Dosage information on selenium in oncology

selenase®
• corrects selenium deficiency
• selenium deficiency – factor for a worse prognosis
• selenium deficiency influences the risk of short- and long-term side effects of cancer therapy

Sodium selenite
• reduces side effects by protecting healthy cells
• selectively cytotoxic against tumor cells
• improves the body’s ability to destroy tumor cells
## Dosage information on selenium in oncology

<table>
<thead>
<tr>
<th>Prevention</th>
<th>Dosage Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>without genetic predisposition</td>
<td>up to 200 µg Se/day(^{[A,B]})</td>
</tr>
<tr>
<td>with genetic predisposition</td>
<td>up to 300 µg Se/day(^{[C,D]})</td>
</tr>
<tr>
<td>Therapy before therapy(^{**})</td>
<td>up to 1,000 µg Se(^{[E-G]})</td>
</tr>
<tr>
<td>on therapy-free days(^{***})</td>
<td>up to 500 µg Se/day(^{[H]})</td>
</tr>
<tr>
<td>After cancer therapy</td>
<td>up to 300 µg Se/day(^{[I]})</td>
</tr>
</tbody>
</table>

* according to dosage, regimes as presented in trials
** as therapy scheme\(^{[L,J]}\)
*** regime of therapy and therapy-free days\(^{[H]}\)

Created according to:


### Selenium to correct selenium deficiency

<table>
<thead>
<tr>
<th>Low selenium status</th>
<th>Selenium deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100 µg/l selenium in serum</td>
<td>&lt; 80 µg/l selenium in serum</td>
</tr>
<tr>
<td>&lt; 120 µg/l selenium in whole blood</td>
<td>&lt; 100 µg/l selenium in whole blood</td>
</tr>
</tbody>
</table>

- until start of cancer therapy
- up to 200 µg selenium per day (tablet or drinking ampoules)
- Costs: approx. € 17 per month or approx. € 200 per year*

- until start of cancer therapy
- up to 300 µg selenium per day (tablet)
- Costs: approx. € 50 per month or approx. € 600 per year*

*calculation based on the marketed dosage forms indicated in parentheses

Created according to: Summary of product characteristics selenase®, biosyn Arzneimittel GmbH, November 2017.

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### Selenium deficiency in cancer patients

- Often reduced selenium status at diagnosis\(^{[11–16]}\)
- Lower selenium status worsens prognosis\(^{[17,18]}\)
Cancer prevention

- Selenium deficiency increases the risk of cancer\(^1,2\)
- Different impact of the selenium status on different types of cancer\(^1\)
- Suboptimal selenium supply in Europe increases colon cancer risk\(^3\)
- Ten-fold increased risk of liver cancer at low selenoprotein P concentration\(^4\)
- Preconditions and options for a preventive effect of selenium:
  - lower selenium status
  - administration of sodium selenite\(^5,48–50\)
  - suitable dosage (not too low, not too high)

### Selenium in cancer prevention

<table>
<thead>
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<th>Low selenium status</th>
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</tr>
<tr>
<td>up to 100 µg selenium per day (tablet or drinking ampoules)</td>
<td>up to 200 µg selenium per day (tablet or drinking ampoules)</td>
</tr>
</tbody>
</table>

Costs:
- approx. €26 per months or approx. €300 per year*
- approx. €50 per months or approx. €600 per year*

*calculation based on the marketed dosage forms indicated in parentheses

Created according to:
Cancer prevention with genetic predisposition

- Selenium reduces DNA damage [6]
- Selenium improves DNA repair mechanisms [7]
- Selenium supplementation improves DNA stability in cases of selenium deficiency [8]
- Highest DNA stability at selenium serum levels between 120–160 μg/l [6]
- Sodium selenite reduces the number of chromosomal breakages in women with BRCA1 mutation [9]
- Sodium selenite can reduce breast cancer risk with BRCA1 mutations [9,10]
DURING THERAPY

Dosage information* and costs of selenium in tumor surgery

<table>
<thead>
<tr>
<th>Dosage information</th>
<th>Costs: approx. € 185**</th>
</tr>
</thead>
<tbody>
<tr>
<td>before surgery[A–C] (i.v. or drinking ampoules)</td>
<td>up to 1,000 µg selenium[A,C]</td>
</tr>
<tr>
<td>intra- or post-operative[A,C] (i.v.)</td>
<td>up to 1,000 µg selenium[A,C]</td>
</tr>
<tr>
<td>per day for 2 weeks[D] (i.v. or drinking ampoules)</td>
<td>1,000 µg selenium</td>
</tr>
</tbody>
</table>

* according to dosages, regimes as presented in trials
** calculation based on the marketed dosage forms of selenase® indicated in parentheses


Tumor surgery

- Surgical interventions lead to a significant decrease in selenium status[19, 20]
- A small increase of the inflammation marker CRP already significantly reduces the selenium status[21]
- Negative impact of the surgery-induced systemic inflammatory response on the therapy success[22, 23]
- Supra-nutritive dose of sodium selenite favors TH1 differentiation[24]
- Peri- and post-operative administration of selenase® improves selenium status[25]
Surgery-related lymphedema

• Reduced volume of surgery-related lymphedema with simultaneous selenase® therapy\(^{[26]}\)

Lymphedema

• Especially affected: breast cancer patients and patients with head and neck tumors
• Only half of those affected obtain therapy\(^{[27]}\)
• The selenium status decreases with increasing severity of lymphedema\(^{[28]}\)
• Sodium selenite shows both biological as well as pharmacological effects\(^{[28]}\)
• Selenium:
  – reduces lymphedema volume\(^{[26,29]}\)
  – raises the effectiveness of physical therapy\(^{[29]}\)
  – reduces the risk of erysipelas\(^{[29,30]}\)
  – improves quality of life scores\(^{[35]}\)
  – reduces side effects
## Dosage information* and costs of selenium in lymphedema

### At increased risk of surgery-related lymphedema*

<table>
<thead>
<tr>
<th>Before surgery[^A] (i.v. or peroral)</th>
<th>Intra- or post-operative[^A] (i.v.)</th>
<th>For 3 weeks[^A] (i.v. or peroral)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,000 µg selenium</td>
<td>1,000 µg selenium</td>
<td>1,000 µg selenium per day</td>
</tr>
</tbody>
</table>

Costs: approx. €265**

### At radiotherapy-induced lymphedema*

<table>
<thead>
<tr>
<th>For 1 week[^B] (i.v. or peroral)</th>
<th>For up to 6 weeks[^C, D] (peroral)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,000 µg selenium per day</td>
<td>500 µg selenium per day</td>
</tr>
</tbody>
</table>

Costs: approx. €320**

### At secondary lymphedema in breast cancer*

<table>
<thead>
<tr>
<th>For 1 week[^B] (i.v. or peroral)</th>
<th>For 2 weeks[^D] (peroral)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,000 µg selenium per day</td>
<td>500 µg selenium per day</td>
</tr>
</tbody>
</table>

Costs: approx. €160**

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Dosage information* and costs of selenium during radiotherapy

To reduce radiotherapy-induced side effects*

<table>
<thead>
<tr>
<th>before radiation**[A] (i.v. or drinking ampoules)</th>
<th>therapy days**[B, C] (drinking ampoules)</th>
</tr>
</thead>
<tbody>
<tr>
<td>up to 1,000 µg selenium</td>
<td>up to 500 µg selenium per day</td>
</tr>
</tbody>
</table>

Costs: approx. €405
(calculation based on example of radiotherapy for 5 days/week for 6 weeks and on the marketed dosage forms of selenase® indicated in parentheses)

* according to dosages, regimes as presented in trials
** regime of therapy and therapy-free days


During radiotherapy

- Negative effect of radiotherapy on selenium status[32]
- Sodium selenite therapy reduces radiotherapy-induced adverse reactions[33]
- Phase III trial:[34, 35]  
  – selenase® reduces radiotherapy-induced diarrhoea  
  – selenase® significantly increases the selenium status  
  – selenase® does not reduce its effectiveness during radiotherapy
During chemotherapy

- Sodium selenite is selectively cytotoxic for tumor cells\(^{36}\)
- Nephroprotective effect of sodium selenite with platinum-based chemotherapy\(^{37}\)
- Reduction of anthracycline-induced cardiac toxicity in case of selenium deficiency\(^{38}\)
- Sodium selenite reduces vinorelbine-induced phlebitis\(^{39}\)
- In combination with sodium selenite reduced side effects due to adjuvant hormone therapy in breast cancer patients\(^{40}\)
- High-dose sodium selenite:
  - reduced infection rate\(^{41}\)
  - cardioprotective effect\(^{42}\)
Dosage information* and costs of selenium after cancer therapy

To improve the immune status\(^*[A]\), for prophylaxis in case of lymphedema\(^*[B, C]\), for elevated cardiotoxicity\(^*[D]\) and osteoporosis risk\(^*[E, F]\)

- continuously
- up to 300 µg selenium per day\(^*[G]\)

**Costs:** approx. €17 per month or €200 per year
(calculation based on the marketed dosage forms of selenase\(^*\))

### At secondary lymphedema in breast cancer*

<table>
<thead>
<tr>
<th></th>
<th>for 1 week(^*[C])</th>
<th>for 2 weeks(^*[H])</th>
</tr>
</thead>
<tbody>
<tr>
<td>(i.v. or drinking ampoules)</td>
<td>1,000 µg selenium per day</td>
<td>500 µg selenium per day</td>
</tr>
</tbody>
</table>

**Costs:** approx. €160
(calculation based on the marketed dosage forms of selenase\(^*\) indicated in parentheses)

*according to dosages, regimes as presented in trials

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\[
\begin{align*}
[A] & \quad \text{Kiremidjian-Schumacher L et al. Biol Trace Elem Res. 2000 Feb; 73(2): 97-111. } \quad \text{Selenium and immunocompetence in patients with head and neck cancer.} \\
[B] & \quad \text{Zimmermann T et al. Biol Trace Elem Res. 2005 Sep; 106(3): 193-203. } \quad \text{Reduction of postoperative lymphedema after oral tumor surgery with sodium selenite.} \\
[D] & \quad \text{Tacyildiz N et al. J Oncol. 2012; 2012: 651630. } \quad \text{Selenium in the prevention of anthracycline-induced cardiotoxicity in children with cancer.} \\
[E] & \quad \text{Hoeg A et al. J Clin Endocrinol Metab. 2012 Nov; 97(11): 4061-70. } \quad \text{Bone turnover and bone mineral density are independently related to selenium status in healthy euthyroid postmenopausal women.} \\
[F] & \quad \text{Beukhof CM et al. PLoS One. 2016 Apr 7; 11(4): e0152748. } \quad \text{Selenium Status Is Positively Associated with Bone Mineral Density in Healthy Aging European Men.} \\
[G] & \quad \text{Summary of product characteristics selenase\(^*\), biosyn Arzneimittel GmbH, November 2017.} \\
\end{align*}
\]
After cancer therapy

• Long-term deterioration of the immune status after chemotherapy\textsuperscript{[43]}
  – sodium selenite to improve the immune status\textsuperscript{[44]}
• Long-term side effects\textsuperscript{[45]}: lymphedema, cardiotoxicity, osteoporosis, second tumors
  – selenase\textsuperscript{®} corrects selenium deficiency
  – improvement of lymphedema\textsuperscript{[20]}
  – balanced selenium status to protect against increased cardiotoxicity\textsuperscript{[38]}
    and risk of osteoporosis\textsuperscript{[46,47]}

selenase\textsuperscript{®}

corrects selenium deficiency
<table>
<thead>
<tr>
<th>selenase® Pharmaceuticals: Prescription Only</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>selenase® T peroral</strong>&lt;br&gt;Oral solution&lt;br&gt;500 μg selenium per drinking bottle</td>
</tr>
<tr>
<td><strong>selenase® 100 μg peroral</strong>&lt;br&gt;Oral solution&lt;br&gt;100 μg selenium per drinking ampoule</td>
</tr>
<tr>
<td><strong>selenase® 300 Mikrogramm Tabletten</strong>&lt;br&gt;Tablets&lt;br&gt;300 μg selenium per tablet</td>
</tr>
<tr>
<td><strong>selenase® T pro injectione</strong>&lt;br&gt;Injection solution&lt;br&gt;1,000 μg selenium per injection bottle</td>
</tr>
<tr>
<td><strong>selenase® T pro injectione</strong>&lt;br&gt;Injection solution&lt;br&gt;500 μg selenium per injection bottle</td>
</tr>
<tr>
<td><strong>selenase® 100 μg pro injectione</strong>&lt;br&gt;Injection solution&lt;br&gt;100 μg selenium per injection ampoule</td>
</tr>
</tbody>
</table>

Active ingredient: sodium selenite pentahydrate
Information from biosyn Arzneimittel GmbH

Brochures

We gladly send you our detailed brochure “Selenium and oncology”. Order by e-mail at: information@biosyn.de (key words “Oncology folder”)

We gladly offer you extensive information on the topics “Selenium in intensive care” and “Selenium and thyroid gland” – for expert groups and patients. Literature for your patients is also available in larger quantities free of charge. Please visit www.biosyn.de for more information.

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You can also find us on coliquio, the free medical network, with our Infocenter Selenium: www.coliquio.de

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selenase®. Active substance: Selenium as sodium selenite pentahydrate. selenase® 100 µg pro injectione, selenase® T pro injectione, selenase® 100 µg peroral, selenase® T peroral: 50 µg selenium per ml. selenase® 300 Mikrogramm Tabletten: 300 µg selenium per tablet. Indications: selenase® 100 µg pro injectione, selenase® T pro injectione, selenase® 100 µg peroral, selenase® T peroral: Proven selenium deficiency that cannot be offset from food sources. Selenium deficiencies may occur as a result of states of malnutrition and malabsorption, as well as in malnourished (e.g. due to complete parenteral nutrition). selenase® 300 Mikrogramm Tabletten: Adults: Treatment of clinically proven selenium deficiency that cannot be compensated by nutritional sources. Composition: selenase® 100 µg pro injectione: 1 ampoule of 2 ml solution for injection contains: 3.33 mg sodium selenite pentahydrate, corresponding to 100 µg (micrograms) selenium. selenase® T pro injectione: 1 injection vial of 1 ml solution for injection contains: 1.67 mg/3.33 mg sodium selenite pentahydrate, corresponding to 500 µg (micrograms) selenium. selenase® 100 µg peroral: 1 drinking ampoule of 2 ml oral solution contains: 3.33 mg sodium selenite pentahydrate, corresponding to 100 µg (micrograms) selenium. selenase® T peroral: 1 ml oral solution contains: 0.167 mg sodium selenite pentahydrate, corresponding to 50 µg (micrograms) selenium. Excipients: Sodium chloride, hydrochloric acid, water for injection. selenase® 300 Mikrogramm Tabletten: 1 tablet contains: 300 microgram selenium, corresponding to 0.999 mg sodium selenite pentahydrate. Excipients: Magnesium stearate (Ph. Eur., vegetable), maize starch, povidone K29/34, sucrose, talc. Contra-indications: Hypersensitivity to sodium selenite pentahydrate or to any of the excipients. Selenosis. Side 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. For selenase® 300 Mikrogramm Tabletten: None known to date when selenase® 300 Mikrogramm Tabletten are used as directed. Interactions: selenase® 300 Mikrogramm Tabletten must not be taken together with reducing agents (e.g. vitamin C). However, selenase® 300 Mikrogramm Tabletten and vitamin C may be administered consecutively with an interval of at least 1 hour between both administrations. Form of administration, size of packages: selenase® 100 µg pro injectione: 10 or 60 ampoules of 2 ml solution for injection. selenase® T pro injectione: 2 or 10 injection vials of 10 ml solution for injection. selenase® 100 µg peroral: 20, 60, 90 or 100 ampoules of 2 ml oral solution. selenase® T peroral: 10 drinking bottles of 10 ml oral solution plus one measuring cup. selenase® 300 Mikrogramm Tabletten: 20, 50, 100 tablets. Prescription only medicine.
Dosage information on selenium in oncology

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