NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance

Kurin Lock for blood culture collection

How we develop NICE medical technologies guidance

If a technology is recommended for use, the specific recommendations are not intended to limit use of other relevant technologies that may offer similar advantages. If the technology is recommended for further evidence generation, it can be used in the NHS to generate further evidence. NICE will review the guidance once new evidence is available. If the technology is recommended for use in research, the recommendations are not intended to preclude the use of the technology but to identify further evidence which, after evaluation, could support a recommendation for wider adoption.

1 Recommendations

1.1 Kurin Lock can be used in the NHS to reduce contamination in blood culture collection in emergency departments with high blood culture contamination rates while more evidence is generated.

Evidence generation

1.2 Evidence should be generated on:

- the resource impact of blood culture test results, including data on length of hospital stay, antibiotic use, further microbiological investigations and medical interventions
- staff adherence to blood culture collection methods
- baseline blood culture contamination rates, and any change in these rates from using Kurin Lock.

Why the committee made these recommendations

Clinical trial evidence suggests that Kurin Lock is a safe and effective way of reducing blood culture contamination rates, compared with standard blood culture collection. It is not clear how it affects other outcomes, like length of hospital stay and antibiotic use, because the clinical trials did not formally record these outcomes.

Kurin Lock costs much more than standard blood culture collection. So, it is more likely that Kurin Lock is cost saving when it is used in emergency departments with high rates of blood culture contamination. The economic modelling is uncertain because of the lack of evidence about how Kurin Lock affects length of hospital stay compared with standard blood culture collection. This means it is uncertain whether Kurin Lock is cost incurring or cost saving.

Evidence generation would help address uncertainties in the clinical and cost-effectiveness evidence. So, Kurin Lock is recommended for use in the NHS while evidence is generated.

2 The technology

Technology

2.1 Kurin Lock (Iskus Health Ltd) is a CE-marked class IIa medical device, intended for use in collecting blood samples to check for the presence of infections. The Kurin Lock device consists of a needle, a flash chamber to collect, isolate and display the first 0.15 ml of blood drawn, and a tube to collect the remaining blood sample, which goes on to be cultured and analysed.

2.2 The company submission lists 14 different versions of the Kurin Lock device. The company stated that there is no impact on the generalisability of evidence across these various versions of the device. It advised that the different versions allow different methods of taking blood culture samples in clinical practice, such as variations in the bottles used to collect samples and taking blood samples from freshly inserted peripheral intravenous cannulas instead of through standard venepuncture.

Care pathway

2.3 People who are suspected to have a bloodstream infection or sepsis have a blood sample collected. The sample is sent to a laboratory for culturing to detect and potentially identify the infection. Current management involves cleaning the injection site with antiseptic, inserting the needle, and collecting blood directly into blood culture collection bottles. Measures such as appropriate skin and bottle preparation, taking cultures from peripheral venepuncture instead of catheters, and training can minimise contamination risk. At least 40 ml of blood should be cultured for optimum detection of bloodstream infections. This requires at least 2 sets of blood culture samples to be taken within a few hours of each other. Kurin Lock could fit in to the pathway by replacing the standard blood culture collection device.

Innovative aspects

2.4 The innovative aspect of Kurin Lock is the flash chamber, which diverts and contains the first 0.15 ml of blood that is drawn during blood sample collection. The intended purpose of this mechanism is to isolate the blood that could contain microbes from the skin at the site of venepuncture. This is to avoid contaminating the blood sample and reduce the rate of false positive bloodstream infection results.

2.5 Blood culture contamination or false-positive blood culture results complicate interpretation, and can have detrimental effects on the patient and health service. For example, people may have unnecessary treatments and may have to extend their hospital stays, and hospital laboratories may do unnecessary further testing.

Intended use

2.6 Kurin Lock is intended for use in secondary care, for people who have blood culture samples taken when bloodstream infections are suspected. This includes in emergency departments, intensive care units and other general inpatient wards. Specific subgroups who may benefit from Kurin

Lock include populations in which taking blood samples may be more difficult, and so the risk of contamination is higher. For example, taking blood samples from children or from intravenous drug users.

Costs

2.7 A Kurin Lock device costs £19.50 (excluding VAT). In usual practice, 2 Kurin Lock devices will be used, so this will cost £39 per patient. All variants of Kurin Lock are the same price.

3 Evidence

NICE commissioned an external assessment group (EAG) to review the evidence submitted by the company. This section summarises that review. Full details of all the evidence are in the project documents on the NICE website.

Clinical evidence

There are 14 publications, comprising 12 studies, that make up the clinical evidence

3.1 The evidence base consists of 12 studies reported across 14 publications with 4 full-text peer-reviewed publications, 5 abstracts and 5 posters. The EAG critically appraised the 4 full-text publications using the JBI Case Series critical appraisal checklist. The remaining 10 abstracts and posters were not formally critically appraised because of a lack of detail. The EAG considered 3 of the full-text publications to be low quality and the other study to be medium quality. For full details of the clinical evidence, see section 4 of the assessment report in the supporting documentation.

It was unclear in the studies how people were selected for blood culture sampling and how contaminated cultures were identified

3.2 Most of the studies did not specify how people were selected to have blood culture collection. Only 1 of the studies described how laboratory analysis would identify contaminated blood cultures (false positives). Most studies were based in the US, and there was variability in clinical practice for referrals to collect blood culture samples and laboratory analysis to

identify contaminated blood cultures. So, the evidence may limit the generalisability of the study results.

Three UK NHS-based studies (not peer reviewed) reported blood culture contamination rates

3.3 There was limited published evidence on blood culture contamination rates in the NHS and the impact Kurin Lock has on this. One of these studies, based in the UK, was unpublished. The UK evidence estimated baseline contaminations of between 5% and 9%. Atta (2022) reported that the contamination fell from 9% to 3.1% with Kurin Lock use, while Hodson (2022) reported a statistically significant change from 6% at baseline to 1.9%.

Other outcomes are estimated based on blood culture contamination rates so the impact of Kurin Lock is uncertain

3.4 Length of stay was not a formal outcome in any of the included studies, but it was briefly discussed in 4 studies. Of these, Atta 2022 and Parsons 2023 were UK NHS based and 2 studies were from the US (Baxter 2020 and Burnie 2021). Both Atta 2022 and Parsons 2023 were posters that based their results on Alahmadi 2010, which investigated length of stay costs associated with false-positive blood cultures in a general hospital in Northern Ireland between July 2007 and July 2008. Kurin Lock was not used in this study, but the bed day findings were used to estimate cost savings in Atta 2022 and Parsons 2023.

3.5 Similarly, the use of antibiotic treatment was not a formal outcome in the published studies. But it was briefly referred to in 3 studies (Baxter 2020, Burnie 2021 and Ostwald 2021a/2021b). The company economic model used vancomycin treatment based on data from studies based in the US. The use of antibiotic treatment in the model was based on contaminated blood culture rates rather than the direct impact of Kurin Lock.

3.6 Staff adherence was discussed briefly in 2 studies reporting the relationship between adherence to using Kurin Lock and the blood culture

contamination rate over a 4-week period. Another study reported that staff adherence ranged between 70% to 75% during a trial use of Kurin Lock.

Cost evidence

Kurin Lock is cost saving compared with standard blood culture collection in both the EAG and company models

3.7 The company submitted a decision tree comparing Kurin Lock with standard blood culture collection in an emergency department in a mixed population setting. In the model, after blood culture collection, empirical antibiotic treatment was started in a proportion of the population based on clinical suspicion of bacteraemia. A length of hospital stay was assumed for everyone who had a blood culture taken. The time horizon of the model was the length of stay in hospital, which could be up to 9 days. The decision model showed that Kurin Lock reduced contaminated blood cultures and led to a shorter length of stay as well as reduced antibiotic treatment compared with standard blood culture collection. This resulted in a cost saving of £73 per person in the company base case and a cost saving of £8 per person in the EAG base case. The main driver for the model was the difference in length of hospital stay between Kurin Lock and standard blood culture collection, and the associated cost.

Length of stay and unnecessary antibiotic use are not formal outcomes in the evidence on Kurin Lock

3.8 Length of stay and unnecessary antibiotic use are not formal outcomes in the evidence on Kurin Lock. So, data for these parameters were taken from other sources, based on false-positive tests. The length of stay was taken from a US emergency department setting (Skoglund 2019). The length of stay for a person with a true negative blood culture in an emergency department was 5 days, and was 7 days for people with a false-positive blood culture and 9 days for people with true positive blood culture. The probability of starting antibiotics and the choice of antibiotic (vancomycin) were also from this paper. The underlying bacteraemia risk was from US data and was assumed to be 7.4%.

There is some evidence of cost savings in the UK but there are limitations to this data

3.9 Atta (2022) and Parsons (2023) based their projected cost savings on the results from Alahmadi 2010, which investigated the costs associated with false-positive blood cultures in a hospital in Northern Ireland, rather than collecting resource use data during the trials. Alahmadi (2010) found there was a cost saving of about £5,000 per contaminated blood culture. The EAG considered that this result was driven by the high proportion of people in the Alahmadi study who were in an intensive care unit, where bed day costs are usually higher than in other hospital settings. This suggested that the cost savings may be overestimated in the Atta (2022) and Parsons (2023) studies. The baseline contamination rate is from Atta (2022) for the company base case. For full details of the cost evidence, see section 4 of the assessment report in the supporting documents.

The EAG changed the decision model parameters to make it more appropriate for decision making

3.10 The EAG agreed with all the clinical parameters in the company model apart from the choice of antibiotic. Clinical experts noted that in practice a wide range of antibiotics may be given. The EAG selected gentamycin for the economic analysis. The change in antibiotic in the EAG model did not have a significant impact on the cost savings of implementing Kurin Lock compared with the company model.

3.11 The most significant change to the decision model was the change of the hospital stay cost. The daily hospital costs in the company base case weighted for the population in the emergency department was £881. This uses a daily cost of a short stay from patient-level data for 1 NHS trust. The EAG considered the hospital stay costs to be high and used an alternative approach to calculate them. It applied a non-elective short stay cost for the first day of admission. For subsequent days, it calculated excess stay costs in line with approaches used previously in NICE assessment reports. This resulted in £1,044 for the first day of admission and £377 daily for the rest of the stay, weighted for the population.

The EAG's changes to the model make Kurin Lock less cost saving

3.12 The EAG base case resulted in a cost saving of £8 per person when using Kurin Lock, whereas the company model reported a cost saving of £73. A probabilistic sensitivity analysis using a 20% variance on the EAG base case showed a 62% probability of Kurin Lock being cost saving. A one-way sensitivity analysis showed that the length and cost of stay, rate of blood culture contamination at baseline and reduction in rate of blood culture contamination from using Kurin Lock all have the potential to make Kurin Lock cost incurring or cost neutral. The results from the sensitivity analysis indicate that at baseline contamination rates of less than 3%, there is low probability of Kurin Lock being cost saving. Contamination rates of more than 9% have a high probability of Kurin Lock being cost saving. The sensitivity analysis (see section 11 of the assessment report in the supporting documents) demonstrated that many factors can influence the cost saving potential of Kurin Lock, and this reflects the uncertainty in the savings in different scenarios.

4 Committee discussion

Clinical-effectiveness overview

The evidence suggests that Kurin Lock reduces blood culture contamination rates

4.1 All 12 studies showed a reduced blood culture contamination rate after introducing Kurin Lock. Most of the studies were based in the US but there were 3 quality improvement studies based in NHS emergency departments. Most of the studies were in adults but there was 1 study in children. Although the evidence base was limited, the committee considered it plausible that Kurin Lock would lead to the positive outcomes associated with reduced blood culture contamination.

More evidence is needed to understand the resource impact of false-positive blood culture results

4.2 There is a lack of direct evidence of the downstream resource impact of using Kurin Lock. By reducing the blood culture contamination rate, the number of false positives should also be reduced. This is expected to have an impact on a patient's length of stay and antibiotic use. The clinical experts advised that there is uncertainty in the length of stay for people who have a blood culture taken and that many factors influence this. The length of stay data used in the economic model was from Skoglund 2019, based in the US. The key parameters were that a person with a true negative blood culture result would have a hospital stay of 5 days, and a person with a false-positive result would have a hospital stay of 7 days. One clinical expert stated that a mean difference of 2 days hospital stay is not plausible in clinical practice. The expert explained that other test results and clinical information are routinely used to help decide if a blood culture result is contaminated. So, in their opinion only a small proportion of people with a false-positive blood culture result would have additional treatment and a longer hospital stay. The committee agreed with the EAG's view that the Alahmadi (2010) study, which estimated longer hospital stays associated with false positives compared with Skoglund 2019, was not generalisable to the NHS because of the high proportion of people in intensive care. The committee agreed that the 2-day difference from Skoglund (2019) may not represent NHS clinical practice, and that further evidence of the resource impact in the NHS should be generated.

4.3 Further evidence is also needed on the impact of false positives on antibiotic treatment. The clinical experts advised that most people with suspected sepsis would start antibiotic treatment before the results of the blood culture test were available. The committee considered that using Kurin Lock is not likely to have a significant impact on antibiotic stewardship. The committee noted that data on staff adherence is also important to determine if this reduces over time or in busy periods, and the impact on blood culture contamination rates.

Relevance to the NHS

There would be no change in practice when using Kurin Lock compared with standard blood culture collection

4.4 According to the clinical experts, Kurin Lock is easy to use and needs minimal training. The clinical experts agreed that Kurin Lock was appropriate for use in the secondary care blood culture sampling pathway, to reduce blood culture contamination rates. It could replace standard blood culture collection in most cases apart from when people have central lines. They advised that Kurin Lock may reduce pressure in the emergency department and improve outcomes for patients by reducing the number of contaminated blood culture samples.

NHS considerations overview

The cost of Kurin Lock is high compared with standard blood culture collection

4.5 The high cost of Kurin Lock compared with standard blood culture collection is a barrier to using it in the NHS, unless there is better evidence showing its impact on resources. One clinical expert commented that his hospital considered the Kurin Lock cost too high and it has explored using an alternative approach to reduce contamination rates. The committee understood that the cost saving from the economic modelling relied on the high device cost being offset by a reduction in resource use, including hospital length of stay, associated with fewer false-positive results. Further evidence generation is needed to show that these cost savings will be realised in NHS clinical practice.

Kurin Lock is most likely to be cost saving in settings with a high baseline contamination rate

4.6 The committee and clinical experts agreed that there are usually higher blood culture contamination rates in the emergency department than other hospital wards, and noted that the economic modelling used an emergency department setting. In published literature, contamination

rates of up to 9% were reported in NHS emergency departments. But clinical experts stated that it could be significantly higher. One clinical expert stated that they had reduced contamination rates through staff training, ensuring samples are not taken from peripheral cannulas and introducing an additional blood bottle, which is used to isolate the first few millilitres from the blood culture sample. They advised that this approach reduced blood culture contamination rates, but the change in practice needs to be regularly reinforced and may be time-consuming. Another expert had trialled this approach before using Kurin Lock and felt that Kurin Lock is easier to adopt, and from their experience works just as well with cannulas as venepuncture.

Cost modelling overview

The EAG's updated model is more plausible than the company's base case and most appropriate for decision making

4.7 The company's base-case model used an emergency department setting. It used a daily ward stay cost taken from patient-level data from 1 NHS trust, which was described as a non-elective short stay cost. This was applied as a daily cost for the duration of the patient stay. The EAG did not have access to this cost data and considered the daily costs very high compared with other economic models for guidance development. The EAG used a non-elective short stay cost as the first day of stay cost, and then calculated excess stay costs for additional days using costs from NHS Cost Collection data. The committee agreed with the changes the EAG made to the company's base-case model. It considered that the lower daily hospital stay cost used by the EAG was appropriate. Accurate information on the costing of the hospital stay and the length of stay would help reduce uncertainty in the economic modelling.

Main cost drivers

The length of stay difference and the cost associated with this affects the cost saving potential of Kurin Lock

4.8 If the difference in length of stay for people with true negative blood culture results and false-positive blood culture results is overestimated, then the cost saving is reduced. This could lead to Kurin Lock being cost incurring rather than cost saving. The EAG confirmed that there is no length of stay difference data directly related to Kurin Lock that can be used instead of the Skoglund (2019) values to reduce the uncertainty of the model results. Because the main driver is the length of stay difference, the committee was cautious in its interpretation of the base-case results.

Cost savings

Kurin Lock is cost saving in the EAG's base case, but the sensitivity analysis indicates uncertainty

4.9 There is uncertainty about the cost effectiveness of introducing Kurin Lock, because the sensitivity analysis showed that it can be cost saving or cost incurring. Probabilistic sensitivity analysis of the EAG model reported a 62% probability that Kurin Lock would be cost saving compared with standard blood culture collection. The committee considered that the lack of evidence on the resource impact from using Kurin Lock is a significant limitation of the economic model. Further evidence generation including information on the length of hospital stay from NHS hospitals using Kurin Lock could be used to revise the economic model.

Conclusion

Evidence generation should provide data to reduce uncertainty in the economic modelling

4.10 The key uncertainties about using Kurin Lock in the NHS are related to its cost effectiveness. Sensitivity analysis showed that Kurin Lock can be cost saving or cost incurring depending on the parameters used,

particularly around the length and cost of hospital stay. The clinical experts advised that length of stay and treatment after a blood culture test is complex and depends on many factors. The committee concluded that evidence generation alongside using Kurin Lock in the NHS would provide an opportunity to collect resource impact data that could inform economic modelling in a future review of the guidance. NICE will review the guidance once new evidence is available.

5 Committee members and NICE project team

Committee members

This topic was considered by NICE's medical technologies advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of the medical technologies advisory committee, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each medical technologies guidance topic is assigned to a team consisting of 1 or more health technology assessment analysts (who act as technical leads for the topic), a health technology assessment adviser and a project manager.

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