AnaConDa-S for sedation with volatile anaesthetics in intensive care

Medtech innovation briefing
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Summary

- The technology described in this briefing is AnaConDa-S. It is a volatile anaesthetic delivery system for use with ventilators to allow people to be sedated using inhaled anaesthetics (isoflurane or sevoflurane).

- The innovative aspects are that it enables sedation to be done using inhaled anaesthetics with standard ventilators in intensive care settings, instead of needing intravenous (IV) anaesthesia.

- The intended place in therapy would be as an alternative to IV sedation of people who need invasive ventilation in an intensive care setting.

- The main points from the evidence summarised in this briefing are from 5 studies, including 1 meta-analysis, with a total of 1,098 people in an intensive care setting. They show that volatile sedation using an AnaConDa device is as effective as IV sedation in people who are invasively ventilated in intensive care, and could reduce the time spent on a ventilator.

- Key uncertainties around the evidence or technology are that there are currently no published UK-based studies and so the outcomes may not be directly generalisable to the NHS.
• The cost of sedation using AnaConDa-S is £118.50 (excluding VAT) for the first 24 hours and £83.50 per subsequent day, in addition to the cost of the volatile anaesthetics used.

The technology

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

AnaConDa-S is a single-use device (replaced every 24 hours or when needed). It is inserted into the breathing circuit of a ventilator between the ET-tube and Y-piece, replacing the heat and moisture exchanger. 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, any 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 exhaled 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.

AnaConDa-S can be used with almost any kind 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 200 ml.

Innovations

The AnaConDa-S device allows people having treatment in intensive care to be sedated with volatile anaesthetics, using ventilators that are already widely used. The company states that volatile anaesthetic use can lead to better control of sedation depth and faster awakening times than intravenous (IV) anaesthetics.

The lower dead space of the AnaConDa-S means that it can be used on smaller adults or children who have smaller minute or tidal ventilation. The company states that general anaesthesia
machines are impractical for intensive care. This is because they need large, bulky equipment and more staff, or staff with a higher level of training, which leads to higher staffing costs. The anaesthetic conserving function of the device could lead to reduced volatile anaesthetics needed and could reduce the environmental impact of volatile anaesthetic use. Scavenging systems (to collect and remove waste anaesthetic gases) used with the device can prevent exposure of staff to volatile anaesthetics (Pickworth et al. 2013).

Current care pathway

Adults who need sedation in intensive care are sedated using IV anaesthetics, primarily propofol or midazolam with alfentanil or morphine. Children in intensive care usually have sedation with IV midazolam and morphine or fentanyl.

The Intensive Care Society guideline on sedation states there are difficulties in delivering and scavenging volatile anaesthetics. There are also concerns about fluoride accumulation (with sevoflurane use) and the dependency of ventilation. Delivery devices, such as AnaConDa, as well as scavenging systems, make using isoflurane and sevoflurane in intensive care safer for staff. Isoflurane has shown safe, effective sedation for up to 96 hours in small studies, with faster awakening than midazolam. Isoflurane has shown similar awakening to propofol. For short-term postoperative sedation (less than 12 hours), desflurane has shown faster awakening and faster mental recovery when compared with propofol. Isoflurane is also a potent bronchodilator and is valuable in treatment for status asthmaticus.

The following publications have been identified as relevant to this care pathway:

- BNF treatment summary on anaesthesia (general)
- BNF for children treatment summary on anaesthesia (general)
- Intensive Care Society guidelines.

Population, setting and intended user

AnaConDa-S is intended to be used as an alternative to IV anaesthetics for sedating people who are invasively ventilated in intensive care. The AnaConDa-S has a tidal volume working range of 200 ml to 800 ml. Volatile anaesthetics should not be used in people with a known history of malignant hyperthermia. Using volatile anaesthetics in pregnant women, especially in the first trimester, could have potential teratogenic or developmental effects on the unborn baby. The AnaConDa-S system could be used for people who need more rapid awakening for assessment; in
people with difficult or limited IV access; or to manage sedation in cases when sedation is difficult despite using multiple sedative agents. Volatile anaesthetics can also be critical in treating severe acute asthma.

AnaConDa-S is for use by medical professionals in an intensive care setting. In the NHS, this would likely be intensivists and intensive care nurses. Usually sedation parameters (such as Richmond Agitation-Sedation Scale [RASS] score and MAC) would be set up by an intensivist and modified if needed by nurses. Administration of isoflurane and sevoflurane using AnaConDa-S should only be done in a setting fully equipped for the monitoring and support of respiratory and cardiovascular function. It should be done by people specifically trained to use inhalational anaesthetic drugs and recognise and manage any adverse effects.

Initial training is provided by the company through an e-learning resource, as well as in-person training. Further training is provided through webinars, quick guides, handouts, memory cards and YouTube videos to reinforce learning and update practitioners on new developments.

**Costs**

**Technology costs**

The cost of the AnaConDa-S starter pack is £115, excluding VAT. The starter pack contains components needed to give sedation for the first 24 hours. It contains an AnaConDa-S, FlurAbsorb-S, FlurAbsorb-S mount, FlurAbsorb accessory kit, gas sample line, nafion line, AnaConDa syringe and a single-use filling adapter with standard threading. A further AnaConDa syringe (£3.50 per syringe) is needed, leading to a total cost of £118.50 for the first 24 hours. For each subsequent day of sedation, there is an additional cost of £83.50 for replacement AnaConDa-S (£60), FlurAbsorb-S (£16.50) and AnaConDa syringes.

Each FlurAbsorb-S filter can be used for 3 syringes of anaesthetic. As an alternative, a FlurAbsorb filter can be used. This costs £40 and can be used for 10 syringes of anaesthetic. Hospitals with Active Gas Scavenging Systems in their intensive care unit do not need FlurAbsorb or FlurAbsorb-S filters.

Anaesthetic for sedation is purchased separately from the AnaConDa-S. Isoflurane costs £3.10 per 24 hours based on using 3 ml per hour. The AnaConDa-S instructions for use state that the expected usage of isoflurane is 2 ml per hour to 7 ml per hour. The cost of 250 ml of isoflurane is £64.68 for a pack of 6 bottles, based on electronic market information tool (eMIT) pricing. Sevoflurane costs £22.94 per 24 hours based on using 5 ml per hour (expected usage 4 ml per hour...
to 10 ml per hour; 250 ml of sevoflurane costs £286.77 for a pack of 6 bottles based on eMIT). Desflurane cannot be used with the AnaConDa-S device and is not routinely used in UK intensive care settings.

There is no increase in staffing needed for sedation using AnaConDa-S compared with IV sedation. Gas monitoring systems are needed for sedation, which would need to be purchased if not already available.

**Costs of standard care**

In standard care, sedation for adults in intensive care is generally done by giving IV propofol or midazolam. The cost of IV propofol (1% emulsion for injection) is £2.38 for a 100-ml vial (10 mg per 1 ml) according to eMIT. The BNF states that for sedation of ventilated adults in intensive care, the dosage is 0.3 mg/kg/hour to 4 mg/kg/hour, adjusted according to response. For IV midazolam, 30 micrograms/kg/hour to 200 micrograms/kg/hour is used at a cost of £1.76 for a 10-mg/2-ml ampule (when bought as a 10-pack) according to eMIT.

The BNF for children states that for children in intensive care who need sedation, IV midazolam is used at 30 micrograms/kg/hour to 120 micrograms/kg/hour for babies and children aged 6 months to 11 years. For children aged 12 years to 17 years, the dosage is 30 micrograms/kg/hour to 200 micrograms/kg/hour. Both dosages are adjusted according to response.

**Resource consequences**

The company states that AnaConDa-S is currently being used in over 30 NHS trusts. Using AnaConDa-S could result in overall cost savings if volatile anaesthetic treatment leads to a reduction in intensive care or hospital stay. The anaesthetic conserving function of the device could lead to a reduction in volatile anaesthetics needed. Because the device is compatible with current ventilators used, no additional ventilators are needed to incorporate it into standard care. However, gas monitors are needed to monitor anaesthesia. The company states that AnaConDa and empty syringes can be disposed of in the general hospital waste. Syringes with larger amounts of residual anaesthetic gas (more than 20 ml) should be disposed of through special hospital waste. Excess volatile anaesthetic should be disposed of using appropriate waste guidelines. Any glass bottles containing anaesthetic residue would need to be incinerated.

**Regulatory information**

AnaConDa-S is CE marked as a class IIa medical device. It received its CE mark in 2017.
The following manufacturer field safety notices or medical device alerts for this technology have been identified.

In January 2020, the Medicines and Healthcare products Regulatory Agency released an urgent field safety notice for AnaConDa-S. This was for a batch of devices incorrectly fitting to select brands of tube extenders. All faulty devices were successfully recalled to Sedana Medical and the safety notice was resolved. The company notes that there were no reported faulty devices in the UK because the tube extenders in question are rarely used. All products in the batch were removed before clinical use.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Volatile anaesthetics may not be suitable for pregnant women. Volatile anaesthesia may particularly benefit children for whom sedation is difficult. Pregnancy and age are protected characteristics under the 2010 Equalities Act.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

There are 5 studies summarised in this briefing. This includes a meta-analysis that compares 8 studies, as well as 2 observational studies. A total of 1,098 people are included in the studies. In addition to the studies included here, there are many other studies published on the earlier version of this device, including 14 randomised controlled trials.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.
Overall assessment of the evidence

Although there is evidence to show the AnaConDa and the newer AnaConDa-S device are comparable, most evidence is based on the original AnaConDa device. There are 2 studies of 33 patients, reporting the effectiveness of the AnaConDa-S, and both of these compare the AnaConDa-S with the original AnaConDa system rather than with standard care. These studies suggest that the 2 versions are comparable in sedation efficiency and that the 'S' version has the benefit of lower carbon dioxide rebreathing.

The published studies on the original AnaConDa device suggest that sedation with volatile anaesthetics using the original AnaConDa device is effective. Two of the studies showed reduced extubation time and 1 showed reduced length of intensive care stay when compared with intravenous (IV) anaesthetics. Although the device is used in the UK, none of the studies were done in the UK so the results may not be generalisable to the NHS.

Marcos-Vidal et al. (2020)

Study size, design and location

**Comparative study of the AnaConDa device to the AnaConDa-S device.** Study in Spain of 23 patients, post-cardiac surgery, sequentially sedated with each device for 60 minutes to assess efficiency of sevoflurane reflection and compare blood gas parameters.

Intervention and comparator

**Intervention:** Inhaled anaesthetic (sevoflurane) through AnaConDa-S.

**Comparator:** Inhaled anaesthetic (sevoflurane) through AnaConDa.

Key outcomes

Both devices enabled sufficient sedation, without altering the quantity of sevoflurane needed. There was reduced arterial partial pressure of carbon dioxide ($p<0.001$) when AnaConDa-S was used. This was potentially because of the reduced dead space in the device.

Strengths and limitations

The study was sufficiently powered to detect differences in efficiency of the devices in retaining anaesthetic. However, only the AnaConDa and AnaConDa-S devices were compared with each other, rather than comparing with standard care. The sedation was only short term, so long-term...
assessment of patient arterial carbon dioxide levels could not be determined.

### Bomberg et al. (2018)

#### Study size, design and location

Crossover study in Germany of 10 patients needing sedation; study compared AnaConDa with AnaConDa-S for 2 hours, to compare carbon dioxide elimination and isoflurane usage.

#### Intervention and comparator

Intervention: Inhaled anaesthetic (isoflurane) through AnaConDa-S.

Comparator: Inhaled anaesthetic (isoflurane) through AnaConDa.

#### Key outcomes

Both devices enabled sufficient sedation, according to Richmond Agitation-Sedation Scale (RASS) scores, without altering the quantity of isoflurane needed. AnaConDa-S led to decreased end-tidal carbon dioxide concentrations compared with AnaConDa.

#### Strengths and limitations

This study was only a small comparison study for the new version of the device and did not compare the AnaConDa-S device with IV anaesthetics. However, it did show that within the same patients, the efficiency of the 2 device versions were comparable.

### Spence et al. (2017)

#### Study size, design and location

A meta-analysis of 8 studies involving 610 patients. This study evaluates the efficacy and safety of volatile anaesthetics, using the original AnaConDa device, compared with IV anaesthetics, for postoperative sedation of adult cardiac surgery patients.

#### Intervention and comparator

Intervention: Inhaled anaesthetic (sevoflurane or isoflurane) through AnaConDa.

Comparator: IV anaesthetic (propofol or midazolam).
Key outcomes

Times to extubation after intensive care admission or stopping sedation were 74 minutes (95% confidence interval [CI] -126 to -23) and 76 minutes (95% CI -150 to -2) less in patients sedated using volatile anaesthetics, respectively. No difference was found in length of intensive care unit or hospital stay. Patients sedated with volatile anaesthetic had lower troponin concentrations (0.71 nanograms/ml; 95% CI 0.23 to 1.2) compared with patients given IV sedation, potentially suggesting reduced cardiac damage.

Strengths and limitations

This study focused on patients sedated after cardiac surgery, used the Cochrane tool to assess risk of bias and evaluated the strength of the research using the GRADE system. This meta-analysis is limited by only including patients at low to moderate risk of adverse outcomes after surgery and there was heterogeneity in the inhalational and IV anaesthetics used. Only 1 study included in the meta-analysis used blinding, leading to a high risk of bias for all other studies. The studies used the original AnaConDa device, not the AnaConDa-S.

Santiago et al. (2018)

Study size, design and location

Prospective observational study in Spain of 23 children (between 1 month and 16 years old) in a paediatric intensive care unit.

Intervention and comparator

Inhaled anaesthetic (sevoflurane) through AnaConDa.

Key outcomes

Children who it was difficult to give sedation to using IV anaesthetics were switched to sevoflurane sedation. The sedation was well tolerated and given for a median of 5 days. Arterial hypotension was seen in 7 patients, all of whom had cardiac surgery. Six patients had withdrawal syndrome and needed IV treatment with dexmedetomidine, clonidine and morphine.

Strengths and limitations

This study was a small single-arm observational study. All children were on prolonged mechanical ventilation and multiple sedation infusions before starting sevoflurane. This study uses the
AnaConDa device, which was then adapted to accommodate a lower tidal volume.

Krannich et al. (2017)

Study size, design and location

Retrospective observational study of 432 adults who had survived cardiac arrests in Germany.

Intervention and comparator

Intervention: Inhaled anaesthetic (isoflurane) through AnaConDa.

Comparator: IV anaesthetic (midazolam).

Key outcomes

Volatile sedation led to reduced time on ventilator (difference of the median time of 98.5 hours; p=0.003) and length of intensive care stay (difference of the median stay of 4.5 days; p=0.006) compared with IV sedation. There was no difference in neurological outcome but more frequent hypocapnia (6.4% compared with 0%; p=0.021) in the volatile sedation group.

Strengths and limitations

This was a retrospective study and so was not randomised or blinded. Some people sedated with volatile anaesthetics were also given IV sedation. This study uses the AnaConDa, not the AnaConDa-S device, which could have contributed to the increased hypocapnia.

Sustainability

Studies show that AnaConDa is environmentally safe in an intensive care setting and reduces isoflurane consumption (Sackey et al. 2005). This reduced consumption is important because volatile anaesthetic vaporisation, including isoflurane and sevoflurane, contribute to global warming (Campbell and Pierce, 2015).

Recent and ongoing studies


• **SED001**: a randomised, controlled, open-label study to confirm the efficacy and safety of sedation with isoflurane in invasively ventilated ICU patients using the AnaConDa administration system. EudraCT number: 2016-004551-67. Status: completed, awaiting publication. Indication: patients in intensive care. Devices: isoflurane or propofol. Date: February 2020. Country: Germany.


**Expert comments**

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE’s view.

Of the experts, 4 out of 5 were familiar with or had used this technology before.

**Level of innovation**

Four experts agreed that this technology is an innovative way to deliver volatile anaesthetics in an
intensive care setting. Two experts noted that conventional volatile anaesthetic systems are impractical for use in intensive care. This is because of bulky equipment and the lack of staff who are trained in using those machines in this setting. One expert commented that the device is compact and comes with a scavenging system, which enables using volatile anaesthetics in this setting. One expert mentioned that being able to use end-tidal concentration as a marker of the cerebral concentration of the sedative agent makes it easier to target appropriate sedation levels. One expert noted that the newer ‘S’ version of the device is a minor innovation to the original device because it allows the device to be used with children and smaller adults. One expert commented that there is an equivalent technology, but they think it is a more complex device than AnaConDa.

**Potential patient impact**

Three experts commented that this device could be lifesaving in severe acute asthma and 1 expert noted that they would use this as a first-line therapy in this instance. One expert also noted that sevoflurane is often more effective for severe asthma. One expert commented that volatile anaesthetic use could lead to potential improvements in lung inflammation and gas exchange in acute respiratory distress syndrome. The experts also stated it can be used to manage sedation in instances when sedation may be difficult. This could be when the patient is having multiple intravenous (IV) and enteral sedative agents; when managing delirium and treating withdrawal symptoms associated with IV agents; providing sedation when there is difficult or limited IV access; treating people with a history of drug or alcohol use; and reducing the use of IV fluid pumps and drugs in times of scarcity.

One expert also commented that the AnaConDa-S can be useful for sedation in people with renal or liver failure because volatile anaesthetics accumulate less in the body. Three experts stated that they found waking times faster using volatile anaesthetics and that, unlike IV sedation, multiple sedative agents are not needed to manage sedation. One expert noted that the faster wake up is particularly relevant after procedures such as cardiac surgery. They also commented that using volatile anaesthetics enhances the ability to make neurological assessments, which is useful when assessing brain injuries. One expert further commented that volatile sedation could reduce the need for agents such as dexmedetomidine to manage post-sedation agitation. One expert noted that volatile anaesthetic removed the need for propofol, which can have negative effects related to cardiac function, propofol infusion syndrome and hyperlipidaemia.

**Potential system impact**

One expert noted that the cost of AnaConDa could be less than standard care because of a
potential reduction in ventilation time and time spent in critical care. However, another expert stated that the effects of using the device on length of patient stay or mortality are limited. Two experts stated that the initial costs would be higher than standard care because gas monitoring systems must be purchased, and time is needed for training and troubleshooting with healthcare staff. However, they believe the ongoing costs would be equivalent to standard care. One expert thought that the costs would be equivalent if not cheaper and that the device also acts as a heat and moisture exchanger, which reduces the need for heated humidifiers. One expert commented that health and safety measures are needed to mitigate risks associated with volatile anaesthetic spillage because they are potentially hazardous substances and an environmental pollutant. One expert noted that the training for using the device was easy and the adoption into their unit was rapid.

General comments

Three experts found AnaConDa-S a useful option for sedation, especially in the subgroups outlined above. These experts would be willing to use the device more routinely going forward. One expert noted that a limitation of the device is that people can experience discomfort when it is disconnected for physiotherapy, to allow for tracheal tube suctioning. Another expert noted that a compatible transport ventilator is needed if people are transported for a scan or theatre. One expert noted that there is some risk associated with saturating the device if it was disconnected and the syringe driver was left on. However, they stated that this is mitigated by using end-tidal concentration monitoring to check the high volatile concentration that this could lead to.

Expert commentators

The following clinicians contributed to this briefing:

- Dr Stephen Playfor, consultant paediatric intensivist, Manchester University NHS Foundation Trust. Dr Playfor has stated that he may contribute to an online workshop for the AnaConDa-S system in the future but has not been offered any payment for this.

- Professor Anil Hormis, consultant in anaesthesia and critical care medicine, Rotherham NHS Foundation Trust. Professor Hormis has received honoraria from Teleflex and Medtronic.

- Dr Jonathan Ball, consultant in intensive care medicine, St George's University Hospitals NHS Foundation Trust. No conflicts declared.

- Dr Mark Blunt, lead critical care consultant, The Queen Elizabeth Hospital King’s Lynn. No conflicts declared.
Dr Guy Glover, consultant in anaesthesia and critical care, Guy's and St Thomas NHS Foundation Trust. Dr Glover has attended an AnaConDa study day, sponsored by Sedana Medical.

Development of this briefing

This briefing was developed by NICE. The *interim process and methods statement* sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.