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| **Protocol title** | **GODIF**Goal directed fluid removal with furosemide in intensive care patients with fluid overload – A randomised, blinded, placebo-controlled trial (GODIF)EudraCT: 2019-004292-40; ClinicalTrials.gov: NCT04180397 |
| **SOP name** | Trial medication |
| **Version** | 1.1 |
| **Applied from** | 04.01 2021 |

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| **Target population**: Site investigators and research staff |
| **Responsible party**: Sponsor, Senior staff specialist and Associate Professor Morten Bestle |
| **Created by**: Coordinating Investigator; Sine Wichmann |
| 1. **Objective**
* To define starting dose of trial drug
* To describe how to adjust the infusion of the trial drug
* To describe how to pause and re-activate trial medication
* To describe stopping criteria
* To ensure uniform working procedures for pausing and re-activation of trial medication
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| 1. **Description:**

**2.1 Starting dose**:0,5-4 ml of trial drug as a bolus injection according to the treating physician’s discretion, followed by infusion of trial drug with 2 ml/hour.**2.2 Adjustment of trial drug infusion**:Infusion of trial drug must be adjusted according to effect and fluid balance. The infusion rate is 0-4 ml/hour. Target is a negative fluid balance of at least 1 ml/kg/hour. Minimum assessment of the effect of trial drug is 3 times a day when the nurses calculate the fluid balance (often at 06:00 am, 2:00 pm and 10:00 pm). It will often be a good idea to assess the infusion rate more often to ensure the reach the target. The infusion rate must be increased until the target is reached. If the target fluid balance cannot be reached on maximum infusion rate of 4 ml/hour – the maximum infusion must continue. When a vial of trial drug is opened – the trial drug must be used within 24 hours. Infusion of trial drug must be replaced with new trial drug every 24 hours or more often.**2.3 Pausing and re-activating trial medication:**When the patient *has reached neutral fluid balance* (+/- 750 ml in cumulative fluid balance) the fluid removal must be stopped. Trial drug must be adjusted to keep the patient’s fluid balance neutral. If possible, the trial drug can be paused. It must be re-activated in case the cumulative fluid balance increases to > +750 ml. Starting bolus should only be administered the first time the trial drug is started.In case *of circulatory instability* (MAP < 50 mmHg *or* lactate ≥ 4.0 *or* mottling beyond the edge of the kneecaps the trial drug must be paused, and the resuscitation algorithm may be started. Fluid bolus of 250-500 mL crystalloids and re-evaluate the circulation within 30 min. Repeat re-evaluation and optional fluid therapy until adequate circulation (lactate < 4.0, MAP > 50 mmHg, and no mottling beyond kneecaps). When all the criteria have been resolved for minimum of 1 hour – restart trial drug at 25% reduced dose (from the dose before resuscitation) for minimum 4 hours before an eventual up regulation in infusion.In case *of escape renal replacement therapy*, the trial drug must be paused, but re-activated when the renal replacement therapy is paused or terminated.**2.4 Stopping criteria:*** Neutral fluid balance
* Discharge from the ICU
* Transferal to another ICU (not participating in GODIF)
* Death in the ICU
* 90 days post randomisation
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| **Responsible party for administration and registration of trial drug:**Site investigators and research staff. |
| **Approved 04.01 2021**: Sponsor, Morten Bestle |