Prescribing Protocol SESLHDPR/576
Tolvaptan in inpatient treatment of hyponatraemia

Health
South Eastern Sydney
Local Health District

Areas where applicable	Inpatient treatment only
Authorised Prescribers	Medical teams on the advice of renal services
Indication for use	Clinically significant euvolaemic or hypervolaemic hyponatraemia in patients: • resistant to intravenous or oral sodium replacement and fluid restriction; AND, • with causes of hyponatraemia excluded
Clinical condition	• Severe hyponatraemia - serum sodium < 125 mmol/L • Euvolaemia or hypervolaemia • Causes of hyponatraemia excluded
Contra-indications	• Hypersensitivity to tolvaptan, benzodiazepine derivatives, or to any excipients • Patients who are unable to sense or appropriately respond to thirst • Patients suffering from hypovolaemic hyponatraemia • Patients with anuria • Urgent need to raise serum sodium acutely • Concomitant strong CYP3A inhibitors
Precautions	• Heart failure • Hypothyroidism and hypoadrenalism – screen before treatment • Severe renal impairment creatinine clearance <10mL/min or chronic dialysis – patients not expected to benefit from tolvaptan • Liver injury or underlying liver disease • Avoid rapid increase in sodium levels • Hypernatremia (potent aquaresis-free water clearance) • Dehydration and hypovolaemia • Hyperkalaemia or drugs that increase serum potassium • Urinary outflow obstruction • Lactose and galactose intolerance • Pregnancy (Category D) • Breastfeeding should be discontinued • High falls risk as occasionally dizziness, weakness or syncope may occur
Place in Therapy	Second line treatment - after intravenous of oral sodium replacement and fluid restriction
Dosage	Initiate treatment with 15 mg orally daily. Increase dose incrementally, first to 30 mg daily and up to a maximum of 60 mg daily if required, at intervals of more than 24 hours. The rate of serum sodium correction should be no more than 10 mmol/L in the first 24 hours.
Duration of therapy	Until serum sodium reaches 130 mmol/L for a maximum of 30 days.

Important Drug Interactions	• Strong CYP3A inhibitors (e.g. ketoconazole, clarithromycin, itraconazole, ritonavir, etc.) should not be co-administered with tolvaptan. • Moderate CYP3A inhibitors (e.g. erythromycin, fluconazole, aprepitant, diltiazem, verapamil) should generally be avoided. • Rifampicin and other CYP3A inducers may reduce effect of tolvaptan. The dose of tolvaptan may have to be increased. • Co-administration of ciclosporin and other P-glycoprotein inhibitors may require dose reduction of tolvaptan • Tolvaptan may increase effects of digoxin, monitor digoxin levels and adjust accordingly
Administration instructions	**Samsca® brand:** Oral administration daily, preferably in the morning, without regard to meals. Tablets should be swallowed without chewing with a glass of water. If patient has swallowing difficulties, refer to Don't Rush to Crush in MIMS monograph **Samsca® brand** tablets should NOT be taken with grapefruit juice.
Monitoring requirements	• Serum sodium daily, increasing less than 12 mmol/L per day. • Serum potassium in patients with serum potassium >5 mmol/L and/or receiving drugs known to increase serum potassium levels • Volume status. • Neurological status during initiation and after titration of dose. • Avoid fluid restriction in the first 24 hours of therapy. • Advise patients to resume fluid restriction following discontinuation of treatment, and continue monitoring sodium and volume status.
Management of complications	Too rapid correction of hyponatraemia can cause osmotic demyelination which may result in dysarthria, mutism, dysphagia, lethargy, affective changes, spastic quadriparesis, seizures, coma and death.In patients receiving tolvaptan who develop **too rapid a rise in serum sodium**, discontinue or interrupt treatment with tolvaptan and consider administration or ingestion of hypotonic fluids as appropriate. Liver function tests should be promptly performed in patients taking tolvaptan who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine or jaundice. If **liver injury** is suspected, tolvaptan should be promptly discontinued, appropriate treatment should be instituted, and investigations should be performed to determine the probable cause. Do NOT reinitiated in patients unless the cause for the observed liver injury is definitively established to be unrelated to tolvaptan treatment.
Basis of Protocol/Guideline:	MIMS Online, Samsca, updated 01 May 2021
Groups consulted in development of this guideline	Nil

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GOVERNANCE	
Enactment date Renewal date	July 2016 June 2022
Expiry date:	July 2025
Ratification date by SESLHD QUM Committee	7th July 2022
Chairperson, QUM Committee	Dr John Shephard
Version Number	3