary reason for exclusion, are available in the preprint article.

1.1.4 Summary of studies included in the effectiveness evidence

Table 2 Summary of studies included in the effectiveness evidence

Study details	Population	Intervention	Comparator	Outcomes
Whear 2025 Study type: Systematic review Studies conducted in: Netherlands, Sweden, Denmark, Italy Setting: Hospitals Funding source: NIHR	Number of participants: 1209 Number of studies: 4 (1 RCT, 3 non-randomised studies) Clinically stable, term and late pre-term (>35 weeks gestation) babies with suspected early-onset sepsis (within the first 72 hours of life) 3 studies included suspected infections only, 1 study included suspected and confirmed infections	<u>Switch to oral antibiotics</u> *Gyllensvärd 2020:* N=59: 3 days IV penicillin (50mg/kg, every 8 to 12 hours) plus amikacin (15mg/kg every 24 hours), followed by 2 days oral amoxicillin (20mg/kg, 3 times per day) *Keij 2022:* N=252: 2 days IV penicillin and gentamicin (dose NR, 3 times per day), followed by 5 days oral amoxicillin (75mg/kg) plus clavulanic acid (18.75mg/kg) per day in 3 doses *Malchau Carlsen 2024:* N=478: 7 days total treatment, of which 1.5 to 2 days IV benzylpenicillin and gentamicin (dose NR),	<u>Continue with IV antibiotics</u> *Gyllensvärd 2020:* N=61: 5 to 7 days IV penicillin (50mg/kg) plus amikacin (15mg/kg every 24 hours) *Keij 2022:* N=252: 7 days IV penicillin and gentamicin (dose NR, 3 times per day) *Malchau Carlsen 2024:* N=53: 7 days IV benzylpenicillin and gentamicin (dose NR)	• Reinfection rate (bacterial reinfection within 28 days of treatment completion; reinfection within 3 days of treatment completion) • Readmission to hospital (readmission within 28 days of treatment completion; readmission within 3 days of treatment completion; readmission due to infection within 60 days of treatment completion; post-discharge admissions timepoint NR) • Adverse events (any adverse event within 35 days of treatment

Study details	Population	Intervention	Comparator	Outcomes
	3 studies included term babies only, 1 study included term and late pre-term babies	followed by oral amoxicillin (50mg/kg, 3 times per day) for remainder of treatment *Manzoni 2009:* N=17: 3 days IV ampicillin and sulbactam (100mg/kg, 3 times per day) plus amikacin (15mg/kg once per day), followed by 5 days oral cefpodoxime proxetil (10mg/kg, once per day)	*Manzoni 2009:* N=37: 8 days IV ampicillin and sulbactam (100mg/kg, 3 times per day) plus amikacin (15mg/kg once per day) for first 3 days	initiation; serious adverse events within 35 days of treatment initiation; complications of treatment timepoint NR; clinical deterioration within intervention (7 days), weight loss on day 4; number of cannulation reinsertion attempts during treatment) • Completion of antibiotic course (protocol violation timepoint NR; treatment discontinuation timepoint NR; oral medication accepted by neonate timepoint NR) • Mortality (within 30 days; in first month of life; timepoint NR) • Breastfeeding rate (exclusively breastfed

Study details	Population	Intervention	Comparator	Outcomes
				at 1 month after treatment completion; exclusively breastfed at discharge) • Sleep good quality (1 week; 1 month) • Duration of hospital stay • Healthcare professional visit (between day 7 and 35)

Abbreviations: IV: intravenous; NIHR: National Institute of Health and Care Research; NR: not reported RCT: randomised controlled trial

See **appendix D** in the technical appendices document for the full evidence table for the existing review.

1.1.5 Summary of effectiveness evidence

Informative statements, that were adapted from GRADE guidelines 26, were used to summarise the evidence. An example of how these informative statements were drafted is provided in **appendix J** in the technical appendices document.

Switching to oral antibiotics versus remaining on intravenous antibiotics

The evidence shows that switching to oral antibiotics probably reduces duration of hospital stay compared to remaining on intravenous antibiotics (Clinical importance: evidence of benefit; Certainty of evidence: moderate) [RCT evidence].

The evidence suggests that switching to oral antibiotics compared to remaining on intravenous antibiotics results in little to no difference for:

- Bacterial reinfection within 28 days of treatment completion (Clinical importance: evidence of no effect; Certainty of evidence: low) [RCT evidence]
- Exclusively breastfed at 1 month after treatment completion (Clinical importance: evidence of no effect; Certainty of evidence: low) [RCT evidence]
- Sleep good quality at 1 week and 1 month (Clinical importance: evidence of no effect; Certainty of evidence: low) [RCT evidence].

The evidence is very uncertain about the effect of switching to oral antibiotics compared to remaining on intravenous antibiotics for:

- Reinfection within 3 days of treatment completion (Clinical importance: evidence of no effect; Certainty of evidence: very low) [observational study evidence]

- Readmission within 28 days of treatment completion (Clinical importance: evidence of no effect; Certainty of evidence: very low) [RCT evidence]
- Readmission within 3 days of treatment completion (Clinical importance: evidence of no effect; Certainty of evidence: very low) [observational study evidence]
- Readmission due to infection within 60 days of treatment completion (Clinical importance: evidence of no effect; Certainty of evidence: very low) [observational study evidence]
- Post-discharge admissions (timepoint NR) (Clinical importance: evidence of no effect; Certainty of evidence: very low) [observational study evidence]
- Any adverse event within 35 days of treatment initiation (Clinical importance: evidence of disbenefit; Certainty of evidence: very low) [RCT evidence]
- Serious adverse events within 35 days of treatment initiation (Clinical importance: evidence of no effect; Certainty of evidence: very low) [RCT evidence]
- Complications of treatment (timepoint NR) (Clinical importance: evidence of no effect; Certainty of evidence: very low) [observational study evidence]
- Clinical deterioration within intervention (7 days) (Clinical importance: evidence of no effect; Certainty of evidence: very low) [RCT evidence]
- Weight loss on day 4 (% of birthweight) (Clinical importance: evidence of no effect; Certainty of evidence: very low) [observational study evidence]

- Protocol violations (timepoint NR) (Clinical importance: evidence of benefit; Certainty of evidence: very low) [RCT evidence]
- Treatment discontinuation (timepoint NR) (Clinical importance: evidence of no effect; Certainty of evidence: very low) [observational study evidence]
- Mortality (timepoint NR) (Clinical importance: evidence of benefit; Certainty of evidence: very low) [observational study evidence]
- Mortality within 30 days (Clinical importance: evidence of no effect; Certainty of evidence: very low) [observational study evidence]
- Mortality in first month of life (Clinical importance: evidence of no effect; Certainty of evidence: very low) [observational study evidence]
- Exclusively breastfed at discharge (Clinical importance: evidence of benefit; Certainty of evidence: very low) [observational study evidence]
- Duration of hospital stay (Clinical importance: evidence of benefit; Certainty of evidence: very low) [observational studies evidence]
- Healthcare professional visit between day 7 and 35 (Clinical importance: evidence of no effect; Certainty of evidence: very low) [RCT evidence].

Note: Some outcomes appear more than once because the included studies were not pooled, due to differences in study design and methodology.

See **appendix F** in the technical appendices document for a GRADE summary table containing full details for all outcomes.

1.1.6 Economic evidence

1.1.6.1 Included studies

A search was not conducted for this evidence review because an existing systematic review from an external source was used. A separate economic search was not undertaken but main outcomes of the review included cost and resource use. Details of the search methods used in the existing review are available in the preprint article.

1.1.6.2 Excluded studies

Details of studies excluded at full text from the existing review, along with the primary reason for exclusion, are available in the preprint article.

1.1.7 Economic model

No original economic modelling was completed for this review question.

1.1.8 Committee discussion and interpretation of the evidence

1.1.8.1 What are the key issues and priorities relating to this question?

The current NICE neonatal infection guideline (NG195) recommends that babies with suspected early-onset neonatal infection who have negative blood cultures and have received antibiotics for more than 36 hours should be reviewed at least once every 24 hours to determine whether it is appropriate to stop antibiotic treatment. For some babies, the continuation of antibiotics is deemed appropriate due to ongoing infection concerns despite negative blood culture. In practice, clinicians may adopt a cautious approach and continue intravenous antibiotics for up to 7 days. This leads to prolonged hospital stays, repeated cannulation, and unnecessary separation of mothers and babies.

NICE does not currently recommend switching from intravenous to oral antibiotics in babies with suspected early-onset neonatal infection, as oral antibiotics were not considered in the previous version of the guideline. Introducing this option could potentially reduce hospital stays and result in cost and capacity savings, while also lowering risks associated with prolonged intravenous therapy, improving parental satisfaction, reducing mother–baby separation, and supporting better breastfeeding rates.

There are potential risks with switching to oral antibiotics, such as overprescribing and unnecessary use of antibiotics, contributing to antimicrobial resistance. A key concern is that clinicians may prescribe oral antibiotics as a precaution, rather than restricting this approach to cases where continuation of antibiotics is clinically indicated. Inappropriate use could result in babies receiving antibiotics without need, thereby increasing the risk of antimicrobial resistance. These concerns can be mitigated by establishing strict eligibility criteria and ensuring parental agreement before discharge. Clear guidance and ongoing monitoring will be essential to maintain safety and effectiveness.

A 2025 systematic review (Whear, 2025) identified new evidence on switching to oral antibiotics from intravenous antibiotics in babies with suspected early-onset infection. Based on this, the committee agreed to review existing recommendations to determine whether switching to oral antibiotics is both effective and safe, and to define clear eligibility criteria for when this can be done safely.

1.1.8.2 Certainty of evidence and the balance of effects

The existing systematic review by Whear (2025) included 4 studies: 1 RCT (which included term and late pre-term babies ≥35 weeks gestation) and 3 non-randomised studies (which included only babies born at term). The existing review was assessed to have unclear risk of bias. This was because although the existing review critically appraised the included studies, it appeared that the findings of the review did not take into account the risk of bias of the included studies, particularly bias due to confounding in non-randomised studies.

A GRADE analysis was conducted by the NICE team, and the certainty of the evidence included in the existing review was rated very low to low for most outcomes. Evidence for all outcomes was downgraded for risk of bias (based on the critical appraisal reported in the existing review: 3 moderate quality and 1 weak quality assessed using the Effective Public Health Practice Project tool, mainly due to a lack of blinding in all studies and not reporting the number of withdrawals in 1 study). All outcomes were also downgraded for inconsistency because they were based on single studies, except for duration of hospital stay which was not downgraded because consistent results were reported by all 4 studies. Other reasons for downgrading included outcome indirectness (readmissions, clinical deterioration, and protocol violations) and population indirectness (1 study included confirmed infections as well as suspected infections). Several outcomes were also downgraded for imprecision.

The committee acknowledged that the published evidence was further limited by small sample sizes, which meant that the studies may not have been

sufficiently powered to detect a difference for rare outcomes (such as bacterial re-infection rate, readmission to hospital, serious adverse events, and mortality). In addition, most of the evidence was from non-randomised studies, which are more prone to bias than RCTs, and none of the published studies were conducted in the UK limiting their applicability.

In terms of benefits, there was moderate certainty evidence from one RCT of a mean reduction of 2.6 days in duration of hospital stay in babies that switched from intravenous to oral antibiotics. The 3 non-randomised studies provided evidence for the same direction of effect (mean reduction of 1 day to 4.4 days across studies) but the evidence was very low certainty. The committee agreed that the observed reduction in hospital stay was clinically meaningful.

The committee noted that there was very low certainty evidence from one RCT suggesting fewer protocol violations in babies that switched to oral antibiotics, which they considered as indirect evidence of a potential benefit for completing the course of antibiotics. However, very low certainty evidence from one non-randomised study suggested no evidence of a difference for treatment discontinuation.

For the outcome of breastfeeding rates, the evidence was mixed; low certainty evidence from one RCT suggested no evidence of a difference at 1 month, while very low certainty evidence from one non-randomised study suggested higher rates of exclusive breastfeeding at discharge in babies that switched to oral antibiotics.

The committee noted that one study suggested evidence of disbenefit for the any adverse event outcome. However, the certainty of this finding was very low. In addition, this outcome included a range of minor adverse events, some of which may not have been related to infection or antibiotic treatment. The evidence for all other adverse event outcomes (serious adverse events, weight loss, clinical deterioration, and complications of treatment) was also very low certainty, but there was no evidence of a difference between

remaining on intravenous antibiotics and switching to oral antibiotics for all outcomes.

Mortality data was reported in 3 non-randomised studies, but the certainty of evidence was very low. In 2 studies, no deaths occurred in either the oral antibiotics group or the intravenous antibiotics group, while the third study reported 2 deaths (not infection related) among babies who remained on intravenous antibiotics and none among those who switched to oral antibiotics. However, the small sample sizes and very low certainty of evidence meant that no conclusions could be drawn.

The evidence suggested little to no difference between switching to oral antibiotics and remaining on intravenous antibiotics for the following outcomes: reinfection rate, hospital readmission, sleep quality, and the number of healthcare professional visits. However, the certainty of evidence was low or very low, making these findings very uncertain. No evidence was identified in the existing review on the impact on gut biome, parental anxiety, parent/child bonding, quality of life, parent perspectives/willingness to give antibiotics, costs to the family, and views and experiences of parents, carers or healthcare professionals.

The committee also considered UK real-world evidence presented by expert witnesses including data from 3 quality improvement initiatives across 9 sites in England currently implementing an oral switch pathway for babies who had received intravenous antibiotics for the first 36 hours. These were term and late pre-term babies who were clinically well, feeding effectively, had negative cultures at 36 hours, met defined C-reactive protein (CRP) thresholds, and had clinician agreement that they were suitable for oral antibiotics. Two of the programmes, Neonatal Oral Antibiotics at Home (NOAH) and the Kent Surrey and Sussex (KSS) Neonatal Oral Switch Initiative, initially used co-amoxiclav as the oral antibiotic. The NOAH programme has already transitioned to amoxicillin at a dose of 30 mg/kg 3 times daily (Aughey and Boxall, 2025), while the KSS programme is currently in the process of making this change. The third programme, Postnatal Early Antibiotic Review for Low-Risk Babies

(PEARL) used amoxicillin at a dose of 30mg/kg 3 times a day throughout. The committee noted that the summary of product characteristics for oral amoxicillin states that for neonates under 7 days, administration should not exceed twice a day.

Data from these sites showed that switching to oral antibiotics reduced the length of hospital stay by 2 to 2.7 days compared with remaining on intravenous antibiotics. Of 331 babies who were switched to oral antibiotics, there were 4 re-presentations at hospital, of which 3 babies were readmitted due to concerns about infection. There were no confirmed cases of late-onset sepsis. All babies completed their oral antibiotic courses. Additional benefits included reduced gentamicin exposure (from ~3 doses to 1.7 per baby), thereby reducing the likelihood of potential ototoxic and nephrotoxic side effects associated with gentamicin, and fewer cannulation attempts.

Qualitative evidence from one site suggested that parents and carers were confident managing their baby's treatment at home. Other impacts reported by parents and carers included going home earlier, improved mental wellbeing, more family support, positive breastfeeding experience, and bonding with their baby. Feedback from healthcare staff was also positive.

The expert witness testimony reported that parents or carers were always given the choice of whether their baby would complete the antibiotic treatment in hospital or go home with oral antibiotics, and very few declined the opportunity for their baby to be sent home with oral antibiotics. The committee acknowledged that the real-world evidence from the expert witness testimony has not yet been peer-reviewed.

The committee were aware of one quality improvement project from one of the sites included in the expert witness testimony (Scally, 2025), which was published after the existing review search had been completed. Key findings from this study of 30 babies that were switched to oral antibiotics were a reduction in median length of stay from 6 to 4 days, no cases of bacterial sepsis within 28 days of treatment completion, and high levels of family satisfaction. Qualitative feedback from parents also highlighted several

positive themes, such as being able to return home sooner, that the oral medication was straightforward to administer and reduced the need for repeated cannulation. Although this evidence was not formally included in the review, the committee took it into account informally during their discussions.

Based on their knowledge, the committee also discussed pharmacokinetic data of oral antibiotics, although this area was not formally reviewed. Recent studies (Keij, 2023 and Barker, 2023) indicated that oral amoxicillin has good bioavailability in neonates (58–87%), but absorption may vary across populations.

Based on the evidence from the existing review and insights from expert witness testimony, the committee agreed that switching from intravenous to oral antibiotics after 36 hours should be considered for babies with suspected early-onset infection born from at least 35 weeks' gestation who meet specific clinical criteria, instead of continuing treatment with intravenous antibiotics as recommended by the previous version of the guideline. This approach can reduce hospital stay, enhance continuity of care for families, and improve the efficient use of neonatal services without increasing the risk of serious adverse outcomes. The committee also agreed that, when a baby is switched to oral antibiotics under this approach it can be considered to send the baby home under the supervision of the neonatal team. The committee noted that the recommendations broadly align with the criteria outlined in the UK Health Security Agency (UKHSA) guidance on the prompt intravenous-to-oral switch (IVOS) of antimicrobials in children and young people, including newborns.

The committee agreed an eligibility criteria for whom this approach could be considered, including a negative blood culture, a reassuring clinical condition with no clinical indicators of ongoing infection (based on those listed in box 2 of the guideline), and a reassuring trend in a previously elevated CRP concentration. The committee also agreed that the baby should remain under the care of the neonatal team until antibiotics are stopped. The committee also agreed that the decision to switch from intravenous to oral antibiotics and the decision to send the baby home with oral antibiotics should be agreed by

a senior neonatologist or paediatrician (consultant level or similar level) to ensure safety.

The committee decided to not recommend any CRP thresholds for switching to oral antibiotics. The CRP thresholds varied across the expert witness testimony sites and only one published study reported using an upper CRP threshold to guide decisions on switching to oral antibiotics. The committee also acknowledged that CRP level may be slightly elevated even without an infection. The committee agreed that decisions about starting, stopping or continuing antibiotic treatment for suspected neonatal infection should not be based on CRP results alone as they should be interpreted in conjunction with the entire clinical picture.

Although most of the studies included in the existing review used either amoxicillin alone (Gyllensvärd 2020; Malchau Carlsen, 2024) or amoxicillin combined with clavulanic acid (Keij, 2022) as the oral antibiotic, none were conducted in the UK, and the combination regimen used by Keij (2022) did not align with BNFC recommended dosing. Based on the UK expert witness testimony and their clinical experience, the committee agreed that oral amoxicillin should be the first choice antibiotic. Amoxicillin was recommended because it is effective against Group B streptococcus (GBS), which is the most common cause of early-onset neonatal infection. The committee also agreed that local microbiological surveillance data should also be considered to guide antibiotic selection based on bacterial resistance data. Based on the expert witness testimony, the committee agreed that a total antibiotic course length of up to 7 days, inclusive of both intravenous and oral treatment was appropriate.

The committee acknowledged that there is currently no BNFC recommended dose of oral amoxicillin for neonates less than 7 days of age. As the BNFC are in the process of reviewing the evidence to recommend an appropriate dosing regimen for this age group, the committee decided not to specify a dose in the recommendations.

The committee also agreed additional safety measures that should be in place before sending a baby home on oral antibiotics, including administering the first oral dose in hospital under supervision, confirming tolerance of oral feeds, confirming that there are no other reasons (unrelated to infection) that meant the baby should stay in hospital (for example, phototherapy for jaundice or the need for the mother to stay in hospital), and ensuring standardised monitoring. This includes keeping the baby under the care of the neonatal team, with at least 2 follow-up consultations (one of which should be once antibiotic treatment has been completed) by appropriately trained staff to maintain continuity and safety. These reviews should also include an assessment of the baby's overall condition and the appropriateness of continuing antibiotic therapy. A minimum of 2 follow-up consultations was recommended based on the evidence and committee consensus. The committee discussed that these follow-up appointments could be conducted via telephone, video conference or face-to-face.

The committee discussed that switching to oral antibiotics and sending babies home may put additional responsibility on parents and carers, who might not feel confident about administering oral antibiotics or recognising signs that their baby is unwell, particularly if it is their first baby. Therefore, the committee agreed that parents' or carers' concerns must be addressed before sending babies home, and that it was the responsibility of healthcare professionals to ensure parents or carers are provided with the required information and training to be competent to administer oral antibiotics and recognise signs that their baby is unwell. They should also be provided with clear information about how to contact the neonatal team if they have concerns. This approach would also help to reduce unnecessary presentations to primary care or A&E.

Given the limited high-quality evidence supporting the switch from intravenous to oral antibiotics in babies with suspected early-onset infection but negative cultures, the committee agreed to make a research recommendation for further research into the effectiveness and safety of switching babies with

suspected early-onset infection from intravenous to oral antibiotics compared with continuing with intravenous antibiotics (see Appendix K).

1.1.8.3 Resources and cost-effectiveness

The Whear 2025 systematic review reported outcomes relevant to resource use and cost-effectiveness. In addition, the committee heard expert witness testimony which provided real-world UK evidence on the potential resource implications of implementing an oral switch pathway for babies who received intravenous antibiotics for the first 36 hours for suspected early onset infection.

In the absence of a formal economic evaluation, the committee used Whear 2025, expert witness testimony and their own clinical experience and expertise to make a qualitative assessment of the cost-effectiveness of switching to oral antibiotics.

They did not believe from the evidence presented or their own expertise and experience that switching to oral antibiotics would lead to worse neonatal outcomes. Whear 2025 provided some evidence that the switch would lead to a reduction in hospital length of stay and Gyllensvärd 2020, one of the included studies in the systematic review, reported that this could lead to savings of €2,700 per patient (£2,372 per patient based on an exchange rate of €1.1382 = £1; source HMRC exchange rate: 1 Jan 2026 to 31 Jan 2026) The committee also noted that oral antibotics are cheaper to administer than intravenous antibiotics.

The expert witnesses estimated that 9,000 to 12,000 babies could be affected by the change in policy, which they believed would translate into 18,000 – 32,000 cot days avoided, based on their local data on reduction in hospital stay. The expert witness testimony estimated that this reduction in hospital stay could translate into a £1900 to £2500 savings per baby and a £17 million to £30 million saving to the NHS, using the 2024/25 national average unit cost for ‘Neonatal Critical Care, Special Care, with External Carer resident’. They also claimed that the revised policy would reduce pressure on NICU (neonatal

intensive care unit) beds and consequently allow the sickest babies to avoid transfers out of region. The committee recognised that there was uncertainty with respect to the actual savings that would be realised. However, they noted that the magnitude of the saving was not an important criteria in determing value for money given an absence of evidence and expert opinion supporting a clinical benefit for intravenous antibiotics.

Therefore, the committtee concluded that a switch to oral antibiotics would be cost-effective, considerably reducing NHS costs without having an adverse impact on neonatal outcomes.

1.1.8.4 Equity

The equality and health inequality assessment (EHIA) identified several disadvantaged groups that may face challenges in managing oral antibiotic therapy for their baby at home, such as people with limited access to follow-up care, unstable housing, lower health literacy, and language barriers. The committee also noted that consideration would need to be given to the demographic characteristics of the local population, such as socioeconomic status, education, ethnicity, and asylum seekers. The committee did not make a specific recommendation for these groups. However, they noted that social and family circumstances should be considered by the clinician when deciding whether it is appropriate to send a baby home with oral antibiotics.

The expert witness testimony highlighted that tailored information and training was provided for parents and carers as part of the oral switch pathway (e.g. multilingual leaflets). They also discussed the benefits for people living in rural areas who may have to travel long distances to the hospital, especially those without access to a car, and reducing the burden of staying in hospital.

The impact of switching to oral antibiotics on health inequalities was not assessed in the existing review due to insufficient evidence.

1.1.8.5 Feasibility

The committee noted that switching to oral antibiotics for babies who are on intravenous antibiotics despite negative blood cultures and being clinically well at 36 hours is already being implemented in some hospitals in the UK and that uptake is likely to increase in the future. From their experience, the committee noted that not all hospitals have outreach, hospital at home, or home antibiotic services and emphasised the importance of robust safety-netting.

1.1.8.6 Other considerations

Evidence from the expert witness testimony highlighted the positive environmental impact of switching to oral antbiotics. A shorter duration of hospital stay, fewer transport-related emissions associated with travelling to the hospital, and decreased use of disposable medical equipment for administering intravenous antibiotics would all contribute to reducing carbon emissions. This approach aligns with NHS net zero goals.

1.1.8.7 Strength of the recommendations

The committee agreed that the published evidence was limited and of mostly very low certainty because it mainly came from non-randomised studies that were conducted in non-UK settings with small sample sizes. They considered the real-world evidence from the expert witness to be compelling, but acknowledged that it had not yet been peer-reviewed and that outcomes were not compared with a control group of babies who remained in hospital on intravenous antibiotics. The committee also recognised that the oral switch pathway is already being implemented in clinical practice and is likely to become more common in the future. However, because of the limitations in the published evidence and the lack of peer-reviewed real-world evidence from expert witness testimony, the committee did not make a strong recommendation, but instead made a ‘consider’ recommendation.

1.1.9 Recommendations supported by this evidence review

This evidence review supports recommendations 1.15.3, 1.22.1 to 1.22.6 and the research recommendation on the clinical and cost effectiveness, and safety, of switching treatment from intravenous to oral antibiotics for babies with suspected early-onset infection compared with remaining on intravenous antibiotics (see Appendix K).

1.1.10 References

1.1.10.1 Effectiveness evidence

Gyllensvärd J, Ingemansson F, Hentz E et al. (2020) C-reactive protein- and clinical symptoms-guided strategy in term neonates with early-onset sepsis reduced antibiotic use and hospital stay: a quality improvement initiative. BMC Pediatrics 20:531

Keij FM, Kornelisse RF, Hartwig NG et al. (2022) Efficacy and safety of switching from intravenous to oral antibiotics (amoxicillin-clavulanic acid) versus a full course of intravenous antibiotics in neonates with probable bacterial infection (RAIN): a multicentre, randomised, open-label, non-inferiority trial. The Lancet Child & Adolescent Health 6(11):799-809

Malchau Carlsen EL, Dungu KHS, Lewis A et al. (2024) Switch from intravenous-to-oral antibiotics in neonatal probable and proven early-onset infection: a prospective population-based real-life multicentre cohort study. Archives of Disease in Childhood - Fetal and Neonatal Edition 109:34-40

Manzoni P, Esposito S, Gallo E et al. (2009) Switch therapy in full-term neonates with presumed or proven bacterial infection. Journal of Chemotherapy 21(1):68-73

Whear R, Abbott R, Aughey H et al. (2025) Effectiveness, cost effectiveness and experiences of switching from intravenous to oral antibiotics in neonates with probable early onset sepsis: a systematic review. medRxiv

1.1.10.2 Economic evidence

Gyllensvärd J, Ingemansson F, Hentz E et al. (2020) C-reactive protein- and clinical symptoms-guided strategy in term neonates with early-onset sepsis reduced antibiotic use and hospital stay: a quality improvement initiative. BMC Pediatrics 20:531

Whear R, Abbott R, Aughey H et al. (2025) Effectiveness, cost effectiveness and experiences of switching from intravenous to oral antibiotics in neonates with probable early onset sepsis: a systematic review. medRxiv

1.1.10.3 Miscellaneous

Aughey H, Boxall K (2025) NOAH Pathway Update: Moving from Co-amoxiclav to Amoxicillin [online; accessed 27 January 2026]

Barker CIS, Kipper K, Lonsdale DO et al. (2023) The Neonatal and Paediatric Pharmacokinetics of Antimicrobials study (NAPPA): investigating amoxicillin, benzylpenicillin, flucloxacillin and piperacillin pharmacokinetics from birth to adolescence. Journal of Antimicrobial Chemotherapy 78(9): 2148-61

Keij FM, Schouwenburg S, Kornelisse RF et al. (2023) Oral and intravenous amoxicillin dosing recommendations in neonates: a pooled population pharmacokinetic study. Clinical Infectious Diseases 77(11):1595–603

Scally N, Leach H, Thakur D et al. (2025) PEARL QIP: postnatal early antibiotic review for low-risk babies – transitioning babies home earlier from the postnatal ward using oral antibiotics. Archives of Disease in Childhood - Education and Practice (forthcoming) Published online first: 9 November 2025