**IMMUCOTHHEL®**

**Effective and less distressing side effects**

**Therapy scheme for superficial urinary bladder carcinoma**

KLH antibodies can recognize and destroy bladder carcinoma cells

- **Oligosaccharides on the KLH surface**
- *Gal(β1–3)GalNAc*

**Antigen-antibody reaction**

- Phagocytosis and dissolution of the tumor cell

**Anti-KLH antibody production**

**Oligosaccharides on the surface of bladder cancer cells**, including *Gal(β1–3)GalNAc*

**Modified according to:**

**IMMUCOTHHEL®**

1 mg, powder for solution for injection / IMMUCOTHHEL® 10 mg, powder for solution for intravesical use

**Active ingredient:** Immunocyanin.

**Indications:** Prevention of bladder carcinoma recurrence after transurethral resection and after failure of established therapies for this indication.

**Composition:** IMMUCOTHHEL® 1 mg: 1 vial with 54.63 mg powder for injections contains 1 mg biotechnically obtained, chromatographically uniform, molecularly standardized immunocyanin. Each vial is accompanied by 1 ampoule with 1 ml solvent. IMMUCOTHHEL® 10 mg: 1 vial with 546.3 mg powder for intravesical instillations contains 10 mg of biotechnically obtained, chromatographically uniform, molecularly standardized immunocyanin. Each vial is accompanied by 1 ampoule with 10 ml solvent. Excipients: Powder: Glycine, sodium hydroxide, sodium chloride, sucrose. Solvent: Water for injections.

**Contra-indications:** Immunosuppression. Known hypersensitivity to proteins foreign to the body.

**Undesirable effects:**

- Hepatobiliary disorders: Rare (≥ 1/10,000 to < 1/1,000): Increase of γ-glutamyl transferase and of glutamate pyruvate transaminase.
- Renal and urinary disorders: Rare (≥ 1/10,000 to < 1/1,000): Urgency, feeling of pressure or pain. Not known (cannot be estimated from the available data): Allergic reactions of the bladder manifesting as sterile leukocyturia.
- General disorders and administration site conditions: Uncommon (≥ 1/1,000 to < 1/100): Subfebrile temperatures are sometimes reported but are reversible after 3 days.

**Interactions:** Specific interactions were not observed. The immunostimulating effect of IMMUCOTHHEL® may be impaired by concurrent immunosuppressive radio- or chemotherapy or by simultaneous administration of corticosteroids.

**Packagings:** IMMUCOTHHEL® 1 mg / 10 mg: 1 vial of 1 mg / 10 mg immunocyanin and 1 ampoule with 1 ml / 10 ml solvent. Subject to prescription.

**Marketing authorization holder:** biosyn Arzneimittel GmbH, Schorndorfer Straße 32, 70734 Fellbach, Germany. Tel.: +49 711 575 32-00, Fax +49 711 575 32-99, e-mail: info@biosyn.de, www.biosyn.de
**IMMUCOTHTEL® – effective and less distressing side effects**

IMMUCOTHTEL® is approved as immunotherapy for the prevention of superficial recurrence of bladder cancer [Tis, Ta-T1 (G1-G3)] after transurethral resection.

**Alternative for BCG failure**

IMMUCOTHTEL® is particularly recommended in case of BCG failure or BCG intolerance. These include severe side effects due to BCG. IMMUCOTHTEL® may provide an alternative to radical cystectomy in patients where the risk, morbidity and limitations on quality of life outweigh the benefits.\(^1\)

**Questions on presensitization**

Pre-sensitization should take place around the time of the TUR. If no positive skin reaction occurs, the presensitization should be repeated. According to a recent study, it is recommended to start instillation after 4 days, even if no reaction is present.\(^2\)

A not insignificant percentage shows no reaction, whereas non-occurrence does not allow a prognosis regarding the response to IMMUCOTHTEL®.\(^2\)

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### Pre-sensitization with IMMUCOTHTEL® 1 mg

- **TUR**
  - Therapy can be started before or during TUR\(^3\)
  - Apply 1 mg s.c. or i.c. in the forearm (positive skin reaction / DTH desired, but not required)

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### Instillation therapy with IMMUCOTHTEL® 10 mg

<table>
<thead>
<tr>
<th>Period</th>
<th>Therapy Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st–2nd month</td>
<td>Initial therapy 20 ml (2 × IMMUCOTHTEL® 10 mg) weekly in week 1 – 6</td>
</tr>
<tr>
<td>3rd–12th month</td>
<td>Maintenance therapy 20 ml (2 × IMMUCOTHTEL® 10 mg) monthly</td>
</tr>
</tbody>
</table>

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### Minor side effect spectrum for IMMUCOTHTEL® compared to BCG

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>IMMUCOTHTEL®</th>
<th>BCG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaise</td>
<td>7%</td>
<td>33%</td>
</tr>
<tr>
<td>Hematuria</td>
<td>7%</td>
<td>26%</td>
</tr>
<tr>
<td>Increased temperature and fever</td>
<td>10%</td>
<td>25%</td>
</tr>
<tr>
<td>Mild and severe cystitis</td>
<td>5%</td>
<td>65%</td>
</tr>
</tbody>
</table>

Modified according to:

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Additional information for KLH/IMMUCOTHTEL®:
- [www.biosyncorp.com](http://www.biosyncorp.com), [www.biosynpharma.com](http://www.biosynpharma.com), [www.biosyn.de](http://www.biosyn.de)

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