

RESEARCH MONOGRAPH . COMPOUND PROFILE

Sevoflurane

A non-pungent fluorinated methyl isopropyl ether with a low blood-gas coefficient enabling fast induction and the dominant inhalational agent for pediatric mask induction.

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ABSTRACT

Sevoflurane (fluoromethyl 2,2,2-trifluoro-1-(trifluoromethyl)ethyl ether; CAS 28523-86-6; molecular formula C₄H₃F₇O; molecular weight 200.05) is a fluorinated methyl isopropyl ether volatile anesthetic synthesized by Ross Terrell at Travenol Laboratories in 1968, brought to clinical use in Japan in 1990, and approved by the FDA in 1995 (Ultane, Sojourn). The minimum alveolar concentration (MAC) at age 40 is 1.8 percent in oxygen; the blood-gas partition coefficient is 0.65, faster than isoflurane (1.4) but slower than desflurane (0.42). The non-pungent character and absence of airway irritation make sevoflurane the agent of choice for inhalational induction of anesthesia, particularly in pediatric patients where intravenous access is established after induction. Mechanism parallels other halogenated ethers (GABA-A positive allosteric modulation, K₂P channel activation, glycine and NMDA effects); the agent is achiral. Hepatic metabolism via CYP2E1 produces hexafluoroisopropanol and inorganic fluoride; the fluoride concentrations approach the historical nephrotoxic threshold associated with methoxyflurane (50 micromolar plasma) during prolonged exposure but published clinical data have not demonstrated nephrotoxicity in humans even with extended cases, attributed to the absence of intrarenal defluorination. The principal residual concern is degradation of sevoflurane in carbon dioxide absorbents (soda lime, Baralyme) at low fresh gas flows producing Compound A, which is nephrotoxic in rats but lacks demonstrated human renal injury within recommended fresh gas flow limits (1 to 2 L/min). Cardiovascular profile is favorable with preserved cardiac output, modest

reduction in systemic vascular resistance, and minimal coronary steal physiology.

1. Compound Identification

Sevoflurane is described as halogenated ether volatile general anesthetic. A non-pungent fluorinated methyl isopropyl ether with a low blood-gas coefficient enabling fast induction and the dominant inhalational agent for pediatric mask induction.

1.1 Class summary

Halogenated ether volatile general anesthetic

1.2 Subtitle

A non-pungent fluorinated methyl isopropyl ether with a low blood-gas coefficient enabling fast induction and the dominant inhalational agent for pediatric mask induction.

2. Abstract

Sevoflurane (fluoromethyl 2,2,2-trifluoro-1-(trifluoromethyl)ethyl ether; CAS 28523-86-6; molecular formula $C_4H_3F_7O$; molecular weight 200.05) is a fluorinated methyl isopropyl ether volatile anesthetic synthesized by Ross Terrell at Travenol Laboratories in 1968, brought to clinical use in Japan in 1990, and approved by the FDA in 1995 (Ultane, Sojourn). The minimum alveolar concentration (MAC) at age 40 is 1.8 percent in oxygen; the blood-gas partition coefficient is 0.65, faster than isoflurane (1.4) but slower than desflurane (0.42). The non-pungent character and absence of airway irritation make sevoflurane the agent of choice for inhalational induction of anesthesia, particularly in pediatric patients where intravenous access is established after induction. Mechanism parallels other halogenated ethers (GABA-A positive allosteric modulation, K2P channel activation, glycine and NMDA effects); the agent is achiral. Hepatic metabolism via CYP2E1 produces hexafluoroisopropanol and inorganic fluoride; the fluoride concentrations approach the historical nephrotoxic threshold associated with methoxyflurane (50 micromolar plasma) during prolonged exposure but published clinical data have not demonstrated nephrotoxicity in humans even with extended cases, attributed to the absence of intrarenal defluorination. The principal residual concern is degradation of sevoflurane in carbon dioxide absorbents (soda lime, Baralyme) at low fresh gas flows producing Compound A, which is nephrotoxic in rats but lacks demonstrated human renal injury within recommended fresh gas flow limits (1 to 2 L/min). Cardiovascular profile is favorable with preserved cardiac output, modest reduction in systemic vascular resistance, and minimal coronary steal physiology.

3. Mechanism of Action

GABA-A positive modulation, K2P channel activation, glycine potentiation, NMDA inhibition. Non-pungent character favored for inhalational induction.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

MAC 1.8 percent in oxygen at age 40; clinical maintenance 1.5 to 2.5 percent end-tidal; induction 6 to 8 percent.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Wallin RF, et al. Sevoflurane: a new inhalational anesthetic agent. *Anesth Analg* 1975.
2. Kharasch ED. Sevoflurane: an inhalation anesthetic. *Anesthesiology* 1995.
3. Ebert TJ, et al. Renal responses to low-flow desflurane, sevoflurane, and propofol in patients. *Anesthesiology* 2000.
4. Eger EI 2nd, et al. Compound A and sevoflurane. *Anesth Analg* 1997.

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