

Medicines Optimisation programme Board (MOPB)

Drug	Tolvaptan
Indication	Hyponatraemia secondary to SIADH (hyponatraemia in cancer patients is the responsibility of NHS England)
Decision	<p>Approved commissioning position in line with East of England Priorities Advisory Committee:</p> <ol style="list-style-type: none"> 1. Tolvaptan is recommended as an option for treating hyponatraemia secondary to SIADH for patients who do not require chemotherapy with proven SIADH with serum sodium <125 mmol/litre with symptoms or <120 mmol/litre without symptoms, where fluid restriction and a ONE week trial of demeclocycline treatment have failed or are contraindicated 2. Course of treatment should not exceed 10 days 3. Treatment should be initiated in secondary care and monitored by a specialist. 4. Prescribing should remain in secondary care. Prescribing in primary care is not recommended. 5. Trusts must notify CCGs on initiation of treatment and provide clinical and outcome data. 6. The responsibility for commissioning tolvaptan for patients requiring chemotherapy is the responsibility of NHS England.
Date	31.05.17
Evidence	<p>Priorities Advisory Committee (PAC) evidence review for Tolvaptan</p>  <p>Item 6 Tolvaptan for hyponatraemia secon</p>

Rationale for recommendation

As stated within the PAC review guidelines do not necessarily reflect current practice within the UK. Following consultation with East of England clinicians it was felt there was a place for Tolvaptan when all other treatments had failed. This correlates with the views of Dr Sennik, Endocrinologist at Princess Alexandra Hospital Harlow (see consultation comments below).

Treatment alternatives and place in therapy

Fluid restriction is first-line treatment for the treatment of hyponatraemia secondary to SIADH. In practice fluid restriction may not always resolve hyponatremia in a timely fashion and restricting fluids for an extended period of time may cause significant discomfort for the patient, and may delay discharge. The European Clinical Practice Guideline on treatment of hyponatraemia recommend increasing intake of osmotic solutes (using oral urea) to enhance clearance of water as a second-line treatment, however this is not an option in the UK as these products are not commercially available.

The use of demeclocycline is not supported by the guidelines but it is used in clinical practice in the UK. It is associated with GI disturbance, renal toxicity and gives an unpredictable response with a slow onset of action. There have been supply problems with demeclocycline over the past few years and although licensed demeclocycline is currently available again, the cost has risen significantly. Feedback from EoE clinicians was in favour of a 1 week trial of demeclocycline if fluid restriction has failed.

Feedback from EoE clinicians indicates that, despite the lack of evidence to support use, there was a place for using tolvaptan in the following patient groups:

- Patients with proven SIADH due to non-cancer indications with serum sodium <125 mmol/litre with symptoms or <120 mmol/litre without symptoms, where fluid restriction and demeclocycline treatment have failed or are contraindicated [4]

Clinicians have indicated that, in practice, a short course of a few days (up to a maximum of 10 days) is required to normalise sodium levels which can then be more readily managed by fluid restriction. Intractable hyponatraemia may prevent discharge in patients who are otherwise suitable for discharge. Whilst tolvaptan is a high cost treatment (£74.68 to £149.36 per day), this would be offset by any reduction in a patient's length of stay. More timely discharge is of particular value for end of life patients where hyponatraemia is delaying their discharge from hospital to home, or to their chosen place of care.

It is acknowledged that there are safety concerns over the use of tolvaptan, but these can be minimized by the use of short courses. It is also noted that the risk/benefit axis shifts in favour of benefit when considering use of tolvaptan in end of life patients, as improvement in symptom control may outweigh any concerns about toxicity.

Due to the risk of over rapid correction of serum sodium levels, treatment should be initiated by a specialist and take place in hospital or in a setting where the patient can be closely monitored for over rapid correction of hyponatraemia (e.g. hospice).

Because of the need for timely treatment of hyponatraemia, it is acknowledged that the IFR route would not be a suitable route for obtaining approval to treat patients with acute hyponatremia due to SIADH.

On initiating treatment with tolvaptan acute trusts should notify CCGs and provide clinical details and outcome data via an agreed proforma.

Financial impact

Hyponatraemia (serum sodium <135 mmol/l) occurs in 15–22% of hospitalized patients. The incidence of moderate and severe hyponatraemia is lower occurring in 1–7% of hospitalized patients. This common disorder remains incompletely understood and often inappropriately managed because of its association with a myriad of underlying disease states, of which SIADH is one.

SIADH and hyponatraemia NDT Plus. 2009 Nov; 2(Suppl 3): iii1–iii4.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2762825/>

Estimated number of patients is difficult to determine, in my knowledge West Essex has only had one application for Tolvaptan for this indication.

Scottish Medicines Consortium:

In the absence of a submission from the holder of the marketing authorisation.

Tolvaptan (Samsca®) is not recommended for use within NHS Scotland for the treatment of adult patients with hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH).

The holder of the marketing authorisation has not made a submission to SMC regarding this product in this indication. As a result we cannot recommend its use within NHS Scotland.

All Wales medicines Strategy Group:

No decision

HMMC have ratified the PAC position:

[http://www.enhertscg.nhs.uk/sites/default/files/content_files/Prescribing/Local Decisions/Endocrine system/Tolvaptan%20for%20hyponatraemia%20secondary%20to%20SIADH.pdf](http://www.enhertscg.nhs.uk/sites/default/files/content_files/Prescribing/Local_Decisions/Endocrine_system/Tolvaptan%20for%20hyponatraemia%20secondary%20to%20SIADH.pdf)

Treatment of hyponatraemia secondary to SIADH - Hospital prescribing ONLY

Cambridge and Peterborough CCG and Addenbrookes:

Treatment of hyponatraemia secondary to SIADH – Hospital prescribing ONLY