Dexmedetomidine

MADE IN GERMANY

Concentrate for Solution for Infusion

The first Dexmedetomidine in Europe indicated for both ICU and procedural sedation.

Dexmedetomidine is a highly selective alpha-2 adrenergic receptor notable for its ability to provide sedation without the risk of respiratory depression.

Dexmedetomidine EVER Pharma is indicated for:

- Sedation of non-intubated adult patients prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation.
- Sedation of adult ICU (Intensive Care Unit) patients requiring sedation level not deeper than arousal in response to verbal stimulation corresponding to Richmond Agitation-Sedation Scale (RASS) 0 to -3.

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Dexmedetomidine EVER Pharma is the first Dexmedetomidine in Europe indicated for both ICU and procedural sedation

200 µg / 2 ml

400 µg / 4 ml

1000 µg / 10 ml

Available in 6 presentations

INNOVATION IN ACTION

EVER PHARMA

Dexmedetomidine EVER Pharma for Procedural Sedation

Sedation of non-intubated adult patients prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation.

- **Unique in that patients remain easily rousable and cooperative[1]**
- **Provides relatively fast onset of sedative properties paralleling natural sleep with easy reversibility providing improved patient safety[1]**
- **Minimal respiratory depression[2]**
- **Similar cardio-respiratory safety profile to midazolam with more efficacious sedation than midazolam in the peri-procedural period[2]**

Dexmedetomidine has advantages over midazolam in terms of reliability, analgesia and patients' and clinicians' satisfaction. Dexmedetomidine and midazolam appear to have a similar cardio-respiratory safety profile when both are carefully titrated. Combined with the use of local anesthesia, dexmedetomidine provides a good alternative for midazolam for procedural sedation.[2]

Procedural Sedation

1. Weerink MAS, Struys MMRF, Hannivoort LN, Barends CRM, Absalom AR, Colin P. Clinical Pharmacokinetics and Pharmacodynamics of Dexmedetomidine. Clin Pharmacokinet. 2017 Aug;56(8):893-913. doi: 10.1007/s40262-017-0507-7
2. Barends, C.R., et al., Dexmedetomidine versus Midazolam in Procedural Sedation. A Systematic Review of Efficacy and Safety. PLoS One, 2017. 12(1): p. e0169525.
3. Candiotti KA, Bergese SD, Bokesch PM, Feldman MA, Wisemandle W, Bekker AY, et al. Monitored anesthesia care with dexmedetomidine: a prospective, randomized, double-blind, multicenter trial. Anesth Analg 2010; 110:47-56.
4. Peng K, Liu HY, Liu SL, Ji FH. Dexmedetomidine-fentanyl Compared With Midazolam-fentanyl for Conscious Sedation in Patients Undergoing Lumbar Disc Surgery. Clin Ther. 2016;38:192-201 e192.

1

Awake fibreoptic intubation (1)

- Bergese SD, Candiotti KA, Bokesch PM, Zura A, Wisemandle W, Bekker AY, Group AS. A Phase IIIb, randomized, double-blind, placebo-controlled, multicenter study evaluating the safety and efficacy of dexmedetomidine for sedation during awake fiberoptic intubation. Am J Ther. 2010;17:586-595. (AWAKE)
- He, X. Y., J. P. Cao, et al. (2014). „Dexmedetomidine for the management of awake fibreoptic intubation." The Cochrane database of systematic reviews 1: CD009798
- Tsai CJ, Chu KS, Lu DV, Wang HM, Lu IC (2010) A comparison of the effectiveness of dexmedetomidine versus propofol target-controlled infusion for sedation during fibreoptic nasotracheal intubation. Anaesthesia 65:254-259

2

Cataract surgery (2)

- Virkkila, M., et al., Dexmedetomidine as intramuscular premedication for day-case cataract surgery. A comparative study of dexmedetomidine, midazolam and placebo. Anaesthesia, 1994. 49(10): p. 853-8.
- Alhashemi JA. Dexmedetomidine vs midazolam for monitored anaesthesia care during cataract surgery. Br J Anaesth. 2006;96:722–726

3

Colonoscopy (3)

- Dere K, Sucullu I, Budak ET et al. A comparison of dexmedetomidine versus midazolam for sedation, pain and hemodynamic control, during colonoscopy under conscious sedation. Eur J Anaesthesiol 2010; 27: 648 – 652

4

Upper endoscopy (4)

- Zhang F, Sun HR, Zheng ZB, Liao R, Liu J. Dexmedetomidine versus midazolam for sedation during endoscopy: A meta-analysis. Exp Ther Med. 2016;11:2519c2524.
- Lee, B. S., J. Ryu, et al. (2014). „Midazolam with meperidine and dexmedetomidine vs. midazolam with meperidine for sedation during ERCP: prospective, randomized, double-blinded trial." Endoscopy 46(4): 291-298.
- Wu, Y., et al., A comparison of propofol vs. dexmedetomidine for sedation, haemodynamic control and satisfaction, during esophagogastroduodenoscopy under conscious sedation. J Clin Pharm Ther, 2015. 40(4): p. 419-25

5

Bronchoscopy (5)

- Goneppanavar U, Magazine R, Periyadka Janardhana B, Krishna Achar S. Intravenous Dexmedetomidine Provides Superior Patient Comfort and Tolerance Compared to Intravenous Midazolam in Patients Undergoing Flexible Bronchoscopy. Pulm Med. 2015;2015:727530

6

Neurosurgery (6)

- Goettel N, Bharadwaj S, Venkatraghavan L, Mehta J, Bernstein M, Manninen PH. Dexmedetomidine vs propofol-remifentanil conscious sedation for awake craniotomy: a prospective randomized controlled trial. Br J Anaesth. 2016;116:811-821
- Shen SL, Zheng JY, Zhang J, Wang WY, Jin T, Zhu J, Zhang Q. Comparison of dexmedetomidine and propofol for conscious sedation in awake craniotomy: a prospective, double-blind, randomized, and controlled clinical trial. Ann Pharmacother. 2013;47:1391-1399
- Rozet I et al. Clinical Experience with Dexmedetomidine for Implantation of Deep Brain Stimulators in Parkinson's Disease. Anesth Analg 2006;103:1224 –8

Vascular surgery (6)

- Bekker AY, Basile J, Gold M, Riles T, Adelman M, Cuff G, Mathew JP, Goldberg JD. Dexmedetomidine for awake carotid endarterectomy: efficacy, hemodynamic profile, and side effects. J Neurosurg Anesthesiol. 2004;16:126-135
- Huncke TK, Candiotti K, Bergese S, Kim S, Bekker A. Prospective, randomized, placebo-controlled study: Dexmedetomidine sedation in vascular procedures. Anesthesiology. 2008;109:A-449
- Huncke, T.K., et al., A prospective, randomized, placebo-controlled study evaluating the efficacy of dexmedetomidine for sedation during vascular procedures. Vasc Endovascular Surg, 2010. 44(4): p. 257-61

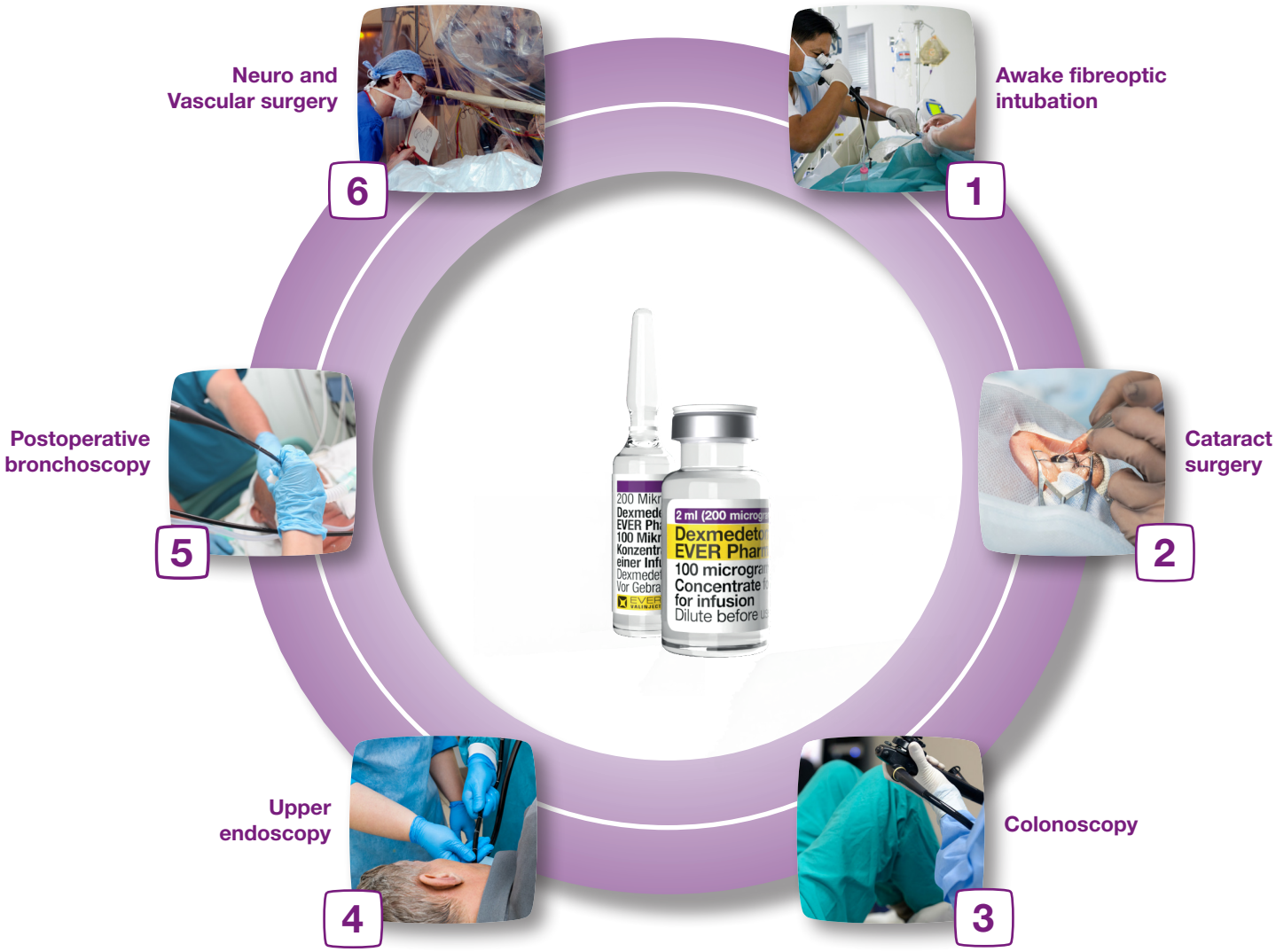
General articles on the pharmacology of dexmedetomidine:

Hannivoort LN et al. Development of an Optimized Pharmacokinetic Model of Dexmedetomidine Using Target-controlled Infusion in Healthy Volunteers. Anesthesiology 2015; 123:357-67

Colin PJ et al. Dexmedetomidine pharmacokinetic–pharmacodynamic modelling in healthy volunteers: 1. Influence of arousal on bispectral index and sedation. Br J Anaesth (2017) 119 (2): 200-210. DOI: https://doi.org/10.1093/bja/aex085

ICU Sedation

1. Jakob SM, Ruokonen E, Grounds RM, et .al. (2012) Dexmedetomodine vs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials. JAMA. 307 (11):1151-60.
2. Riker RR, Shehabi Y, Bokesch PM et. al. (2009) Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial (SEDCOM). JAMA. 301 (5): 489-99.



Compared to Midazolam, a recent systematic review concluded that Dexmedetomidine provides more comfort during the procedure for the patient and clinician[2]

Initiation of Procedural Sedation:

- **For adult patients:** A loading infusion of 1.0 microgram/kg over 10 minutes. For less invasive procedures such as ophthalmic surgery, a loading infusion of 0.5 micrograms/kg given over 10 minutes may be suitable.
- **For awake fiberoptic intubation in adult patients:** A loading infusion of 1 microgram/kg over 10 minutes.
- **For patients over 65 years of age:** A dose reduction should be considered.
- **For adult patients with impaired hepatic function:** A dose reduction should be considered

Maintenance of Procedural Sedation:

- **For adult patients:** The maintenance infusion is generally initiated at 0.6 microgram/kg/hour and titrated to achieve desired clinical effect with doses ranging from 0.2 to 1 microgram/kg/hour. The rate of the maintenance infusion should be adjusted to achieve the targeted level of sedation.
- **For awake fiberoptic intubation in adult patients:** A maintenance infusion of 0.7 microgram/kg/hour is recommended until the endotracheal tube is secured.
- **For patients over 65 years of age:** A dose reduction should be considered.
- **For adult patients with impaired hepatic function:** A dose reduction should be considered

Dexmedetomidine EVER Pharma for sedation of adult ICU patients

Sedation of adult ICU (Intensive Care Unit) patients requiring sedation level not deeper than arousal in response to verbal stimulation corresponding to Richmond Agitation-Sedation Scale (RASS) 0 to -3

- Patient ability to communicate and cooperate with staff significantly improved[1]
- As effective as propofol and midazolam for light to moderate sedation (RASS score 0 to -3)[1]
- Compared to midazolam, dexmedetomidine-treated patients spent less time on the ventilator, experienced less delirium, and developed less tachycardia and hypertension. The most notable adverse effect of dexmedetomidine was bradycardia[2]
- Shorter time to extubation than standard sedatives[1,2]

ICU Sedation
1. Jakob SM, Ruokonen E, Grounds RM, et .al. (2012) Dexmedetomodine vs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials. JAMA. 307 (11):1151-60.
2. Riker RR, Shehabi Y, Bokesch PM et. al. (2009) Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial (SEDCOM). JAMA. 301 (5): 489-99.

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Indications

For sedation of non-intubated adult patients prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation.

For sedation of adult ICU (Intensive Care Unit) patients requiring sedation level not deeper than arousal in response to verbal stimulation (corresponding to Richmond Agitation-Sedation Scale (RASS) 0 to -3).

Active Ingredient

Dexmedetomidine hydrochloride

Excipients

Sodium chloride, Water for injections

Presentations

- **200 µg/2 ml** concentrate for solution for infusion
- **400 µg/4 ml** concentrate for solution for infusion
- **1000 µg/10 ml** concentrate for solution for infusion

Strength

Each 1 ml of concentrate contains dexmedetomidine hydrochloride equivalent to 100 micrograms dexmedetomidine.

Stability

- **Unopened:** 48 months, does not require any special temperature storage conditions. Keep the ampoules or vials in the outer carton in order to protect from light.
- **After 1st Opening:** Use Immediately. Ampoules and vials are intended for single patient use only.
- **After dilution:** Chemical and physical stability of the diluted infusion (Infusion Solution Stability) has been demonstrated for 48 hours at 25°C and at refrigerated conditions (2 °C – 8 °C).

Primary Packaging

Type I colourless glass ampoules; 2, 5 or 10 ml (with filling volumes of 2, 4 and 10 ml)
Type I colourless glass vials; 2, 5 or 10 ml (with filling volumes of 2, 4 and 10 ml)
Bromobutyl rubber stopper with fluoropolymer coating

Pack sizes

200 µg/2 ml | Vials: 4, 5; Ampoules: 5, 25
400 µg/4 ml | Vials: 4, 5; Ampoules: 4, 5
1000 µg/10 ml | Vials: 4, 5; Ampoules: 4, 5

Dexmedetomidine EVER Pharma 100 micrograms/ml concentrate for solution for infusion
Composition: Each 1 ml of concentrate contains dexmedetomidine hydrochloride equivalent to 100 micrograms dexmedetomidine. List of excipients: Sodium chloride, Water for injections, Therapeutic indications: 1. For sedation of adult ICU (Intensive Care Unit) patients requiring sedation level not deeper than arousal in response to verbal stimulation (corresponding to Richmond Agitation-Sedation Scale (RASS) 0 to -3). 2. For sedation of non-intubated adult patients prior to and/or during diagnostic or surgical procedures requiring sedation, i.e. procedural/awake sedation. Contraindications: Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Advanced heart block (grade 2 or 3) unless paced. Uncontrolled hypotension. Acute cerebrovascular conditions. Side effects: very common: bradycardia, hypotension, hypertension, respiratory depression, common: hyperglycaemia, hypoglycaemia, agitation, myocardial ischaemia or infarction, tachycardia, nausea, vomiting, dry mouth, withdrawal syndrome, hyperthermia, uncommon: metabolic acidosis, hypoalbuminaemia, hallucination, atrioventricular block, cardiac output decreased, cardiac arrect, dyspnoea, apnoea, abdominal distension, drug ineffective, thirst, unknown: polyuria. More information available in the summary of product characteristics. Only available on prescription. Last update: March 2020, Marketing Authorisation Holder: EVER Valinject GmbH, Oberburgau 3, 4866 Unterach am Attersee, Austria.

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