selenase® in intensive care

Dosage recommendations

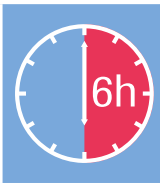
selenase®

- reduces nosocomial infections
- shortens the hospital stay
- corrects selenium deficiency

we are research

biosyn®

High-dose for sepsis – so that selenium is effective

Day 1		Start of therapy ideally within 6 hours after admission to ICU [II]
	As bolus	2,000 [I–III] µg Se
	Subsequently as continual infusion	1,500 [I–III] µg Se
At least 7 days [I]	Maintenance therapy	1,500 [III] µg Se / day

I Huang TS et al. PLoS One. 2013; 8(1): e54431. Effect of parenteral selenium supplementation in critically ill patients: a systematic review and meta-analysis.

II Chelkeba L et al. Ann Intensive Care. 2015 Dec; 5(1): 29. The effect of parenteral selenium on outcomes of mechanically ventilated patients following sepsis: a prospective randomized clinical trial.

III Manzanares W et al. Intensive Care Med. 2011 Jul; 37(7): 1120-7. High-dose selenium reduces ventilator-associated pneumonia and illness severity in critically ill patients with systemic inflammation.

selenase® for sepsis

- High-dose sodium selenite (selenase®) significantly reduces nosocomial infections [1–4]
- The hospital stay of sepsis patients is significantly shortened by three days for those treated with sodium selenite [5]
- Only high-dose sodium selenite (selenase®) is able to remedy the massive selenium deficiency of sepsis patients [5,6]
- There is no negative effect at kidney dysfunction [5]

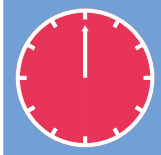
selenase® for cardiac surgery		
Day 1	Bolus ideally within 30 minutes after administration of anesthesia; termination of the bolus before initiation of the cardiopulmonary bypass	
	Intraoperative as bolus (for about 30 min.)	2,000 [I, II] µg Se
	Bolus directly after admission to ICU	2,000 [I, II] µg Se
From day 2 of the ICU stay	Maintenance therapy	1,000 [I, II] µg Se / day

I Stoppe C et al. Nutrition. 2013 Jan; 29(1): 158-65. Selenium blood concentrations in patients undergoing elective cardiac surgery and receiving perioperative sodium selenite.

II Stoppe C et al. Trials. 2014 Aug 28; 15: 339. SodiUm SeleniTe Adminstration IN Cardiac Surgery (SUSTAIN CSX-trial): study design of an international multicenter randomized double-blinded controlled trial of high dose sodium-selenite administration in high-risk cardiac surgical patients.

Significance of selenium in cardiac surgery

- An intraoperative decrease of selenium is associated with the postoperative development of multi-organ failure[7]
- The postoperative decrease of selenium concentration is not attributed to the use of a heart-lung machine[8]
- Perioperative administration of selenase® prevents the strong postoperative decrease of selenium concentration[9]

Sodium selenite for burns*		
Day 1		Start of therapy preferably within 12 hours after admission to ICU
	As continuous infusion	~350–1,000 [I–II] µg Se
14 days for burns <60 % of the body surface [I]	Maintenance therapy	~350–1,000 [I–II] µg Se/day

*together with zinc and copper in the trials

I Berger MM et al. Crit Care. 2006; 10(6): R153. Reduction of nosocomial pneumonia after major burns by trace element supplementation: aggregation of two randomised trials.

II Prescribing information selenase®, biosyn Arzneimittel GmbH, as of July 2017.

Sodium selenite for burns

Sodium selenite*

- reduces the number of infections [10]
- improves wound healing [11, 12]
- shortens the antibiotic treatment [10]
- shortens the ICU stay [10, 13]

*together with zinc and copper in the trials

selenase® after resuscitation		
Day 1	Beginning of treatment directly after resuscitation or ICU admission	
	As continuous infusion	1,000 [I] µg Se
Day 2 – 5	Maintenance therapy	1,000 [I] µg Se / day

I Adapted according to Reisinger J et al. Am J Emerg Med. 2009 Feb; 27(2): 176-81. Does early administration of selenium improve neurological outcome after cardiac arrest?

selenase® after resuscitation

- Low selenium level in the post-resuscitation phase[14]
- Length of resuscitation correlates negatively with the selenium level[15]

Sodium selenite for stroke*		
Day 1	Bolus directly after admission to ICU	2,000 [I] µg Se
Day 2 – 5	Maintenance therapy	1,000 [I] µg Se / day

* ongoing clinical trial

I NCT020505295 "Selenium and ischemic stroke outcome".

By now a randomized, double-blinded, placebo controlled trial with the title "Selenium and ischemic stroke outcome" (NCT02505295) is under way, which investigates whether administration of 2,000 µg selenium in form of selenase® directly after patient admission plus 1,000 µg selenium per day (selenase®) for five days reduces mortality and neurological damage.

Sodium selenite for stroke

- Stroke patients show significantly reduced selenium levels [16]
- High glutathione peroxidase concentration correlates with low neurological deficiency and a positive outcome after a stroke [16]
- Significantly reduced selenoprotein P concentration in patients after an acute stroke [17]
- Reduced selenoprotein P status is associated with a significantly higher risk for stroke [17]

Compatibility

Yes	No
• 5 % glucose solution • Ringer solution • Carbohydrate solutions (stability 72 hours (3 days)) • Colloidal volume expander solutions (stability 72 hours (3 days)) • Electrolyte solutions with increased potassium concentration (stability 48 hours (2 days)) • Crystalloid electrolyte solutions (stability 48 hours (2 days)) • Amino acid solutions without cysteine (stability 36 hours (1.5 days)) • Fat emulsions (stability 24 hours (1 day)) • Vitamin solutions (without vitamin C) • Solutions without reducing agents	• Cytostatic agent solutions [a] • Amino acid solutions that contain cysteine [b] • Solutions that contain glutathione (GSH) [c] • Vitamin solutions that contain vitamin C [d]

[a] selenase® should generally be administered 1 hour before cytostatic agent application for timely incorporation in the endogenous protective systems.

[b, c] SH groups react with Na-selenite; Na-selenite can no longer satisfy its task as a radical scavenger.

[d] Selenium (Se^{+IV}) in sodium selenite is reduced by vitamin C to the elementary selenium (Se^{0}) and is thereby ineffective.

Robinson MF et al. N Z Med J. 1985 Aug 14; 98(784): 627-9. Effect of a megadose of ascorbic acid, a meal and orange juice on the absorption of selenium as sodium selenite.

Ip C. J Natl Cancer Inst. 1986 Jul; 77(1): 299-303. Interaction of vitamin C and selenium supplementation in the modification of mammary carcinogenesis in rats.

Example scheme volumes

Bolus (within 6 hours)	2,000 µg selenium (40 ml selenase® T pro injectione) in 100 ml saline within one hour [l]
Continuous infusion (at least 7 days)	1,500 µg selenium (30 ml selenase® T pro injectione) in 250 ml saline during 12 hours for 14 days [l]

l Chelkeba L et al. Ann Intensive Care. 2015 Dec; 5(1): 29. The effect of parenteral selenium on outcomes of mechanically ventilated patients following sepsis: a prospective randomized clinical trial.

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5. Bloos F et al. JAMA Intern Med. 2016 Sep 1; 176(9): 1266-76. Effect of Sodium Selenite Administration and Procalcitonin-Guided Therapy on Mortality in Patients With Severe Sepsis or Septic Shock: A Randomized Clinical Trial.
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Selenium in guidelines

	Premature babies	Infants with low birth weight	Critically ill		Sepsis patients	Burn patients
			Children and adolescents	Adults		
Parenteral Nutrition in Paediatrics S3-Guideline of the DGEM [1]	×		×			
ESPEN/ESPGHAN Guidelines on paediatric parenteral nutrition [2]		×				
ESPEN Guidelines on Parenteral Nutrition: Intensive Care [3]				×	×	
ESPEN endorsed recommendations: Nutritional therapy in major burns [4]						×
The Canadian Critical Care Nutrition Guidelines in 2013 [5]				×	×	

1. Jochum F et al. Aktuelle Ernährungsmedizin 2014; 39; e99-e147.
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3. Singer P et al. Clin Nutr. 2009 Aug; 28(4): 387-400.
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5. Dhaliwal R et al. Nutr Clin Pract. 2014 Feb; 29(1): 29-43.

Products for injection therapy

Prescription only

selenase® 100 µg pro injectione	selenase® T pro injectione	selenase® T pro injectione
100 µg selenium / injection ampoule	500 µg selenium / injection vials	1,000 µg selenium / injection vials
		
10 and 50 ampoules with 2 ml solution for injection	2, 10, 30 (3 × 10) and 50 (5 × 10) glass vials with 10 ml solution for injection	2, 10, 30 (3 × 10) and 50 (5 × 10) glass vials with 20 ml solution for injection

Subject to sale in pharmacies

selenase® 50 Mikrogramm Injektionslösung (selenase® 50 microgram injection solution)

50 µg selenium / injection ampoule

New

10 (N2) and 50 ampoules with 1 ml solution for injection

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biosyn Arzneimittel GmbH

World market leader for high-dose selenium injections

biosyn Arzneimittel GmbH is a pharmaceutical and biotech company based in Fellbach, Germany. It specializes in trace elements, is a world market leader for high-dose selenium injections, developer and operator of two unique GMP manufacturing operations for producing active ingredients, and in the biotech sector, is actively involved in the production of glycoprotein isolated from the Megathura crenulata, a sea snail found in California. 70 percent of our sales turnover is realized outside of Germany – in 26 countries all around the world.

With products geared to the areas of intensive care, oncology and endocrinology, biosyn is a partner to hospitals and physicians in private practice, as well as to naturopathic physicians and holistic health practitioners. We pursue research and development and evaluate the current medical-scientific literature as well as engage in modern online marketing. Our mid-sized family enterprise places great value on an open, engaged and customer-oriented corporate culture.

Information on biosyn Arzneimittel GmbH

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- Selenium and stroke
- Overview of intensive care trials

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selenase®

Active substance: Sodium selenite pentahydrate. selenase® 100 µg pro injectione, selenase® T pro injectione, selenase® 50 Mikrogramm Injektionslösung: 50 µg selenium per ml. **Indications:** selenase® 100 µg pro injectione, selenase® T pro injectione, selenase® 50 Mikrogramm Injektionslösung: Confirmed selenium deficiency that cannot be corrected by diet. Selenium deficiency can occur in conditions of maldigestion or malabsorption, as well as in malnutrition (e.g. total parenteral nutrition). **Composition:** selenase® 100 µg pro injectione: 1 ampoule of 2 ml solution for injection contains: 0.333 mg sodium selenite pentahydrate, corresponding to 100 µg (micrograms) selenium. selenase® T pro injectione: 1 injection vial of 10 ml / 20 ml solution for injection contains: 1.67 mg / 3.33 mg sodium selenite pentahydrate, corresponding to 500 µg / 1000 µg (micrograms) selenium. selenase® 50 Mikrogramm Injektionslösung: 1 ampoule of 1 ml solution for injection contains as active substance 0.167 mg sodium selenite pentahydrate corresponding to 50 µg selenium in an 0.9 % aqueous NaCl-solution. Excipients: Sodium chloride, hydrochloric acid, water for injections. **Contra-indications:** Selenium poisoning. **Undesirable effects:** None known to date if the medicinal product is administered according to prescription. For selenase® 100 µg pro injectione, selenase® T pro injectione: General disorders and administration site conditions: Frequency not known (cannot be estimated from the available data): after intramuscular administration local pain at the site of administration has been reported. **Form of administration, size of packages:** selenase® 100 µg pro injectione: 10 or 50 ampoules of 2 ml solution for injection. selenase® T pro injectione: 2 or 10 injection vials of 10 ml solution for injection, hospital-size pack 30 (3 × 10) or 50 (5 × 10) injection vials of 10 ml solution for injection, 2 or 10 injection vials of 20 ml solution for injection, hospital-size pack 30 (3 × 10) or 50 (5 × 10) injection vials of 20 ml solution for injection. selenase® 50 Mikrogramm Injektionslösung: 10 and 50 ampoules respectively of 1 ml solution for injection. selenase® 100 µg pro injectione, selenase® T pro injectione: **Subject to prescription.** selenase® 50 Mikrogramm Injektionslösung: **Subject to sale in pharmacies.**
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selenase® in intensive care

Dosage recommendations

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