NHS
Greater Glasgow and Clyde

CLINICAL GUIDELINE

Hepato-Renal Syndrome (HRS) with Acute Kidney Injury (AKI)

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Approval Group:	Medicines Utilisation Subcommittee of ADTC

Important Note:

The Intranet version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

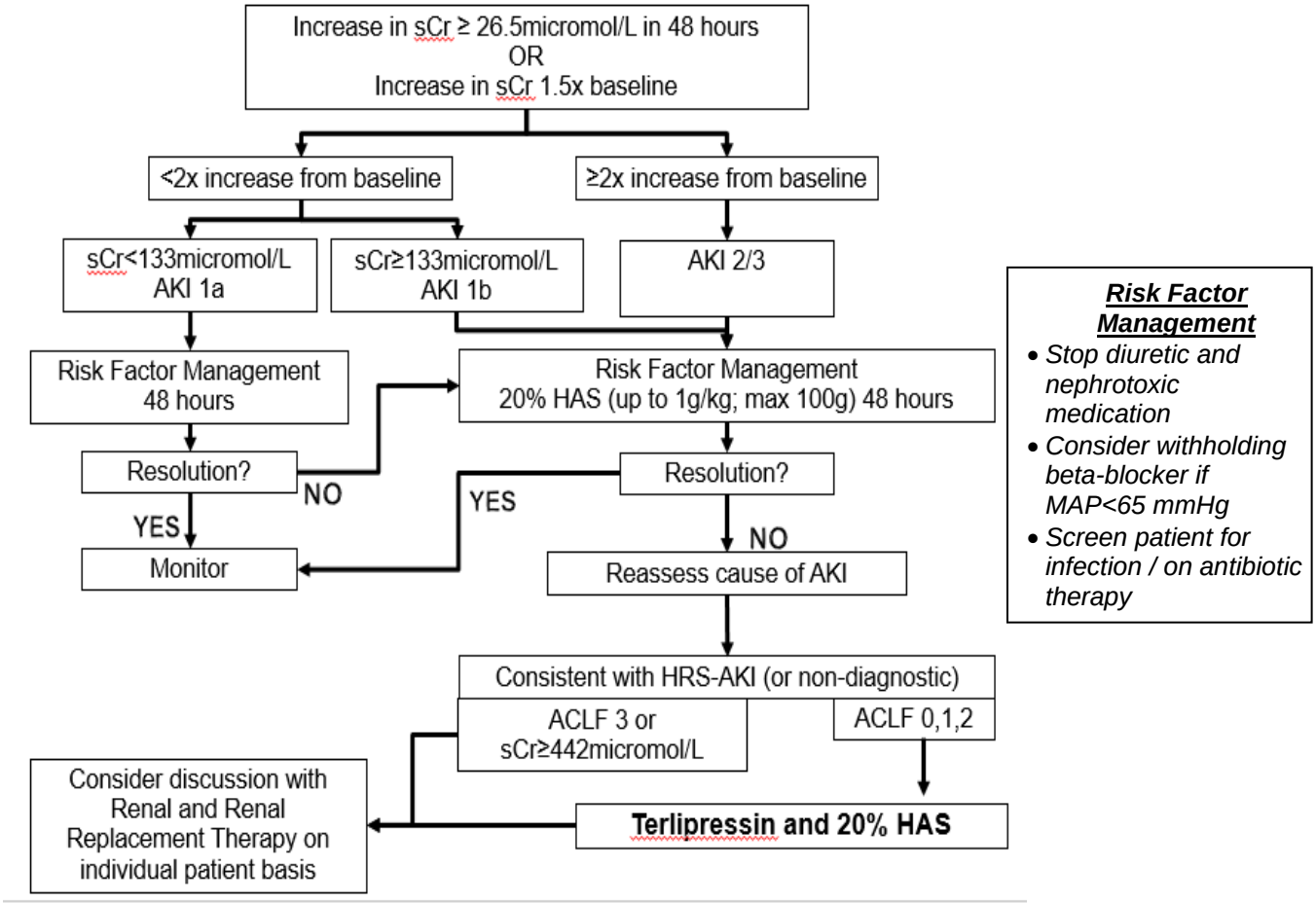
Treatment of Hepato-Renal Syndrome (HRS) with Acute Kidney Injury (AKI)

Diagnostic criteria HRS-AKI:

- AKI: an increase in serum Creatinine (sCr) ≥26.5 micromol/L within 48 hours or an increase in sCr ≥50% from baseline (1.5x baseline).
- Cirrhosis with ascites and absence of shock.
- No current or recent treatment with nephrotoxic drugs.
- Absence of other causes of kidney disease (absence of urine protein:creatinine ratio >50mg/micromol, microhaematuria or abnormal renal US).

Urine Electrolytes can be helpful in assessing AKI in advanced liver disease: Fractional excretion of urea (FeUrea) < 21% suggestive of HRS; FeUrea >21% & <33% suggestive of prerenal disease; FeUrea >33% suggestive of tubulointerstitial disease; Urine Na <20 and Fractional excretion of sodium (FeNa) <1% suggestive of prerenal disease or HRS.

Management Approach to HRS-AKI



Human Albumin Solution (HAS) Infusion

- Day 1: HAS 20% (20g albumin per 100ml) 1g/kg, up to a maximum of 100g (usually 2-5 bottles)
- Day 2 and thereafter in combination with terlipressin: HAS 20% 20-40g per day (1-2 bottles per day) +/- supplementary fluid as clinically indicated.

Terlipressin Administration:

THIS GUIDANCE SHOULD NOT BE USED FOR VARICEAL BLEEDING

Terlipressin for the treatment of HRS-AKI should only be commenced after discussion with a gastroenterology consultant or specialist registrar

Cautions and Contraindications to terlipressin: see SPC and BNF
Terlipressin can be given in boluses throughout the day **or** as a continuous infusion: continuous infusion has been associated with fewer side-effects and better tolerance.

Terlipressin should be avoided if sCr ≥ 442micromol/L, Acute-on-Chronic Liver Failure (ACLF) grade 3 and/or a Model for End-stage Liver Disease (MELD) score ≥39, unless the clinical benefits are believed to outweigh the risks.

Terlipressin Continuous Intravenous Infusion Treatment:
Terlipressin can be administered as a continuous intravenous infusion by syringe pump over 24 hours. The starting dose of 2mg terlipressin acetate over 24 hours can be increased to a maximum of 12mg of terlipressin acetate over 24 hours.
The infusion should be administered, through a dedicated cannula and not mixed with other drugs. See the table below for information on how to prepare the infusion for administration.

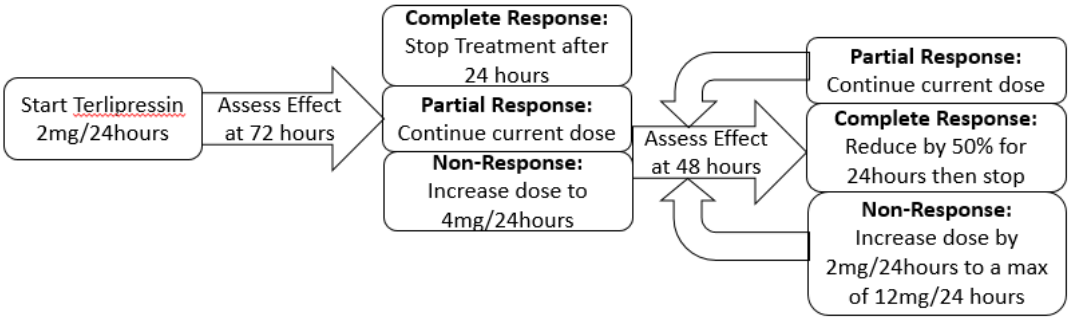
At the time of publication, terlipressin acetate 1mg/8.5ml (0.12mg/ml) solution for injection is the preparation available for use within NHS GGC. Use of this preparation in HRS is off label.

Monitoring
The following should result in **immediate** cessation of the infusion and review:

(1) Acute respiratory distress
(2) Cardiovascular complications: arrhythmia (including HR>120 bpm or HR <45 bpm or new atrial fibrillation); hypertension (>180/120 mmHg); chest pain
(3) Peripheral ischaemia: painful or cold extremities
(4) Abdominal pain associated with at least two of: (i) forceful bowel movements, (ii) abdominal tenderness or distension, (iii) nausea and vomiting, or (iv) bloody stools

Assessment of Response and Dose Alteration

Assess response 72 hours after starting terlipressin, and thereafter every 48 hours.
Changes in sCr are relative to the time of starting the terlipressin (pre-treatment sCr).



Complete Response
- Reduction in sCr to ≤ 26.5 µmol/l of the pre-treatment sCr

Partial response
- Reduction in sCr by ≥25% but without Complete Response

Non-Response
- Rise or <25% reduction in sCr

Duration of treatment
Until Complete Response or up to 14 days

Further information Refer to MHRA Drug Safety Update (March 2023) Terlipressin: new recommendations to reduce risks of respiratory failure and septic shock in patients with type 1 hepatorenal syndrome - GOV.UK (www.gov.uk)

	Terlipressin acetate					
	Intravenous Continuous Infusion for Hepato-Renal Syndrome					
Dose in 24 hours (mg)	**2mg**	**4mg**	**6mg**	**8mg**	**10mg**	**12mg**
Total amount in syringe (mg)	**2mg**	**4mg**	**3mg**	**4mg**	**5mg**	**4mg**
Name of diluent	Glucose 5%	Glucose 5%	Glucose 5%	Glucose 5%	Glucose 5%	Glucose 5%
Total volume in syringe	48ml	48ml	48ml	48ml	48ml	48ml
Drug concentration (mg/ml)	0.04mg/ml	0.08mg/ml	0.06mg/ml	0.08mg/ml	0.10mg/ml	0.08mg/ml
Drug dose per hour (mg/hr)	0.08mg/hr	0.17mg/hr	0.25mg/hr	0.33mg/hr	0.42mg/hr	0.50mg/hr
Route	IV	IV	IV	IV	IV	IV
Infusion rate (ml/hr)	2ml/hour	2ml/hour	4ml/hour	4ml/hour	4ml/hour	6ml/hour
Syringe to be changed	every 24 hours	every 24 hours	every 12 hours	every 12 hours	every 12 hours	every 8 hours
	Terlipressin has a low pH and may cause venous irritation and tissue damage in cases of extravasation. If a central venous access device is unavailable, administer via large peripheral vein and monitor insertion site closely using a recognised phlebitis scoring tool. Re-site cannula at first signs of inflammation. *Stability data* 1. *Personal communication, Medical Information, Alliance Pharmaceuticals, 22/09/23* 2. *Cavallin, M. et al. Terlipressin given by continuous intravenous infusion versus intravenous boluses in the treatment of hepatorenal syndrome: a randomized controlled study. Hepatology **63**, 983-992 (2016)*					