Baxter CONTRAfluran ZeoSys Medical GmbH

Sustainable Anaesthesia with CONTRAfluran™ Gas Capture System

Let's clear the air.

Baxter is proud to announce a partnership with ZeoSys that will allow hospitals to capture exhaled anaesthetic gases, preventing their release into the atmosphere!

Introducing CONTRAfluran™ Anaesthetic Gas Capture System:

- ✓ Innovation
- ✓ Ease-of-use
- ✓ 99% capture of a patient's exhaled anaesthetic gas in the operating room[1]

At Baxter, we take our corporate responsibilities seriously and we constantly aim to meet our mission to save and sustain lives.

Sustainable anaesthesia

How CONTRAfluran™ works

CONTRAfluran™ environmental benefit

SAFETY INFORMATION

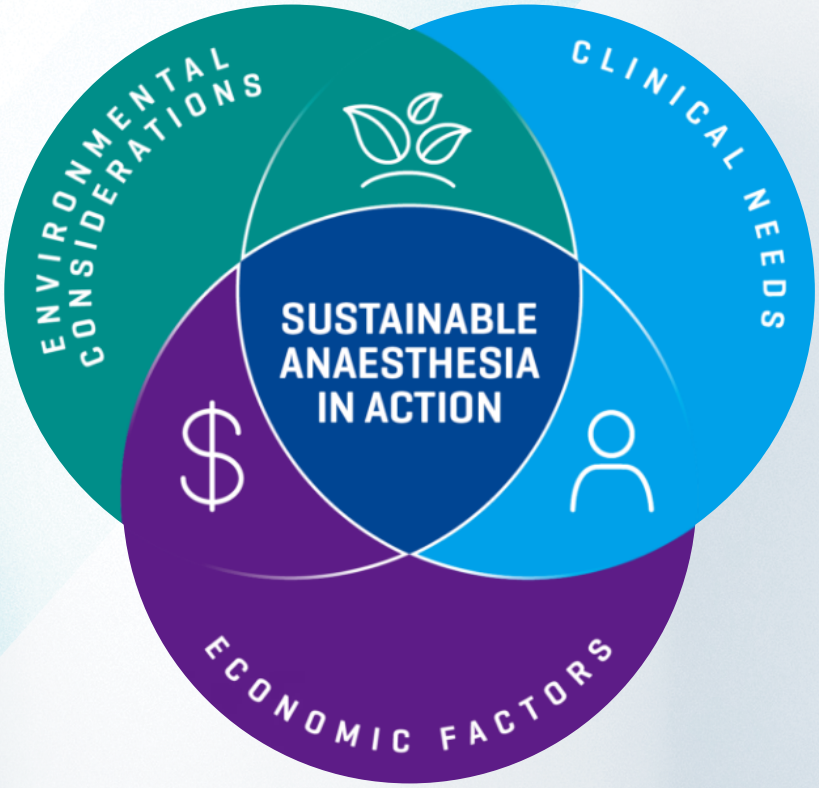
REFERENCES

What is “Sustainable” Anaesthesia?

To make any solution a long-term one, it must drive:

- ✓ Economic benefit
- ✓ Clinical needs
- ✓ Environmental success

Economic, clinical, and ecological processes are interconnected. When all three needs are met, we have sustainability.[2,3]



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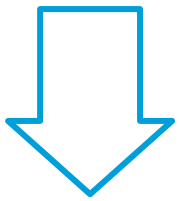
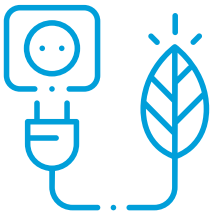
Baxter is committed

to delivering life-sustaining products while simultaneously working to minimise the impact these products have on the environment. We strive to use energy, water and raw materials efficiently, while reducing waste and greenhouse gas (GHG) emissions.

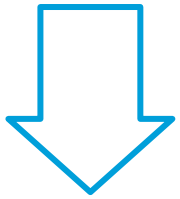
15%
REDUCTION
in GHG emissions globally[4*]





94%
ELECTRICITY from renewable sources in Europe[4]

8%
REDUCTION
in water consumption globally[4†]



Baxter is recognised as a **leader in climate impact** by the Carbon Disclosure Project (CDP), a non-profit organisation which drives companies to build a truly sustainable economy.[5]

Baxter has reported on the Carbon Disclosure Project (CDP) since its inception in 2003, and rated as **A/A- leadership position for the last 5 consecutive years**.[5]

CDP
DISCLOSURE INSIGHT ACTION

*Compared with 2015.
†Compared with 2015 and indexed to revenue.

SAFETY INFORMATION
REFERENCES

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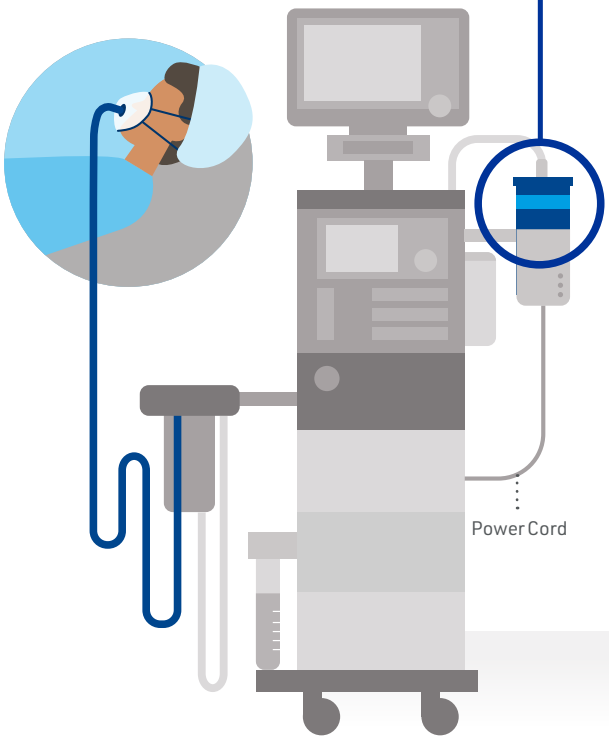
How CONTRAfluran™ works

Anaesthetic gas capture allows hospitals to collect exhaled desflurane and sevoflurane in the surgical suite, instead of expelling gas into the atmosphere.

The CONTRAfluran™ Gas Capture System

- ✓ Captures both sevoflurane and desflurane, preventing their release into the atmosphere
- ✓ Easy-to-use indicator and audible alarm signify when the canister is full and needs replacement
- ✓ Simple-to-install, space-efficient system for the operating theatre
- ✓ Potentially reduces energy consumption and costs associated with an Anaesthetic Gas Scavenging System (AGSS)



SAFETY INFORMATION
REFERENCES

Baxter
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CONTRAfluran™ can reduce your Carbon Footprint

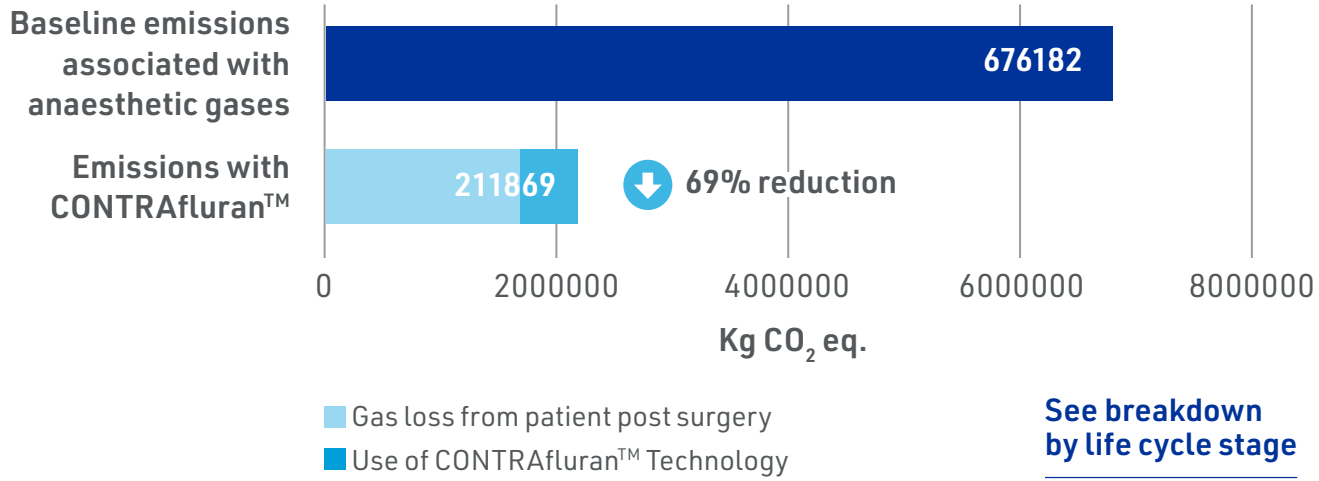
Baxter commissioned an independent life cycle assessment on the CONTRAfluran™ Anaesthetic Gas Capture System. This assessed the benefits of the technology on reducing hospital emissions as well as the carbon impact of the technology itself, compared to baseline without CONTRAfluran™.

Once regulatory approval for all life cycle stages is granted, analysis for this scenario found:[6*]

69%

REDUCTION
in greenhouse gas emissions after implementing the CONTRAfluran™ system compared to baseline[6*]

ANNUAL LIFE CYCLE CLIMATE CHANGE EMISSIONS: 50 OPERATING THEATRES[6*]



See breakdown by life cycle stage

*Scenario assumptions: 1) Sevoflurane and desflurane anaesthetic gas emissions with the CONTRAfluran™ technology in use in 50 operating rooms, running at mean operation hours (10.17 hrs/day) for 1 year; 2) Manufacture of sevoflurane and desflurane from data in previous LCA study: sevoflurane – 20.625 kg CO_2 eq per kg; desflurane – 37.25 kg CO^2 eq per kg; 3) Use of an inhaled anaesthetic mix of 66 % sevoflurane, 34% desflurane, with a potential loss included of 25% of both gases after surgery (due to patient retention); 4) Included the impact of savings from switching off hospital scavenging system, *which would contribute 43,100 kg CO_2 eq.*

SAFETY INFORMATION

REFERENCES

Baxter
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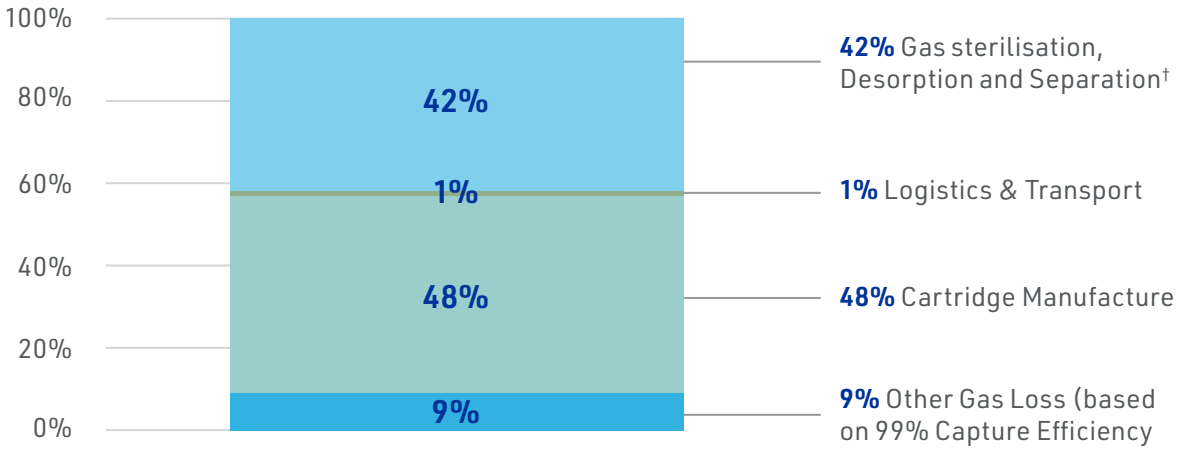
We are Committed to Reducing Climate Impact at Every Life Cycle Stage

CLIMATE CHANGE IMPACT DURING USE OF CONTRAFLURAN™ TECHNOLOGY (ONCE REGULATORY APPROVAL FOR ALL STAGES IS GRANTED)[6*]



The life cycle stages which contribute most to the carbon footprint of CONTRAfluran™ are the cartridge manufacture and the gas desorption process†, which can be improved over time

Logistics and **Transport** utilise existing delivery arrangements (reverse logistics) and contribute less than 1% of emissions

N.B. There is also a carbon 'benefit' of the technology resulting from anaesthetic gas manufacture avoided through re-use.†

*Scenario assumptions: 1) Sevoflurane and desflurane anaesthetic gas emissions with the CONTRAfluran™ technology in use in 50 operating rooms, running at mean operation hours (10.17 hrs/day) for 1 year; 2) Manufacture of sevoflurane and desflurane from data in previous LCA study: sevoflurane – 20.625 kg CO_2 eq per kg; desflurane – 37.25 kg CO_2 eq per kg; 3) Use of an inhaled anaesthetic mix of 66 % sevoflurane, 34% desflurane, with a potential loss included of 25% of both gases after surgery (due to patient retention); 4) Included the impact of savings from switching off hospital scavenging system, *which would contribute 43,100 kg CO_2 eq.*

†Once regulatory approval is granted.

SAFETY INFORMATION REFERENCES

Baxter

CONTRAfluran

Desflurane

PRESCRIBING INFORMATION – UK

Name and composition: Desflurane 100% v/v Inhalation vapour, liquid.

Indications: Inhalation agent for induction and/or maintenance of anaesthesia in adults, maintenance of anaesthesia in paediatrics.

Dosage and Route: *See SPC for full details*. Administration by inhalation using vapouriser specifically designed for use with desflurane and dose individualised based on patient's response. MAC decreases with increasing age. Opioids or benzodiazepines decrease the amount of desflurane to produce anaesthesia. Desflurane decreases the required dose of neuromuscular blocking agents. *Induction*: Inspired concentrations of 4–11% usually produces surgical anaesthesia in 2–4 minutes. Not for induction in children or paediatrics. *Maintenance*: In adults, 2–6% with concomitant nitrous oxide or 2.5–8.5% in oxygen or enriched air. In infants and children, 5.2–10% with or without nitrous oxide. Not for use in non-intubated children under 6 years old. Monitor blood pressure and heart rate during maintenance. Concentrations of 1–4% have been used successfully in chronic renal/hepatic impairment and renal transplant.

Side effects: See SmPC for detail. May cause dose-dependent cardio-respiratory depression. Nausea and vomiting has been reported postoperatively – may be due to a range of factors and common following surgery under general anaesthesia. Common (≥1/100 – <1/10) Pharyngitis, breath holding, headache, conjunctivitis, nodal arrhythmia, bradycardia, tachycardia, hypertension, apnea, cough, laryngospasm, salivary hypersecretion, increased creatinine phosphokinase, ECG abnormal.

Precautions: Only to be administered by people trained in administration of general anaesthesia with appropriate emergency measures available. Monitor blood pressure and heart rate as part of evaluation of the depth of anaesthesia. Caution in children with asthma or recent upper airway infection. Caution in use with LMA or face mask in children under 6 years. May trigger malignant hyperthermia. Inhaled anaesthetics have been associated with increases in serum potassium, cardiac arrhythmias, and death in children during the postoperative period. This has been reported in patients with latent or overt neuromuscular disease. Use of suxamethonium has been associated with most cases. Reports of QT prolongation, very rarely associated with torsade de points (in exceptional cases, fatal). Prompt and vigorous treatment for hyperkalaemia and arrhythmias recommended. Disruption of hepatic function, icterus and fatal liver necrosis have been reported with halogenated anaesthetics. May increase CSF pressure but attention to maintain CPP. Maintenance of normal hemodynamics is import in patients with coronary artery disease. Rapid increase in end-tidal concentration may increase heart rate and blood pressure. Hypotension and respiratory depression increases as anaesthesia deepens. Use in hypovolaemia, hypotension and debilitated patients has not been investigated, a lower concentration is recommended. Carbon dioxide absorbers should not dry out. Appropriate analgesia should be administered at the end of surgery or early in PACU. Caution with repeated anaesthesia in a short period of time. Desflurane has been associated with some glucose elevation intra-operatively. Safety of desflurane has not been established in obstetric procedures.

Contra-indications: Not to be used if general anaesthesia in contra-indicated, known hypersensitivity to halogenated agents, known susceptibility to malignant hyperthermia or with history of hepatitis due to halogenated inhalational agents. Not for use as an induction agent in paediatrics. Not for induction in patients at risk of coronary artery disease or where increases in heart rate or blood pressure are undesirable. Desflurane is not indicated for use during pregnancy and lactation.

Interactions: MAC reduced by concomitant N2O administration. Concomitant administration of opioids or benzodiazepines show a marked reduction in MAC. Neuromuscular blocks are potentiated by desflurane.

Overdose: Discontinue desflurane, establish clear airway and initiate assisted/controlled ventilation with pure oxygen. Support and maintain adequate haemodynamics.

Legal category: POM

Basic NHS price: £80.00 per 240ml bottle (FDG9632ALUN)

Market Authorisation number and holder: PL 0116/0327 – Baxter Healthcare Limited, Caxton Way, Thetford, Norfolk. IP24 3SE.

Date of Preparation: January 2019.

REFERENCES

Baxter

CONTRAfluran

Sevoflurane

PRESCRIBING INFORMATION – UK

Name and composition: Sevoflurane Baxter, 100%, inhalation vapour, liquid. **Indications:** Induction and maintenance of general anaesthesia in adults and children.

Posology and Method of Administration: Premedication should be selected according to the need of the individual patient, and at the discretion of the anaesthesiologist. *Induction*. Individualise and titrate dose according to age, clinical status and patient response. May use after short acting barbiturate or intravenous induction agent. 0.5-1.0% in oxygen, with or without nitrous oxide, increasing by 0.5-1.0% increments as required (maximum 8%). Surgical anaesthesia usually produced in less than two minutes by inhalation of up to 5% in adults and up to 7% in children. *Maintenance*. 0.5-3% in oxygen with or without nitrous oxide. *Emergence*. Emergence times are generally short; therefore, patients may require post-operative pain relief earlier. *Elderly*. MAC decreases with increasing age. The average concentration to achieve MAC in an 80 year old is approximately 50% of that required in a 20 year old. *Paediatric population*. See Summary of Product Characteristics for MAC values for paediatric patients according to age. **Side effects:** *See SPC for detail*. As with all potent inhalational anaesthetics, can produce dose-dependent cardiac respiratory depression. Most of the adverse reactions are mild to moderate and transient. Nausea and vomiting reported postoperatively - may be due to a range of factors and is common following surgery under general anaesthesia. Most common in adults: hypotension, nausea and vomiting, in elderly patients: bradycardia, hypotension and nausea, in paediatric patients: agitation, cough, vomiting and nausea. *Very common* – agitation, bradycardia, hypotension, cough, nausea, vomiting. *Common* - somnolence, headache, dizziness, tachycardia, hypertension, respiratory disorder, respiratory depression, laryngospasm, airway obstruction, salivary hypersecretion, pyrexia, chills, abnormal blood glucose, abnormal liver function test, abnormal white blood cell count, increased blood fluoride, hypothermia. *Uncommon* – Confusion, Atrioventricular block complete, cardiac arrhythmias (including ventricular arrhythmias), atrial fibrillation, extrasystoles (ventricular, supra-ventricular, bigeminy-linked), apnoea, asthma, hypoxia, serum creatinine increased, *Unknown frequency* – Anaphylactic and anaphylactoid reactions, hypersensitivity, convulsion, dystonia, increased intracranial pressure, cardiac arrest, ventricular fibrillation, Torsades de Pointes, ventricular tachycardia, electrocardiogram QT prolongation, bronchospasm, dyspnoea, wheezing, breath holding, pancreatitis, hyperkalemia, muscle rigidity, hepatitis, hepatic failure, hepatic necrosis, jaundice, tubulointerstitial nephritis, dermatitis contact, pruritus, rash, swelling face, urticaria, chest discomfort, hyperthermia malignant, edema, seizures most frequently in paediatric use. **Precautions:** Only to be administered by people trained in general anaesthesia with appropriate emergency facilities. Monitor continuously, including electrocardiogram, blood pressure, oxygen saturation and end tidal carbon dioxide. The concentration being delivered must be known exactly and must be accomplished by using a vaporizer calibrated specifically for sevoflurane. Individualise dose based on patient's response as hypotension and respiratory depression increase as anaesthesia deepens. Due to sevoflurane insolubility in blood, haemodynamic changes may be more rapid than some other volatile agents. Cautious dosing for patients in any of these groups – weakened patients, hypovolaemic, hypotensive or otherwise haemodynamically compromised, impaired renal function (monitor post-operatively), obstetrics (consider uterus relaxation and haemorrhage), recent previous exposure to sevoflurane or other halogenated hydrocarbons, coronary artery disease (maintain haemodynamics to avoid myocardial ischaemia), in ICP-reducing procedures, seizures, underlying liver problems, concomitant drugs associated with liver dysfunction or haemodynamic compromise, history of hepatic injury, jaundice, unexplained fever or eosinophilia following other inhalational anaesthetics, pregnancy and lactation. Assess emergence before discharging from the post-anaesthesia care unit. Rapid emergence may prompt early post-operative pain relief and, in children, may evoke brief agitation and hinder cooperation. Dystonic movements seen in children. Consider risk of malignant hyperthermia, fatal outcomes have been reported. Associated with rare increases in serum potassium and cardiac arrhythmias and postoperative death in paediatric patients. Patients with latent or overt neuromuscular disease, particularly Duchenne muscular dystrophy appear to be most vulnerable. Most cases were associated with concomitant use of succinylcholine. Consider QT prolongation, caution should be exercised when administering sevoflurane to susceptible patients. Isolated cases of ventricular arrhythmia in paediatric patients with Pompe's disease. Caution should be exercised when administering sevoflurane to patients with mitochondrial disorders. Regularly replace CO2 absorbent lime, considering risk of exothermic reaction if dries out. Animal studies indicate a potential for renal injury at low flow rates. Sevoflurane exposure should not exceed 2 MAC hours at flow rates 1 to <2 L/min. Fresh gas flow rates < 1 L/min are not recommended. High prevalence and degree of bradycardia have been reported in children with Down syndrome during and following sevoflurane induction. **Contraindications:** Known or suspected hypersensitivity to sevoflurane or other halogenated anaesthetics, history of unexplained moderate to severe hepatic dysfunction with jaundice, history of confirmed hepatitis, fever and eosinophilia after sevoflurane, known or suspected genetic susceptibility to malignant hyperthermia. Patients in whom general anaesthesia is contraindicated. **Interactions:** Nitrous oxide, benzodiazepines or opiates decrease the MAC of sevoflurane. When combined with the opioids fentanyl, alfentanil or sufentanil may lead to synergistic fall in heart rate, blood pressure and respiratory rate. Increases the effect of non-depolarising muscle relaxants. May increase the negative ionotropic, chronotropic and dromotropic effects of beta blockers. Sensitisation of the myocardium to the arrhythmogenic effect of exogenously administered adrenaline. Metabolism may be increased by agents that increase the activity of cytochrome P450 isoenzyme CYP2E1 (eg isoniazid, alcohol). Concomitant use of sevoflurane and isoniazid can potentiate the hepatotoxic effect of isoniazid. Risk of acute hypertension with indirect-acting sympathomimetics (eg amphetamines, ephedrine). Observed atrioventricular impairment of conduction with verapamil. Severe hypotension and delayed emergence in patients treated long-term with St John's Wort. Sevoflurane is compatible with barbiturates. **Overdose:** Symptoms include respiratory depression and circulatory insufficiency. Discontinue anaesthetic and institute supportive measures. Maintain patient's airway and stable cardiovascular function. **Legal category:** POM **Marketing Authorisation Number and Holder:** PL 00116/0420 Baxter Healthcare Limited, Caxton Way, Thetford, Norfolk. IP24 3SE. UK **Basic NHS Price** £123 per 250ml aluminium bottle - **Date of preparation:** June 2020 Further information available upon request.

REFERENCES

Baxter

CONTRAfluran

Desflurane

PRESCRIBING INFORMATION – Ireland

Name and composition: Suprane inhalation vapour, solution. Desflurane 100 % v/v **Indications:** Inhalation agent for induction and maintenance of anaesthesia in adults and maintenance in intubated infants and children under 12 years. Not recommended for induction in paediatrics. Dental anaesthesia restricted to hospitals / day care units only **Dosage and Route:** Inhalation via specific vaporiser designed for use with Suprane. Administration must be individualized based on patient's responses. *Induction*. In adults, starting concentration of 3% is recommended, increasing dose between 0.5-1.0% increments every 2-3 breaths. Inspired concentrations of 4-11% usually produces surgical anaesthesia in 2-4 minutes. Higher concentrations up to 15% may be used, in such cases administration of oxygen should be 30% or above. After induction with intravenous drugs, desflurane can be started at 0.5-1.0 MAC. Desflurane should be administered at 0.8 MAC or less, and in conjunction with a barbiturate induction and hyperventilation until cerebral decompression in patients with known or suspected increases in cerebrospinal fluid pressure. Attention to be paid to maintain cerebral perfusion pressure. *Maintenance*. 2-6% with concomitant nitrous oxide or 2.5-8.5% in oxygen or oxygen enriched air. Surgical levels of anaesthesia may be sustained with a reduced concentration of desflurane when nitrous oxide is used. 5.2-10% desflurane with or without nitrous oxide in children under 12 years of age or intubated infants. Up to 18% has been administered for short periods – ensure 25% oxygen for high concentrations with nitrous oxide. Desflurane is not approved for maintenance of anaesthesia in children 12-18 years of age. 1-4% in nitrous oxide/oxygen has been successful in chronic renal/hepatic impairment and renal transplant. **Side effects:** *See Summary of Product Characteristics for detail.* May cause a dose-dependent cardio-respiratory depression. *Very common:* Nausea, vomiting *Common:* Pharyngitis, breath holding, headache, conjunctivitis, nodal arrhythmia, bradycardia, tachycardia, hypertension, apnea, cough, laryngospasm, salivary hypersecretion, increased creatinine phosphokinase, ECG abnormalities *Other side effects:* Coagulopathy, hypokalaemia, hyperkalaemia, metabolic acidosis, agitation, dizziness, convulsions, ocular icterus, myocardial infarction, myocardial ischaemia, arrhythmia, cardiac arrest, Torsade de Pointes, ventricular failure, ventricular hypokinesia, atrial fibrillation, electrocardiogram QT prolonged, vasodilation, malignant hypertension, haemorrhage, hypotension, shock, hypoxia, respiratory arrest, respiratory failure, respiratory distress, bronchospasm, haemoptysis, pancreatitis acute, abdominal pain, hepatic failure, hepatic necrosis, hepatitis, cytolytic hepatitis, cholestasis, jaundice, abnormal hepatic function, liver disorder, urticaria, erythema, myalgia, rhabdomyolysis, hyperthermia malignant, asthenia, malaise, electrocardiogram ST-T change, electrocardiogram T wave inversion, transaminase increased, alanine aminotransferase increased, aspartate aminotransferase increased, blood bilirubin increased, coagulation test abnormal, ammonia increased, increased blood glucose levels, agitation postoperative, dizziness, migraine, tachyarrhythmia, palpitations, eye burns, blindness transient, encephalopathy, ulcerative keratitis, ocular hyperemia, visual acuity reduced, eye irritation, eye pain, fatigue, accidental exposure, skin burn sensation, drug administration error. **Precautions:** Only to be administered by people trained in general anaesthesia. All patients should be constantly monitored, including ECG, BP, oxygen saturation and end tidal carbon dioxide with appropriate emergency facilities for resuscitation available. Hypotension and respiratory depression increases with depth of anaesthesia. Use in hypovolaemic or hypotensive patients has not been extensively investigated. Not for use in patients prone to bronchoconstriction. Caution in repeated anaesthesia with halogenated agents in a short period of time. Desflurane causes a rise in blood sugar levels during anaesthesia. All necessary precautions should be taken to ensure carbon dioxide adsorbents are not allowed to dry out. Desflurane may trigger malignant hyperthermia. In such cases discontinue the triggering agents, administer dantrolene sodium and apply supportive therapy. Renal failure may appear later, monitor urine flow and sustain if possible. Fatal outcomes due to malignant hyperthermia have been reported. Inhaled anaesthetic agents has been associated with rare increases of potassium resulting in cardiac arrhythmias, some fatal. Patients with latent and overt muscular dystrophies, particularly Duchenne muscular dystrophy appear most vulnerable. Early and aggressive intervention to treat hyperkalaemia and arrhythmias is recommended. Use with caution in children with asthma or history of recent upper airway infection. Not approved for maintenance in children 12-18 years of age. Not approved for non-intubated paediatric patients or non-intubated children. Caution in children with LMA, in particular for children 6 years old or younger. Children emerging from anaesthesia may experience brief state of agitation that may hinder cooperation. Caution when administering to patients susceptible to QT prolongation, very rarely associated with torsade de pointes. Disruption of hepatic function, icterus and fatal liver necrosis have been reported. May cause sensitivity hepatitis. Cirrhosis, viral hepatitis or other pre-existing hepatic disease may be a reason to select an alternative agent. Desflurane may produce a dose-dependent increase in cerebrospinal fluid pressure when administered to patients with space occupying lesions. In patients with coronary artery disease marked increases in pulse rate, mean arterial pressure and levels of epinephrine and norepinephrine are associated with rapid increase in desflurane concentrations. Desflurane should not be the sole anaesthetic agent for induction in patients at risk of coronary artery disease or when increases in heart rate or blood pressure are undesirable. After rapid increase in concentration of desflurane an increase in heart rate and blood pressure may not represent inadequate anaesthesia. Increases in heart rate and blood pressure without a rapid increase in desflurane concentration may be interpreted as light anaesthesia. Supportive analgesia should be administered at the end of the procedure or early in the post-anaesthesia care unit. Safety of desflurane has not been established for use in obstetric procedures. Desflurane is a uterine relaxant and reduces uterine-placental blood-flow. Desflurane is not indicated for use during pregnancy and lactation. **Contraindications:** Not to be used if general anaesthesia is contraindicated, known sensitivity to halogenated agents, or known or genetic susceptibility to malignant hyperthermia. Not for use in patients undergoing dental procedures outside a hospital or day care unit. Not for use in patients with liver dysfunction, jaundice, unexplained fever, leukocytosis or eosinophilia after previous halogenated anaesthetic administration. Not for use for induction in patients undergoing CABG. Not for use as an induction agent in paediatrics. **Interactions:** MAC for desflurane is reduced by concomitant nitrous oxide administration. Muscle relaxants are potentiated by desflurane. Increasing doses of fentanyl show a marked reduction in MAC. Midazolam showed a small reduction in MAC. **Overdose:** In the event of overdose or what may appear to be overdose, discontinue or minimize exposure to desflurane, establish an airway and initiate assisted or controlled ventilation with 100% oxygen, support and maintain adequate haemodynamics. **Legal category:** POM **Marketing Authorisation Number and Holder:** PA 2299/023/001 – Baxter Holding B.V. Kobaltweg 49, 3542CE Utrecht, Netherlands **Date of preparation:** June 2020. Further information available upon request.

REFERENCES

Baxter

CONTRAfluran

Sevoflurane

PRESCRIBING INFORMATION - Ireland

Name and composition: Sevoflurane Baxter, 100%, inhalation vapour, liquid. **Indications:** Induction and maintenance of general anaesthesia in adults and children.

Posology and Method of Administration: Premedication should be selected according to the need of the individual patient, and at the discretion of the anaesthesiologist. *Induction*. Individualise and titrate dose according to age, clinical status and patient response. May use after short acting barbiturate or intravenous induction agent. 0.5-1.0% in oxygen, with or without nitrous oxide, increasing by 0.5-1.0% increments as required (maximum 8%). Surgical anaesthesia usually produced in less than two minutes by inhalation of up to 5% in adults and up to 7% in children. *Maintenance*. 0.5-3% in oxygen with or without nitrous oxide. *Emergence*. Emergence times are generally short; therefore, patients may require post-operative pain relief earlier. *Elderly*. MAC decreases with increasing age. The average concentration to achieve MAC in an 80 year old is approximately 50% of that required in a 20 year old. *Paediatric population*. See Summary of Product Characteristics for MAC values for paediatric patients according to age. **Side effects:** *See SPC for detail.* As with all potent inhalational anaesthetics, can produce dose-dependent cardiac respiratory depression. Most of the adverse reactions are mild to moderate and transient. Nausea and vomiting reported postoperatively - may be due to a range of factors and is common following surgery under general anaesthesia. *Very common* – agitation, bradycardia, hypotension, cough, nausea, vomiting. *Common* - somnolence, headache, dizziness, tachycardia, hypertension, respiratory disorder, respiratory depression, laryngospasm, airway obstruction, salivary hypersecretion, pyrexia, chills, abnormal blood glucose, abnormal liver function test, abnormal white blood cell count, increased blood fluoride, hypothermia. *Uncommon* – Confusion, atrioventricular block complete, cardiac arrhythmias (including ventricular arrhythmias), atrial fibrillation, extrasystoles (ventricular, supra-ventricular, bigeminy-linked), apnoea, asthma, hypoxia, serum creatinine increased. *Unknown frequency* – Anaphylactic and anaphylactoid reactions, hypersensitivity, convulsion, dystonia, increased intracranial pressure, cardiac arrest, ventricular fibrillation, Torsades de Pointes, ventricular tachycardia, electrocardiogram QT prolonged, bronchospasm, dyspnoea, wheezing, breath holding, pancreatitis, hyperkalaemia, muscle rigidity, hepatitis, hepatic failure, hepatic necrosis, jaundice, tubulointestinal nephritis, dermatitis contact, pruritus, rash, swelling face, urticaria, chest discomfort, hyperthermia malignant, edema, seizures most frequently in paediatric use. **Precautions:** Only to be administered by people trained in general anaesthesia with appropriate emergency facilities. Monitor continuously, including electrocardiogram, blood pressure, oxygen saturation and end tidal carbon dioxide. The concentration being delivered must be known exactly and must be accomplished by using a vaporizer calibrated specifically for sevoflurane. Individualise dose based on patient's response as hypotension and respiratory depression increase as anaesthesia deepens. Due to sevoflurane insolubility in blood haemodynamic changes may be more rapid than some other volatile agents. Cautious dosing for patients in any of these groups – weakened patients, hypovolaemic, hypotensive or otherwise haemodynamically compromised, impaired renal function (monitor post-operatively), obstetrics (consider uterus relaxation and haemorrhage), recent previous exposure to sevoflurane or other halogenated hydrocarbons, coronary artery disease (maintain haemodynamics to avoid myocardial ischaemia), in ICP-reducing procedures, seizures, underlying liver problems, concomitant drugs associated with liver dysfunction or haemodynamic compromise, history of hepatic injury, jaundice, unexplained fever or eosinophilia following other inhalational anaesthetics, pregnancy and lactation. Assess emergence before discharging from the post-anaesthesia care unit. Rapid emergence may prompt early post-operative pain relief and, in children, may evoke brief agitation and hinder cooperation. Dystonic movements seen in children. Consider risk of malignant hyperthermia, fatal outcomes have been reported. Associated with rare increases in serum potassium and cardiac arrhythmias and postoperative death in paediatric patients. Patients with latent or overt neuromuscular disease, particularly Duchenne muscular dystrophy appear to be most vulnerable. Most cases were associated with concomitant use of succinylcholine. Consider QT prolongation, caution should be exercised when administering sevoflurane to susceptible patients. Isolated cases of ventricular arrhythmia in paediatric patients with Pompe's disease. Caution should be exercised when administering sevoflurane to patients with mitochondrial disorders. Regularly replace CO2 absorbent lime, considering risk of exothermic reaction if dries out. Animal studies indicate a potential for renal injury at low flow rates. Sevoflurane exposure should not exceed 2 MAC hours at flow rates 1 to <2 L/min. Fresh gas flow rates < 1 L/min are not recommended. High prevalence and degree of bradycardia have been reported in children with Down syndrome during and following sevoflurane induction. **Contraindications:** Known or suspected hypersensitivity to sevoflurane or other halogenated anaesthetics, history of unexplained moderate to severe hepatic dysfunction with jaundice, history of confirmed hepatitis, fever and eosinophilia after sevoflurane, known or suspected genetic susceptibility to malignant hyperthermia. Patients in whom general anaesthesia is contraindicated. **Interactions:** Nitrous oxide, benzodiazepines or opiates decrease the MAC of sevoflurane. When combined with the opioids fentanyl, alfentanil or sufentanil may lead to synergistic fall in heart rate, blood pressure and respiratory rate. Increases the effect of non-depolarising muscle relaxants. May increase the negative inotropic, chronotropic and dromotropic effects of beta blockers. Sensitisation of the myocardium to the arrhythmogenic effect of exogenously administered adrenaline. Metabolism may be increased by agents that increase the activity of cytochrome P450 isoenzyme CYP2E1 (eg isoniazid, alcohol). Concomitant use of sevoflurane and isoniazid can potentiate the hepatotoxic effect of isoniazid. Risk of acute hypertension with indirect-acting sympathomimetics (eg amphetamines, ephedrine). Observed atrioventricular impairment of conduction with verapamil. Severe hypotension and delayed emergence in patients treated long-term with St John's Wort. Sevoflurane is compatible with barbiturates. **Overdose:** Symptoms include respiratory depression and circulatory insufficiency. Discontinue anaesthetic and institute supportive measures. Maintain patient's airway and stable cardiovascular function. **Legal category:** POM **Marketing Authorisation Number and Holder:** PA2299/031/001 Baxter Holding B.V., Kobaltweg 49, 3542CE Utrecht, Netherlands. **Date of preparation:** June 2020. Further information available upon request.

REFERENCES

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CONTRAfluran

ZeoSys
Medical GmbH

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Adverse Events and any drug or medical device product quality complaints (including suspected defective medicines or medical device adverse incidents) should be reported. For the UK reporting forms and information can be found at www.mhra.gov.uk/yellowcard. For Ireland report to the Health Products Regulatory Authority (HPRA) using a Yellow Card obtained from the HPRA, via the online system (www.hpra.ie) or by telephone on +353 (0)1-6764971.

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