NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology consultation document

AnaConDa-S for sedation with volatile anaesthetics in intensive care

How medical technology guidance supports innovation

NICE medical technologies guidance addresses specific technologies notified to NICE by companies. The 'case for adoption' is based on the claimed advantages of introducing the specific technology compared with current management of the condition. This case is reviewed against the evidence submitted and expert advice.

If the case for adopting the technology is supported, the specific recommendations are not intended to limit use of other relevant technologies that may offer similar advantages. 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 AnaConDa-S is recommended as an option for delivering inhaled sedation in an intensive care setting when the volatile anaesthetics isoflurane or sevoflurane are being considered.

1.2 Further research is recommended to identify any groups of patients that could benefit from inhaled sedation with AnaConDa-S. Find out more in the section on further research.

1.3 Cost modelling shows that, over 30 days, AnaConDa-S is cost saving compared with intravenous propofol sedation by £4,393.20 per adult. In children, AnaConDa-S is also cost saving compared with intravenous midazolam sedation by £3,396.85 per child. These savings are from

reduced time on mechanical ventilation, which may shorten the length of time in intensive care for the patient.

Why the committee made these recommendations

AnaConDa-S is used in intensive care settings when people need inhaled sedation. The evidence for AnaConDa-S includes people with a wide range of conditions. But there were not enough people for each condition in the studies to identify who would particularly benefit from inhaled sedation with AnaConDa-S. Also, there is no published evidence on using AnaConDa-S in children. So, further research is recommended to identify the groups that could benefit from using the technology.

Evidence suggests that time to people waking up from sedation is shorter with inhaled sedation (using AnaConDa-S) than with intravenous sedation, but that a reduction in time on mechanical ventilation is uncertain. It is also uncertain if using AnaConDa-S shortens a person's length of stay in intensive care. Because these are the key drivers of cost savings, the cost analysis results are also uncertain. Even with these uncertainties, AnaConDa-S is still cost saving in both children and adults and shows promise as an option for use in intensive care settings for sedation with volatile anaesthetics, when sedation with isoflurane or sevoflurane is being considered.

2 The technology

Technology

2.1 The Anaesthetic Conserving Device-S (AnaConDa-S; Sedana Medical) is a volatile anaesthetic delivery system to give isoflurane or sevoflurane to people who are mechanically ventilated, usually in an intensive care setting.

2.2 AnaConDa-S is a single-use device (replaced every 24 hours or earlier when needed). The device can be inserted into either the breathing circuit of a ventilator between the endotracheal tube and Y piece, replacing the heat and moisture exchanger (standard placement) or in the inspiratory port of the ventilator (alternative placement). Liquid anaesthetic is injected through the anaesthetic agent line, into a porous rod in the AnaConDa-S

device where the anaesthetic is vaporised. The vaporised anaesthetic is then inhaled by the patient with the inspiration flow from the ventilator. With continued breathing, most of the anaesthetic agent that has not been absorbed by the lungs is exhaled and adsorbed by an active carbon filter in the device. On further inhalation, the anaesthetic is desorbed from the filter and transported back to the lungs, reducing the amount of anaesthetic agent wasted. The AnaConDa-S device also contains a bacterial and viral filter and a gas analyser port. This port is used to measure the exhalated anaesthetic concentration in minimal alveolar concentration (MAC value; a relative measure of the level of anaesthesia) or end-tidal concentration [Fet%]). Side stream or mainstream gas monitors, which can measure concentrations of carbon dioxide and anaesthetic gases, must be used to continually monitor anaesthesia. These will need to be purchased separately if not already available. AnaConDa-S is also recommended to be used with a gas scavenging system. This can be either via a passive system like the manufacturer's FlurAbsorb and FlurAbsorb-S products, or via an active scavenging system. This is usually built in the hospital system to capture volatile anaesthetics in operating theatres.

2.3 AnaConDa-S can be used with most kinds of ventilator, except high-frequency ventilators. It was launched in the UK in 2017 and is a newer version of the AnaConDa device (available in the UK since 2005), which is now only available on request in the UK. The AnaConDa-S has a lower dead space of 50 ml (compared with 100 ml in the original device) and works with tidal volumes as low as 90 ml. The lower dead space allows AnaConDa-S to be used on smaller adults or children who have smaller minute or tidal ventilation.

Care pathway

2.4 Adults who need sedation in intensive care have sedation with intravenous sedatives and analgesics, primarily propofol or midazolam with alfentanil, fentanyl or morphine. Children in intensive care usually have sedation with intravenous midazolam and morphine or fentanyl.

2.5 Volatile anaesthetics are not licensed for sedation in intensive care units but are licensed for inducting and maintaining anaesthesia in operating theatres. However, clinical experts reported that sedation is a continuum to anaesthesia. The off-label use of volatile anaesthetics in sedation is widely accepted and is not considered to be harmful. The choice of type of sedation and sedative agents to be used is made by trained clinicians.

2.6 Expert advice suggests the technology is being used in the NHS as an alternative to intravenous sedation in:

- people who need mechanical ventilation that are difficult to sedate (both adults and children)
- people who have severe bronchospasms that need mechanical ventilation (both adults and children)
- people who need mechanical ventilation after cardiac surgery and cardiac arrest
- people in whom intravenous access is difficult or not possible.

Innovative aspects

2.7 The innovative aspect is that AnaConDa-S is the only device that allows conserved delivery of inhaled anaesthetic in an intensive care setting in both adults and children.

Intended use

2.8 AnaConDa-S is intended to be used as an alternative to intravenous anaesthetics for people who need sedation and are mechanically ventilated in intensive care. The AnaConDa-S has a tidal volume working range of 200 ml to 800 ml when used in standard placement. Small tidal volume (90 ml) can be achieved when AnaConDa-S is used in the alternative placement.

2.9 AnaConDa-S is for use by healthcare professionals, trained to use inhalational anaesthetic drugs and recognise and manage any adverse effects, in an intensive care setting. In the NHS this would likely be intensivists and intensive care nurses.

Costs

2.10 AnaConDa-S is available for purchase as a pack of 6 for [redacted] This includes component materials for 6 patient set-ups and approximately 5 treatment days each (30 treatment days in total). The costs used in the economic modelling were:

- Device cost: [redacted] per full course per patient (10.9 days sedation)
- Consumables (FlurAbsorb, syringes, new fill adapter, measure line, nafion tubing, accessories kit): [redacted] per patient
- Multi-gas analyser: £36.61
- Total cost of isoflurane administration: £110.78 per patient

For more details, see the website for AnaConDa-S.

3 Evidence

NICE commissioned an external assessment centre (EAC) 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

The main clinical evidence comprises 21 studies

3.1 The EAC assessed 21 full text comparative studies. Thirteen were randomised controlled trials, 5 retrospective studies, 1 prospective study, and 1 study collected data prospectively for the AnaConDa-S arm but utilised retrospective data for the intravenous arm. Fifteen abstracts identified were not included in the evidence review. The EAC focused on primary studies only and did not extract data from 1 meta-analysis to avoid duplication of data. There was no published evidence on using AnaConDa-S in children.

3.2 All included studies were peer-reviewed, and none were done in the UK. The included studies covered 6 population groups:

- People after cardiac surgery (8 studies, 798 people)

- People after cardiac arrest having therapeutic temperature management (3 studies, 816 people)
- People with acute respiratory distress syndrome patients (2 studies, 88 people)
- People with various surgical indications (2 studies, 270 people)
- People having head and neck surgery who need a tracheostomy (1 study, 29 people)
- People with pulmonary disorders (1 study, 30 people)
- People with over 12 hour (1 study, 40 people) and 24 hour sedation needs (2 studies, 361 people).

For full details of the clinical evidence, see section 3 of the assessment report. Find the assessment report in the supporting documentation file in the project documents on the NICE website.

Clinical experts identified 3 particularly important clinical outcomes

3.3 The EAC, after consultation with clinical experts, identified 3 outcomes of particular clinical importance: time on mechanical ventilation, wake up time and sedation efficiency. Other outcomes reported across the 21 included studies were: intensive care and hospital length of stay, cognitive and neurological status, cardiac, renal and hepatic markers and blood gas results.

Evidence shows that inhaled sedation using AnaConDa-S consistently leads to faster wake up time and maintains adequate sedation but time on mechanical ventilation is uncertain

3.4 Wake up time, usually reported as extubation time (the time from stopping the sedative infusion to taking out the endotracheal tube), was measured in 6 studies and found to be significantly shorter in the volatile sedation arms compared with the intravenous arms across all the heterogeneous populations. The EAC concluded that sedation given using AnaConDa-S offers benefit over intravenous sedation in terms of wake up time, but this is likely attributed to using the volatile sedatives that AnaConDa-S allows to be used rather than the device itself.

3.5 Inhaled sedation using isoflurane delivered with AnaConDa-S was non-inferior to propofol in maintaining adequate sedation (time spent at the desired sedation depth) without rescue medications in a large randomised clinical trial (n=301, Meiser 2021).

3.6 Eleven publications reported time on mechanical ventilation. The difference in time on mechanical ventilation between the volatile arms and the intravenous arms was uncertain because only 3 studies reported statistically significant differences (matched analysis of Krannich 2017, Rohm 2008 & 2009) and the rest of the studies found non-significant differences in time on ventilation.

There is uncertainty in the evidence on length of stay for inhaled sedation and intravenous sedation

3.7 All included studies were inconclusive about the measured outcomes for length of stay. The studies looked at different sedative drug combinations and any differences between groups are likely to be because of these drug differences as well as the variables involved in patient treatment and are unlikely to be solely attributed to using the device.

Evidence is inconclusive for other outcomes that benefit patients

3.8 Eight studies reported on cognitive and neurological outcomes, 9 studies reported on cardiac, renal and hepatic biochemical markers and 6 studies reported on patient blood gas results. Most of the studies were not statistically significant in lowering the incidence of delirium, lowering organ-specific biomarkers and improving oxygenation compared with intravenous sedatives.

Cost evidence

The company's cost analysis model compares inhaled sedation using the AnaConDa-S device with intravenous sedation

3.9 The company's cost model compared inhaled isoflurane with intravenous propofol. The cost model had a 30-day time horizon and included adult patients needing mechanical ventilation for 24 hours or longer in intensive care. The clinical input parameters included the mean body weight of people having sedation in intensive care, the time on mechanical ventilation (mean in days) and the length of stay in intensive care (mean in days). The company also submitted a scenario analysis that compared inhaled isoflurane with intravenous midazolam. The EAC adapted this analysis to extrapolate the cost analysis in children. The EAC inputted an average body weight of 12 kg for a child but did not change the other clinical paraments. For full details of the cost evidence, see section 4 of the assessment report.

AnaConDa-S device remains cost saving in the EAC's updated model

3.10 The EAC agreed with the company's cost model overall. The EAC noted that the time on mechanical ventilation and the length of stay in intensive care were based on the results of a post-hoc analysis done in a subset of people [redacted] from the original randomised clinical trial (n=301, Meiser 2021). This subgroup consisted of people that did not have their sedation approach switched after the 48 hour randomisation period. The EAC corrected some costs, added the cost of training for switching from intravenous to inhaled sedation and found that AnaConDa-S remained cost saving by £4,393.20 per adult.

The company cost analysis results are robust but there is uncertainty around the clinical inputs that drive cost savings

3.11 Sensitivity analysis indicated that the cost analysis was robust to changes to drug doses, drug costs and to the addition of training costs with AnaConDa-S. The EAC threshold analysis showed that, if time on mechanical ventilation is the same for both methods of sedation, inhaled

sedation using AnaConDa-S was cost saving compared with intravenous propofol when the duration of non-ventilated intensive care days was in the region of 0.5 days to 0.6 days lower. However, the length of stay in intensive care and time on mechanical ventilation, were sourced from the post hoc analysis in a subset of study patients from Meiser 2021. These outcomes were not the primary outcomes of the trial and they were not included in the publication.

Exploratory analysis suggests that inhaled sedation with AnaConDa-S is cost saving in children

3.12 The EAC used the cost analysis model comparing inhaled isoflurane with intravenous midazolam to explore the economic impact of using inhaled sedation in children. Clinical parameters were informed from Krannich 2017. The cost analysis estimated a cost saving of £3,396.85 per child. The clinical experts considered it reasonable to assume that children have a similar response to intervention to adults.

4 Committee discussion

Clinical-effectiveness overview

AnaConDa-S is an efficient delivery system for using inhaled sedation in an intensive care setting without needing a scavenging system

4.1 Experts explained that AnaConDa-S is the only device that allows delivery of inhaled sedation in an intensive care setting without the need for a gas scavenging system. The alternative would be to use an anaesthetic trolley or machine used for general anaesthesia with a gas scavenger, but the clinical experts said that intensive care units are not routinely equipped with scavenging systems. The experts also said that before AnaConDa-S was implemented, patients needing inhaled sedation with vaporisers had to be transferred to operating theatres where scavenging systems for volatile anaesthetics are built into the hospital system (that is, the exhaust port of the anaesthetic circuit or ventilators are connected to the operating theatre scavenging system). The committee concluded that AnaConDa-S

is an efficient delivery system for inhaled sedation in an intensive care setting not equipped with scavenging systems.

No published clinical evidence is available on using AnaConDa-S in children

4.2 Although no clinical evidence in children was presented to the committee, a clinical expert said that AnaConDa-S has been used for 15 years in their paediatric intensive care and it is an effective way of delivering inhaled sedation. No major contraindications exist for using inhaled sedation in children, apart from malignant hyperthermia susceptibility. The EAC extrapolation of the efficacy of inhaled sedation from adults to children considered it reasonable to assume that children respond similarly to the intervention to adults. The committee accepted the assumption and concluded that AnaConDa-S is a useful option for allowing delivery of volatile sedation in children.

Evidence shows that inhaled sedation using AnaConDa-S is consistently associated with faster wake up time

4.3 Six clinical studies (5 randomised controlled trials [RCTs] and 1 comparative non-RCT) reported statistically significant differences in wake up between the intravenous sedation and the inhaled sedation using AnaConDa-S. The EAC reported that the extubation time is likely dependent on the type of sedative agent used rather than using the AnaConDa-S device itself. Nevertheless, the clinical experts agreed that using inhaled sedation delivered with AnaConDa-S leads to more predictable wake up time in people having sedation for long time and this is useful when patients need to be woken quickly to make clinical assessments.

The evidence for replacing intravenous sedation with inhaled sedation delivered by AnaConDa-S is uncertain because of heterogeneity

4.4 The 21 studies had heterogenous patient populations that included people after cardiac surgery (9 studies), people after cardiac arrest having therapeutic temperature management (3 studies), people with acute

respiratory distress syndrome (2 studies), patients with various surgical indications (2 studies), people having head and neck surgery who need a tracheostomy (1 study), people with pulmonary disorders (1 study) and people with over 12 hour (1 study) and 24 hour sedation needs (2 studies). The committee concluded that there was uncertainty about which specific patient population would benefits more from using inhaled sedation. But, based on expert advice, it agreed that AnaConDa-S should be an available option for delivering inhaled sedation in intensive care settings when considered clinically appropriate.

Length of stay in intensive care and the time on mechanical ventilation depend on the underlying condition

4.5 Clinical experts said that the length of stay in intensive care and the time on mechanical ventilation are outcomes that depend on a patient's underlying condition. The committee understood that this means it is particularly challenging to show evidence of benefit for length of stay in the context of a clinical study. However, clinical experts explained that using inhaled sedation can reduce the time on mechanical ventilation and shorten the time the patient stays in intensive care after extubation by some hours. The committee concluded that type of sedation used was likely to only have a small effect on the length of stay in intensive care or time on mechanical ventilation.

AnaConDa-S delivered inhaled sedation is useful for sparing intravenous agents during emergency situations

4.6 Clinical experts reported that during the SARS-COV-2 pandemic, inhaled sedation using AnaConDa-S has been used to preserve intravenous sedative agents that could potentially be in limited supply. The committee concluded that AnaConDa-S is a useful option to spare intravenous sedative agents during unexpected emergency situations when large number of people need mechanical ventilation such as in the recent SARS-COV-2 pandemic.

Side effects and adverse events

Adverse events associated with using AnaConDa-S are uncommon but inhaled sedation is contraindicated in some patients

4.7 The committee heard that were no reported safety concerns around using the AnaConDa-S device. It understood that people in intensive care have highly complex needs and as such most adverse events will be due to the different medications to achieve sedation, rather than using the AnaConDa-S device itself. The only adverse event linked to the device is blockage, which can also happen in heat and moisture exchangers at a similar rate. There are adverse events associated with using volatile anaesthetic drugs. Volatile anaesthetics are contraindicated in patients with malignant hyperthermia susceptibility. Clinical experts said that using volatile anaesthetics in pregnant women, especially in the first trimester, involve clinical judgment in the risk/benefit balance to the unborn foetus and risk to the woman. The committee concluded that using AnaConDa-S is safe.

4.8 There are other adverse events associated with using volatile anaesthetia listed in the British National Formulary.

Other patient benefits or issues

Some evidence shows inhaled sedation seems to be beneficial to patients

4.9 Clinical experts explained that there are benefits for patients when volatile sedatives are used such as liver, lung and cardiac protection. The EAC reported better awareness quality (1 study) and lower incidence of delirium (1 study) in the AnaConDa-S group compared with the intravenous group.

Clinical experts suggest AnaConDA-S may be more beneficial in some patient subgroups

4.10 The clinical experts agreed that inhaled sedation is likely to be beneficial in the following subgroups:

- People who are difficult to sedate
- People with acute bronchospasm
- People with acute respiratory distress syndrome
- People having multiple sedative agents
- Peoples with overdose that need a fast wake up
- People who need neurological assessment after a cardiac attack
- Elderly people at high risk of delirium
- Children with resistant status epilepticus
- People with difficult intravenous access
- People with hypoxia.

NHS considerations overview

Children and adults having sedation with inhaled volatiles using AnaConDa-S can be transported for transfer within hospital

4.11 While uncommon, clinical experts said that patients can be transported for additional tests or procedures within hospitals using AnaConDa-S. If transport ventilators do not have scavenging system built in, canisters containing activated carbon, such as FlurAbsorb, can be added to the transport trolley.

Training

Only health care professionals trained in inhaled anaesthetic drugs can use AnaConDa-S

4.12 The clinical experts said that the company offers face-to-face training and an e-learning module for intensive care nurses and intensivists. The clinical experts noted that the company training resources were highly effective.

Environmental impact

AnaConDa-S may minimise the release of greenhouse gases

4.13 Volatile anaesthetic drugs are potent greenhouse gases. However, the company claims that the conservation of gases within AnaConDa-S and using scavenging systems can reduce the release of gases into the atmosphere. The company also claims that AnaConDa-S would be associated with a lower consumption of volatile sedatives compared with other delivery systems for volatile sedation. The committee was concerned about the environmental effect of increased use of anaesthetic gases and was unsure about the company claims on the efficacy of their scavenging systems. They noted that there was a lack of evidence comparing AnaConDa-S with other vaporisers used for delivering volatile sedation. Nevertheless, the committee concluded that there was plausible promise that AnaConDa-S would minimise release of greenhouse gases.

Cost modelling overview

Economic modelling is limited by the uncertainty in some clinical inputs and its relevance to the NHS clinical pathway

4.14 The committee accepted the EAC's changes to the company model, which showed inhaled sedation delivered with AnaConDa-S was cost saving when compared with intravenous sedation. However, the committee agreed that the modelled clinical scenario comparing intravenous sedation with inhaled sedation using AnaConDa-S does not reflect the average UK duration of time on mechanical ventilation in intensive care so has limited applicability (mean time on mechanical ventilation used in the model was [redacted] days whereas experts reported 5 days to 7 days in the UK). The committee also noted that the clinical evidence used to populate the model had substantial limitations, which affected the robustness of the model and the certainty of the results.

Main cost drivers

Because of the outcomes measured in the study, the cost savings are not certain

4.15 The committee concluded that the evidence about length of stay in intensive care and the time on mechanical ventilation reported in the post-hoc analysis from Meiser 2021 trial was very weak. Because these inputs were the key drivers that led AnaConDa-S to be cost saving, there was uncertainty if using AnaConDa-S would be cost saving. Despite these uncertainties, the committee noted that AnaConDa-S has a low threshold to be cost saving. The EAC's threshold analysis found that AnaConDa-S was cost saving when duration of non-ventilated days in intensive care was 12 hours shorter than that of intravenous. The committee concluded that AnaConDa-S was likely to be the cost saving.

Scenario analyses

AnaConDa-S remains cost saving in all analysed scenarios

4.16 The committee noted that AnaConDa-S remained cost saving in all scenario analyses presented. However, the robustness of the estimates of length of stay in intensive care and time on mechanical ventilation were uncertain. The committee concluded that the uncertainty in the clinical inputs could led to inaccuracies in the cost savings calculated.

Cost savings

AnaConDa-S is likely to be cost saving compared with intravenous sedation in both adults and children

4.17 The EAC reported that in modelling, AnaConDa-S is cost saving compared with intravenous sedation by £4,393.20 per adult patient and by £3,396.85 per child. The committee concluded that AnaConDa-S was likely to be cost saving compared with propofol or midazolam but recognised the limitations in the underpinning clinical evidence which made the size of the potential cost savings uncertain.

Further research

Further good quality research is needed to address uncertainties about the population for whom AnaConDa-S is most appropriate

4.18 The committee recognised that AnaConDa-S is an efficient and safe way of delivering volatile anaesthetics in intensive care units. The committee concluded that further research is needed to address uncertainties in the appropriate population where AnaConDa-S would be recommended for use compared with standard care. It concluded that, although there is clear evidence that inhaled sedation using AnaConDa-S can lead to faster wake time, the evidence around the decrease in length of stay in intensive care and time on mechanical ventilation are more difficult to because of the complexity of the underlying conditions of people in intensive care unit.

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 appraised. 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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ISBN: [to be added at publication]

Addendum 1: Corrected Training Costs

MT582 AnaConDa-S for sedation with volatile anaesthetics in intensive care

Impact of Calculation Correction on Cost Savings

A calculation error in the cost of training has been corrected by the EAC. Training costs have been reduced to £62.16 per patient. The impact of this change has been to increase the cost savings associated with inhaled sedation using the AnaConDa device when compared with propofol.

Table 1: Propofol versus Isoflurane

Model	Cost of Intervention (Inhaled isoflurane using AnaConDa-S)	Cost of Comparator (IV Propofol)	Cost Saving
Company Base-case	£15,999.43	£19,647.73	£3,648.31
EAC Preferred Values	£18,703.83	£23,097.03	£4,393.20
Scenario 1: Days on ventilation are different for the sedation methods			
Company Scenario 1 (difference in ventilator days and ICU days between IV and inhaled sedation)	£15,507	£20,004	£4,497
Using EAC Preferred Values	£17,842.21	£23,797.63	£5,955.42
Scenario 2: ICU length of stay for total study population			
Company Scenario 2 (difference in ventilator days and ICU day in population including switchers)	£20,107.00	£21,141.66	£1,034.66
Using EAC Preferred Values	£23,166.41	£25,300.15	£2,133.74
Scenario 3: Sevoflurane for inhaled sedation			
EAC Additional Scenario: Sevoflurane for inhaled sedation with AnaConDa	£19,751.42	£23,097.03	£3,345.61

Similarly, the reduction in training costs results in increased cost savings with AnaConDa compared with Midazolam (table 2).

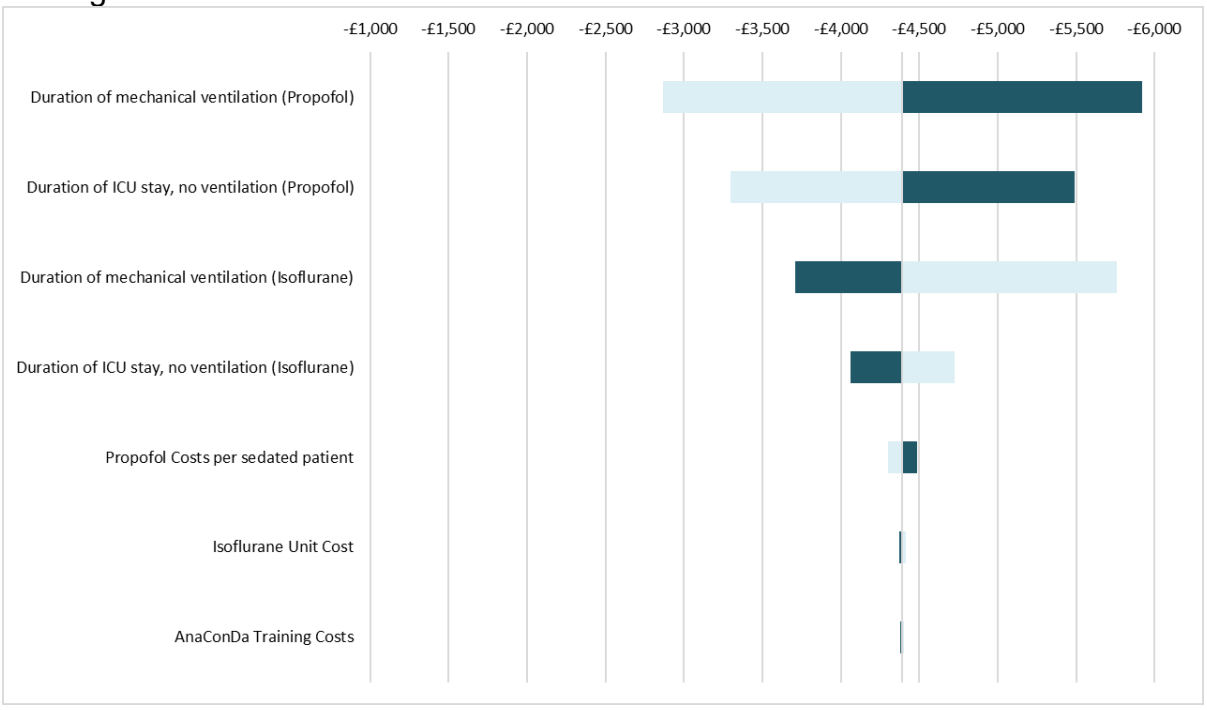
Table 2: Midazolam versus Isoflurane

Model	Cost of Intervention (Inhaled isoflurane using AnaConDa-S)	Cost of Comparator (IV Midazolam)	Cost Saving
Company Scenario	£10,161.28	£15,919.55	£5,758
EAC preferred inputs (Adult patients)	£12,508.88	£19,157.57	£6,648.69
EAC preferred inputs (Pediatric Patients)	£6,883.58	£9,720.99	£3,396.85

Sensitivity Analysis (AnaConDa vs Propofol)

Updated sensitivity analysis suggests that with the lower cost of training, AnaConDa remains cost saving even when duration of ICU stay is slightly longer with AnaConDa. This is because, with changes the EAC made to propofol costs (see Assessment Report) the cost of sedation with AnaConDa becomes marginally cheaper than with propofol per patient per day.

The EAC note that there is considerable uncertainty around the accuracy of the training costs and should be considered with caution.



		Duration of Additional ICU Stay													
		AnaConDa													
	-£4,393.20	18	17	16.5	16.3	15.5	15	14.5	14.2	13.5	13	12.5	12.4	11.5	10.5
Propofol	18	-£550.95	-£1,465.77	-£1,923.18	-£2,106.15	-£2,838.00	-£3,295.41	-£3,752.82	-£4,027.27	-£4,667.64	-£5,125.05	-£5,582.46	-£5,673.94	-£6,497.28	-£7,412.10
	17	£363.87	-£550.95	-£1,008.36	-£1,191.33	-£1,923.18	-£2,380.59	-£2,838.00	-£3,112.45	-£3,752.82	-£4,210.23	-£4,667.64	-£4,759.12	-£5,582.46	-£6,497.28
	16.5	£821.28	-£93.54	-£550.95	-£733.92	-£1,465.77	-£1,923.18	-£2,380.59	-£2,655.04	-£3,295.41	-£3,752.82	-£4,210.23	-£4,301.71	-£5,125.05	-£6,039.87
	16.3	£1,004.24	£89.42	-£367.99	-£550.95	-£1,282.81	-£1,740.22	-£2,197.63	-£2,472.07	-£3,112.45	-£3,569.86	-£4,027.27	-£4,118.75	-£4,942.09	-£5,856.91
	15.5	£1,736.10	£821.28	£363.87	£180.90	-£550.95	-£1,008.36	-£1,465.77	-£1,740.22	-£2,380.59	-£2,838.00	-£3,295.41	-£3,386.89	-£4,210.23	-£5,125.05
	15	£2,193.51	£1,278.69	£821.28	£638.31	-£93.54	-£550.95	-£1,008.36	-£1,282.81	-£1,923.18	-£2,380.59	-£2,838.00	-£2,929.48	-£3,752.82	-£4,667.64
	14.5	£2,650.92	£1,736.10	£1,278.69	£1,095.72	£363.87	-£93.54	-£550.95	-£825.40	-£1,465.77	-£1,923.18	-£2,380.59	-£2,472.07	-£3,295.41	-£4,210.23
	14.2	£2,925.36	£2,010.54	£1,553.13	£1,370.17	£638.31	£180.90	-£276.51	-£550.95	-£1,191.33	-£1,648.74	-£2,106.15	-£2,197.63	-£3,020.97	-£3,935.79
	13.5	£3,565.74	£2,650.92	£2,193.51	£2,010.54	£1,278.69	£821.28	£363.87	£89.42	-£550.95	-£1,008.36	-£1,465.77	-£1,557.25	-£2,380.59	-£3,295.41
	13	£4,023.15	£3,108.33	£2,650.92	£2,467.95	£1,736.10	£1,278.69	£821.28	£546.83	-£93.54	-£550.95	-£1,008.36	-£1,099.84	-£1,923.18	-£2,838.00
	12.5	£4,480.56	£3,565.74	£3,108.33	£2,925.36	£2,193.51	£1,736.10	£1,278.69	£1,004.24	£363.87	-£93.54	-£550.95	-£642.43	-£1,465.77	-£2,380.59
	12.4	£4,572.04	£3,657.22	£3,199.81	£3,016.85	£2,284.99	£1,827.58	£1,370.17	£1,095.72	£455.35	-£2.06	-£459.47	-£550.95	-£1,374.29	-£2,289.11
	11.5	£5,395.38	£4,480.56	£4,023.15	£3,840.18	£3,108.33	£2,650.92	£2,193.51	£1,919.06	£1,278.69	£821.28	£363.87	£272.39	-£550.95	-£1,465.77
	10.5	£6,310.20	£5,395.38	£4,937.97	£4,755.00	£4,023.15	£3,565.74	£3,108.33	£2,833.88	£2,193.51	£1,736.10	£1,278.69	£1,187.21	£363.87	-£550.95
		£15,915.81	£15,000.99	£14,543.58	£14,360.61	£13,628.76	£13,171.35	£12,713.94	£12,439.49	£11,799.12	£11,341.71	£10,884.30	£10,792.82	£9,969.48	£9,054.66

Addendum 2: Breakdown of costs and impact of removing daily sedation interruption and dose renewals

During the draft guidance meeting, the clinical experts requested a breakdown of the costs by sedation approach. This information is presented below – it should be noted that all results are based on a corrected cost of training.

Daily Sedation Interruption and Dose Renewals: These are included in the model for IV Sedation (Propofol) only.

The costs in the model are outlined in table 3.

Table 3: Cost by sedation approach

Sedation Approach	Cost per patient per day	Total cost for duration of sedation (10.9 days)
Propofol	£152.01 £43.34 is the cost of Propofol and £108.67 is the cost of the daily sedation interruption/dose renewal.	£1,656.94
Isoflurane	£95.76 £10.16 is the cost of isoflurane and £85.60 is the additional equipment costs for AnaConDa	£1,043.83

Based on the corrected training costs, if the daily sedation interruption and dose renewal costs are removed from the model, the cost savings associated with AnaConDa reduce from £4,393.20 to £3,208.71. This is for the base case, where the duration of ventilation is the same in both arms. In two-way sensitivity analysis (table 2), again with duration of ventilation equal in both arms, AnaConDa remains cost saving provided there is a reduction of 0.7 days overall ICU stay.

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		Duration of Additional ICU Stay AnaConDa													
	-£3,208.71	18	17	16.5	16.3	15.5	15	14.5	14.2	13.5	13	12.5	12.4	11.5	10.5
Propofol	18	£633.54	-£281.28	-£738.69	-£921.66	-£1,653.51	-£2,110.92	-£2,568.33	-£2,842.78	-£3,483.15	-£3,940.56	-£4,397.97	-£4,489.45	-£5,312.79	-£6,227.61
	17	£1,548.36	£633.54	£176.13	-£6.84	-£738.69	-£1,196.10	-£1,653.51	-£1,927.96	-£2,568.33	-£3,025.74	-£3,483.15	-£3,574.63	-£4,397.97	-£5,312.79
	16.5	£2,005.77	£1,090.95	£633.54	£450.57	-£281.28	-£738.69	-£1,196.10	-£1,470.55	-£2,110.92	-£2,568.33	-£3,025.74	-£3,117.22	-£3,940.56	-£4,855.38
	16.3	£2,188.73	£1,273.91	£816.50	£633.54	-£98.32	-£555.73	-£1,013.14	-£1,287.58	-£1,927.96	-£2,385.37	-£2,842.78	-£2,934.26	-£3,757.60	-£4,672.42
	15.5	£2,920.59	£2,005.77	£1,548.36	£1,365.39	£633.54	£176.13	-£281.28	-£555.73	-£1,196.10	-£1,653.51	-£2,110.92	-£2,202.40	-£3,025.74	-£3,940.56
	15	£3,378.00	£2,463.18	£2,005.77	£1,822.80	£1,090.95	£633.54	£176.13	-£98.32	-£738.69	-£1,196.10	-£1,653.51	-£1,744.99	-£2,568.33	-£3,483.15
	14.5	£3,835.41	£2,920.59	£2,463.18	£2,280.21	£1,548.36	£1,090.95	£633.54	£359.09	-£281.28	-£738.69	-£1,196.10	-£1,287.58	-£2,110.92	-£3,025.74
	14.2	£4,109.85	£3,195.03	£2,737.62	£2,554.66	£1,822.80	£1,365.39	£907.98	£633.54	-£6.84	-£464.25	-£921.66	-£1,013.14	-£1,836.48	-£2,751.30
	13.5	£4,750.23	£3,835.41	£3,378.00	£3,195.03	£2,463.18	£2,005.77	£1,548.36	£1,273.91	£633.54	£176.13	-£281.28	-£372.76	-£1,196.10	-£2,110.92
	13	£5,207.64	£4,292.82	£3,835.41	£3,652.44	£2,920.59	£2,463.18	£2,005.77	£1,731.32	£1,090.95	£633.54	£176.13	£84.65	-£738.69	-£1,653.51
	12.5	£5,665.05	£4,750.23	£4,292.82	£4,109.85	£3,378.00	£2,920.59	£2,463.18	£2,188.73	£1,548.36	£1,090.95	£633.54	£542.06	-£281.28	-£1,196.10
	12.4	£5,756.53	£4,841.71	£4,384.30	£4,201.34	£3,469.48	£3,012.07	£2,554.66	£2,280.21	£1,639.84	£1,182.43	£725.02	£633.54	-£189.80	-£1,104.62
	11.5	£6,579.87	£5,665.05	£5,207.64	£5,024.67	£4,292.82	£3,835.41	£3,378.00	£3,103.55	£2,463.18	£2,005.77	£1,548.36	£1,456.88	£633.54	-£281.28
	10.5	£7,494.69	£6,579.87	£6,122.46	£5,939.49	£5,207.64	£4,750.23	£4,292.82	£4,018.37	£3,378.00	£2,920.59	£2,463.18	£2,371.70	£1,548.36	£633.54
		£17,100.30	£16,185.48	£15,728.07	£15,545.10	£14,813.25	£14,355.84	£13,898.43	£13,623.98	£12,983.61	£12,526.20	£12,068.79	£11,977.31	£11,153.97	£10,239.15

The impact of removing the daily sedation interruption and dose renewal costs on cost savings for each of the scenarios is outlined in table 4.

Table 4: Cost savings without daily sedation interruption and dose renewal for scenarios (based on corrected training costs)

Scenario	Company	EAC (with daily sedation interruption and dose renewal)	EAC (without daily sedation interruption and dose renewal)
Difference in ventilation days	£4,497	£5,955.42	£4,462.26
Mechanical ventilation and ICU duration for the whole population (switchers included)	£1,034.66	£2,133.74	£721.05
Sevoflurane	N/A	£3,345.61	£2,161.12

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