Dosing of selenase®
for sepsis, heart surgery, stroke, burns and after reanimation

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
	As bolus	2,000 [I–III] µg Se
	Subsequently as continual infusion	1,500 [I–III] µg Se
At least 7 days	Maintenance therapy	1,500 [I–III] µg Se/day

I 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.

II 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.

III 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.

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]

[1] 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. https://www.ncbi.nlm.nih.gov/pubmed/21445641

[2] Andrews PJ, et al. BMJ. 2011 Mar 17; 342: d1542. doi: 10.1136/bmj.d1542. Randomised trial of glutamine, selenium, or both, to supplement parenteral nutrition for critically ill patients. http://www.ncbi.nlm.nih.gov/pubmed/21415104

[3] 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. https://www.ncbi.nlm.nih.gov/pubmed/26429356

[4] Dhaliwal R, et al. Nutr Clin Pract. 2014 Feb; 29(1): 29-43. The Canadian critical care nutrition guidelines in 2013: an update on current recommendations and implementation strategies. https://www.ncbi.nlm.nih.gov/pubmed/24297678

[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. https://www.ncbi.nlm.nih.gov/pubmed/27428731

[6] Angstwurm MW, et al. Crit Care Med. 2007 Jan; 35(1): 118-26. Selenium in Intensive Care (SIC): results of a prospective randomized, placebo-controlled, multiple-center study in patients with severe systemic inflammatory response syndrome, sepsis, and septic shock. http://www.ncbi.nlm.nih.gov/pubmed/17095947

selenase® for cardiac surgery		
1 week before	Elective cardiac surgery	500[I] µg Se/day oral
Day 1	Bolus ideally within 30 minutes after administration of anaesthesia; 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. doi: 10.1016/j.nut.2012.05.013. 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.

selenase® for cardiac surgery

- The selenium status correlates with the extent of cardiac damage [1]
- An intraoperative decrease of selenium is associated with the postoperative development of multi-organ failure [2]
- The postoperative decrease of selenium concentration is not attributed to the use of a heart-lung machine [3]
- Perioperative administration of selenase® prevents the strong postoperative decrease of selenium concentration [4]

[1] Altekin E, Coker C, Şişman AR, Onvural B, Kuralay F, Kirimli O. J Trace Elem Med Biol. 2005; 18(3): 235-42. The relationship between trace elements and cardiac markers in acute coronary syndromes. http://www.ncbi.nlm.nih.gov/pubmed/15966572

[2] Stoppe C, Schälte G, Rossaint R, Coburn M, Graf B, Spillner J, Marx G, Rex S. Crit Care Med. 2011 Aug; 39(8): 1879-85. doi: 10.1097/CCM.0b013e3182190d48. The intraoperative decrease of selenium is associated with the postoperative development of multiorgan dysfunction in cardiac surgical patients. http://www.ncbi.nlm.nih.gov/pubmed/21460705

[3] Stevanovic A, Coburn M, Menon A, Rossaint R, Heyland D, Schälte G, Werker T, Wonisch W, Kiehntopf M, Goetzenich A, Rex S, Stoppe C. PLoS One. 2014 Aug 13; 9(8): e104222. doi: 10.1371/journal.pone.0104222. The importance of intraoperative selenium blood levels on organ dysfunction in patients undergoing off-pump cardiac surgery: a randomised controlled trial. http://www.ncbi.nlm.nih.gov/pubmed/25118980

[4] Stoppe C, Spillner J, Rossaint R, Coburn M, Schälte G, Wildenhues A, Marx G, Rex S. Nutrition. 2013 Jan; 29(1): 158-65. doi: 10.1016/j.nut.2012.05.013. Selenium blood concentrations in patients undergoing elective cardiac surgery and receiving perioperative sodium selenite. http://www.ncbi.nlm.nih.gov/pubmed/23010420

Sodium selenite for stroke		
Day 1		Start of therapy ideally within 6 hours after admission to ICU
	Bolus directly after admission to ICU	1,000 [I] µg Se
	Then as continuous infusion	500 [I] µg Se
From day 2 of the ICU stay	Maintenance therapy	500 [I] µg Se/day

I 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?

Sodium selenite for stroke

- Stroke patients show significantly reduced selenium values [1]
- High glutathione peroxidase concentration correlates with low neurological deficiency and a positive outcome after a stroke [1]
- Significantly reduced selenoprotein P concentration in patients after an acute stroke [2]
- Reduced selenoprotein P status is associated with a significantly higher risk for stroke [2]

In the meantime a randomized, double-blind placebo-controlled study is being conducted with the title "Selenium and ischemic stroke out-come" (NCT02505295), which monitors whether 2,000 µg selenium administered immediately after admission of the patient in the form of selenase® as well as 1,000 µg selenium per day (selenase®) for 5 days reduces mortality and neurological damages.

[1] Zimmermann C, Winnefeld K, Streck S, Roskos M, Haberl RL. Eur Neurol. 2004; 51(3): 157-61. Antioxidant status in acute stroke patients and patients at stroke risk. http://www.ncbi.nlm.nih.gov/pubmed/15073440

[2] Koyama H, Abdulah R, Ohkubo T, Imai Y, Satoh H, Nagai K. Nutr Res. 2009 Feb; 29(2): 94-9. doi: 10.1016/j.nutres.2009.01.002. Depressed serum selenoprotein P: possible new predicator of increased risk for cerebrovascular events. http://www.ncbi.nlm.nih.gov/pubmed/19285599

Sodium selenite for burns		
Day 1		Start of therapy ideally within 12 hours after admission to ICU
	Then as continuous infusion	500 [I–III] µg Se
14 days for burns <60 % of the body surface 21 days for burns ≥60 % of the body surface	Maintenance therapy	500 [I–III] µg Se/day

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 Berger MM, et al. Am J Clin Nutr. 2007 May; 85(5): 1293-300. Trace element supplementation after major burns modulates antioxidant status and clinical course by way of increased tissue trace element concentrations.

III Berger MM, et al. Am J Clin Nutr. 2007 May; 85(5): 1301-6. Trace element supplementation after major burns increases burned skin trace element concentrations and modulates local protein metabolism but not whole-body substrate metabolism.

Sodium selenite for burns

Sodium selenite

- reduces the number of infections [1]
- improves wound healing [2, 3]
- shortens the antibiotic treatment [1]
- shortens the hospital stay [1, 4]

[1] Berger MM, Eggimann P, Heyland DK, Chioléro RL, Revelly JP, Day A, Raffoul W, Shenkin A. Crit Care. 2006; 10(6): R153. Reduction of nosocomial pneumonia after major burns by trace element supplementation: aggregation of two randomised trials. http://www.ncbi.nlm.nih.gov/pubmed/17081282

[2] Berger MM, Baines M, Raffoul W, Benathan M, Chiolero RL, Reeves C, Revelly JP, Cayeux MC, Sénéchaud I, Shenkin A. Am J Clin Nutr. 2007 May; 85(5): 1293-300. Trace element supplementation after major burns modulates antioxidant status and clinical course by way of increased tissue trace element concentrations. http://www.ncbi.nlm.nih.gov/pubmed/17490965

[3] Berger MM, Binnert C, Chiolero RL, Taylor W, Raffoul W, Cayeux MC, Benathan M, Shenkin A, Tappy L. Am J Clin Nutr. 2007 May; 85(5): 1301-6. Trace element supplementation after major burns increases burned skin trace element concentrations and modulates local protein metabolism but not whole-body substrate metabolism. http://www.ncbi.nlm.nih.gov/pubmed/17490966

[4] Berger MM, Spertini F, Shenkin A, Wardle C, Wiesner L, Schindler C, Chiolero RL. Am J Clin Nutr. 1998 Aug; 68(2): 365-71. Trace element supplementation modulates pulmonary infection rates after major burns: a double-blind, placebo-controlled trial. http://www.ncbi.nlm.nih.gov/pubmed/9701195

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

I 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 reanimation

- Low selenium status in the post-reanimation phase [1]
- Length of reanimation correlates negatively with the selenium level [2]
- Early administration of selenase® improves the neurological outcome of patients after cardiac arrest [3]

[1] Fink K, Moebes M, Vetter C, Bourgeois N, Schmid B, Bode C, Helbing T, Busch HJ. Crit Care. 2015 Feb 26; 19(1): 58. Selenium prevents microparticle-induced endothelial inflammation in patients after cardiopulmonary resuscitation. http://www.ncbi.nlm.nih.gov/pubmed/25886988

[2] Busch HJ: Neue klinische Daten bei reanimierten Patienten. Satelliten-Symposium „Selen - neue Therapieoption zur Reduktion von Reperfusionsschäden. 20. Symposium Intensivmedizin + Intensivpflege 17.-19. Februar 2010, Bremen.

[3] Reisinger J, Höllinger K, Lang W, Steiner C, Winter T, Winter A, Mori M, Lindorfer A, Kiblböck D, Siostrzonek P. Am J Emerg Med. 2009 Feb; 27(2): 176-81. doi: 10.1016/j.ajem.2008.01.020. Does early administration of selenium improve neurological outcome after cardiac arrest? http://www.ncbi.nlm.nih.gov/pubmed/19371525

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)	• Cytostatic agent solutions [1] • Amino acid solutions that contain cysteine [2] • Solutions that contain glutathione (GSH) [3] • Vitamin solutions that contain vitamin C [4]

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

[2, 3] SH groups react with Na-selenite; Na-selenite can no longer act as a radical scavenger.

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

Robinson MF, Thomson CD, Huemmer PK. 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.

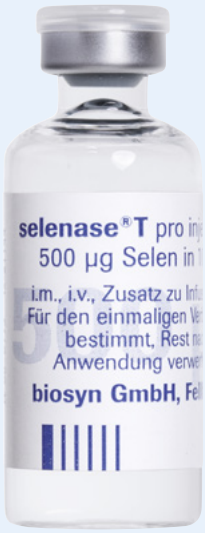
Volumes

Bolus (within 6 hours)	2,000 µg selenium (40 ml selenase® T pro injectione) in 100 ml saline within one hour [I]
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 [I]

[I] 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.

Products for injection therapy

Prescription only

selenase® 100 µg pro injectione	selenase® T pro injectione
100 µg selenium / injection ampoule	500 µg selenium / injection vials
	
10 (N2) and 50 ampoules with 2 ml solution for injection	2, 10 (N2), 30 (3 × 10) and 50 (5 × 10) glass vials with 10 ml solution for injection

selenase®

selenase® 100 µg/T pro injectione: Active substance: Sodium selenite pentahydrate, 50 µg selenium per ml. **Indications:** Proven selenium deficiency that cannot be offset from food sources. Selenium deficiencies may occur as a result of states of maldigestion and malabsorption, as well as in malnutrition (e.g. due to complete 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. Excipients: Sodium chloride, hydrochloric acid, water for injections. **Contraindications:** Selenium poisoning. **Undesirable effects:** *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. Subject to prescription 01/17 e

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.
[2] Koletzko B, et al. J Pediatr Gastroenterol Nutr. 2005 Nov; 41 Suppl 2: S1-87.
[3] Singer P, et al. Clin Nutr. 2009 Aug; 28(4): 387-400.
[4] Rousseau AF, et al. Clin Nutr. 2013 Aug; 32(4): 497-502.
[5] Dhaliwal R, et al. Nutr Clin Pract. 2014 Feb; 29(1): 29-43.

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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.

GMP-compliant production of sodium selenite at biosyn:
Vacuum drying system for targeted crystallization of metallic salts with defined portions of hydrated ingredients


WIBObarrier
WIBObarrier

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