1. What are NutriLock™ and TauroLock™ products?

NutriLock $^{\mathbb{M}}$ and TauroLock $^{\mathbb{M}}$ products are catheter lock solutions for tunneled and non-tunneled vascular access and port systems for the prevention of catheter-related infections and catheter flow problems.

2. What are the active ingredients of NutriLock™ and TauroLock™ products?

NutriLock $^{\text{M}}$ contains taurolidine as an antimicrobial ingredient. In addition to taurolidine, TauroLock $^{\text{M}}$ solutions contain 4 % citrate for the maintenance of catheter patency. There are three product variants that combine taurolidine and citrate with one more ingredient:

- TauroLock™-HEP100 also contains 100 IU/ml heparin.
- TauroLock™-HEP500 also contains 500 IU/ml heparin.
- Taurol ock™-U25.000 also contains 25.000 IU urokinase.

3. Are there special formulas for persistent patency issues?

In addition to taurolidine and 4 % citrate, TauroLock™-HEP100 contains 100 IU/ml heparin to improve patency. TauroLock™-HEP500 contains 500 IU/ml heparin.

The most effective prophylaxis against catheter occlusion is ensured with the regular use of TauroLock™-U25.000, which contains 25,000 IU urokinase (5,000 IU/ml), taurolidine, and 4 % citrate. This combination reduces flow problems in the catheter substantially (read more about lock solutions in dialysis in the documents under "Brochures"). Which catheter lock solution will prove most advantageous depends on the patient's individual situation. Alternating use (e.g. TauroLock™-HEP500, TauroLock™-U25.000) is feasible

4. Why should I use NutriLock™ or TauroLock™ products?

Heparin and 4 % citrate only have anticoagulant effects, but no bactericidal properties. Consequently, contamination of the catheter can lead to bacteremia.

TauroLock[™] solutions are used to prevent both infections and occlusions in catheter and port systems. NutriLock[™] acts prophylactically against catheter infections. Prophylactic use of TauroLock[™] solutions prevents the formation of biofilm and thus maintains the flow rate in the catheter or port.

The fibrinolytic activity of TauroLock™-U25.000 further improves patency by dissolving already formed clots.



5. Are TauroLock™ products known to have side effects?

Due to the citrate content (citrate content: 4 %), an overly rapid application into the bloodstream can lead to mild hypocalcemic effects (e.g. metallic taste)

6. Why is the citrate content in TauroLock™ products limited to 4 %? Would a higher ratio be better for anticoagulation?

A citrate concentration of 4 % is recommended by US regulatory authorities and others.

- In the context of one case of fatality, the FDA issued an advisory not to use a product with a higher citrate content (Tricitrasol, 46.7 %). Lock solutions of this type had to be recalled from the US market. Their use is no longer approved.
- Likewise, over-instillation of less than 1 ml per lumen of a 30 % citrate solution induced transient cardiac arrest in two cases in the Netherlands (Punt et al. Clinical Nephrology 2008. DOI: 10.5414/cnp69317).
- A high citrate content (46.7 %) can also lead to embolic events which might be triggered by protein precipitation (Willicombe et al. American Journal of Kidney Diseases 2010. DOI: 10.1053/j.ajkd.2009.06.037 / Schilcher et al. Nephrol Dial Transplant 2012. DOI: 10.1093/ndt/gfs048).

7. How should I use NutriLock™ and TauroLock™ products?

- Before instilling the lock solution, flush the vascular access system with at least 10 ml of physiological saline with the pulsatile flushing technique.
- Use a suitable syringe to remove NutriLock™ or a TauroLock™ solution from the container.
- Instill the lock solution into the access device in a quantity sufficient to fill the lumen completely. The specific filling volume is stated in the instructions for use of the access system and must be strictly followed.
- NutriLock™ or TauroLock™ solutions remain inside the access system until the next treatment. Before starting the next treatment, the lock solution must be aspirated.
- Flush the vascular access system with 10 ml of physiological saline.



8. Are NutriLock™ or TauroLock™ products known to have unwanted effects? What happens if TauroLock™ solutions enter the patient's body?

Once the lock solutions enter the body, their antimicrobial ingredient is degraded extremely quickly. The degradation produces taurine, an amino acid naturally present in the body.

All TauroLock™ solutions can cause mild hypocalcemia (common, e.g. metallic taste). These mild adverse effects can be avoided by slow instillation (considering the volume of the device) or by use of a citrate-free lock solution (NutriLock™). In addition, TauroLock™, TauroLock™-HEP100, TauroLock™-HEP500, and TauroLock™-U25.000 might cause an anaphylactic reaction (very rare). Bleeding may also not be completely excluded for TauroLock™-HEP100 and TauroLock™-HEP500 (very rare). TauroLock™-U25.000 may also lead to bleeding events (very rare).

9. How should I proceed if NutriLock™ or TauroLock™ products cannot be aspirated before the next treatment?

Prior to the next treatment, NutriLock^{\mathbb{M}} and all TauroLock^{\mathbb{M}} solutions must be aspirated and discarded. If NutriLock^{\mathbb{M}} cannot be aspirated, slow flushing of NutriLock^{\mathbb{M}} may be considered. If aspiration is not possible or if the healthcare professional decides that aspiration of TauroLock^{\mathbb{M}}, TauroLock^{\mathbb{M}}-HEP100, TauroLock^{\mathbb{M}}-HEP500, and TauroLock^{\mathbb{M}}-U25.000 is not appropriate (blood in the catheter, e. g. in parenteral nutrition), slow flushing (not more than 1 ml per 3 seconds) of the catheter lock solution may be considered.

Taurolidine and citrate do not induce any systemic effect. The potential systemic anticoagulant effect of heparin and of urokinase needs to be considered if flushed. Regular flushing with TauroLock™-HEP100, TauroLock™-HEP500, or TauroLock™-U25.000 may increase the risk of allergic reaction. In infants and children less than two years of age, flushing of NutriLock™, TauroLock™, TauroLock™-HEP100, and TauroLock™-HEP500 should only be performed if aspiration is not possible. All products should not be used in women during pregnancy or breastfeeding, since there is no data available on these patient groups. Likewise, TauroLock™-U25.000 should not be used in children due to a lack of data. The safety and efficacy of NutriLock™ have not been investigated in children before skeletal maturity. Due to the content of citrate, flushing of TauroLock™ solutions should be performed very slowly (not more than 1 ml per 8 seconds). Please read the instructions for use before applying a lock solution.

10. In which contexts have NutriLock™ and TauroLock™ products been approved, specifically?

NutriLock™ and TauroLock™ solutions have been approved as medical devices with CE registration.



11. How can I order NutriLock™ and TauroLock™ products?

If you would like to place an order, please contact us at <u>order@transcutan.com</u>. You can also place an order directly through our website. We will process your request as soon as possible. For costumers outside Sweden - please contact the manufacturer at www.taurolock.com.

12. What quantities can I order of NutriLock™ and TauroLock™ products?

Please visit our website under the "Products" section for more information.

13. Do NutriLock™ and TauroLock™ products affect the catheter?

The effect of NutriLock™ and TauroLock™ solutions on various catheter materials (polyurethane, silicone) has been investigated. All types of catheters remain undamaged, even in long-term tests.

14. I have been using heparin for a lock solution. Can I switch directly to TauroLock™ products?

Current findings show that a heparin 5,000 IU/ml solution can be replaced by TauroLock™-HEP500. The use of heparin can thus be reduced drastically. Please note that there is an increased probability of biofilm with viable organisms and endotoxin, as heparin has no antimicrobial efficacy. This may lead to anaphylactic reactions in case biofilm enters the bloodstream. TauroLock™-HEP500 is the product of choice in dialysis, whereas TauroLock™-HEP100 is used primarily in haematology/oncology or with paediatric patients. TauroLock™-HEP100 or TauroLock™-HEP500 must be aspirated before the next treatment.

15. Can I take coagulation test samples from a catheter locked with a TauroLock™ solution without falsifying the results?

Blood drawn from catheters locked with TauroLock™ products must not be used for measurements of blood parameters.

The above-mentioned information is taken from <u>www.taurolock.com</u>.

