

Demeclocycline shared care guideline

Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)

Specialist details	Patient identifier
Name: _____	
Location: _____	
Tel: _____	Date: _____

Introduction

Demeclocycline is a tetracycline derivative and is thought to act by directly blocking the renal tubular effect of antidiuretic hormone. It decreases tubular reabsorption of water and thus lowers concentration of urine, in effect causing a form of nephrogenic diabetes insipidus.

Licensed indications: for the treatment of chronic hyponatraemia associated with the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) secondary to malignant disease, where water restriction is ineffective and the patient does not have concomitant cirrhosis.

Unlicensed indications: demeclocycline is also sometimes prescribed for SIADH in the setting of non-malignant disease, particularly chronic respiratory disorders.

Whether therapy for hyponatraemia should be continued after discharge from the hospital depends on the aetiology of the SIADH, as many causes of inpatient hyponatremia are transient and resolve with treatment of the underlying comorbidity.

All patients who are to continue on therapy as an outpatient must have an identified specialist sharing care with the GP.

Advice will be given by the hospital specialist to the GP on the frequency of monitoring, and when to request advice.

Adult dosage and administration

Initial dose: 900 - 1200mg orally daily in divided doses. Treatment must be continued for several days to achieve maximal diuretic effects, so 3 - 4 days may be required before reviewing the dose.

Maintenance dose: 600 - 900mg orally daily in divided doses.

Regular assessment of the patient's need to continue demeclocycline and their response to therapy is required.

Available as: demeclocycline 150mg capsules.

Hospital specialist responsibilities

- Shared care is likely to be applicable to a small number of patients. The consultant who is discharging the patient from hospital must seek agreement on any monitoring required from the GP before discharge on an individual basis.
 - **If the discharging consultant considers it more appropriate for another specialty such as clinical chemistry or endocrinology to share this care with the GP then they should directly contact the relevant consultant to request and agree this prior to discharge.**
- Assess the suitability of the patient for this continued treatment. Any need for ongoing fluid restriction should be discussed with the patient prior to discharge.
- Provide the patient/carer with relevant (preferably written) information on use, side effects and need for monitoring of medication.
- Advise the GP on the dose to be prescribed and any dose adjustment appropriate, including when therapy may be reduced and/or stopped.
- Advise the GP on arrangements for secondary care planned follow up and review, including planned frequency of review.
- Advise the GP what routine monitoring will be completed by the specialist and what monitoring the GP will be responsible for. The frequency and targets for monitoring are individual and specific to each patient.
- In conjunction with GP, monitor response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP if required and respond to issues raised by the GP.

Table 1. Monitoring: frequency and targets for monitoring should be individualised

Test	Hospital specialist	GP	Hospital specialist
	Baseline	During treatment	At hospital review
U&Es, eGFR	✓	Frequency required may vary and will be advised on an individual patient basis by the specialist as clinically indicated	At any review appointment or as clinically indicated
Serum and urine osmolality*	✓		
FBC	✓		As clinically indicated
LFTs			

* The assessment of serum and urine osmolality may require overview from a specialist (clinical chemist, endocrinologist, oncologist or other experienced physician).

GP responsibilities

- Prescribe demeclocycline as requested by the specialist. Continued prescribing is unusual outside of oncology or endocrinology but is appropriate for patients attending regular review.
- Arrange and record ongoing monitoring as advised by specialist (see Table 1), ensuring practice systems are in place to recall patients for monitoring blood tests.
- Communicate the results of monitoring to the consultant. In conjunction with the consultant, monitor response to treatment and need to continue therapy.
- Report any adverse drug reactions to specialist and the usual bodies (eg. MHRA/CHM).
- Ensure no drug interactions with other medicines especially other tetracycline antibiotics.

Contraindications , precautions and adverse effects

Contraindications: demeclocycline is contraindicated in patients with acute porphyria, patients who are pregnant or breast-feeding, children under 12 years of age, patients with a history of hypersensitivity to tetracyclines and patients with renal impairment.

Adverse effects include:

- GI disturbances, nausea, vomiting, diarrhoea and rarely dysphagia and oesophagitis have been reported.
- In common with other tetracyclines, transient increases in liver function test values, hepatitis, jaundice and hepatic failure have been reported rarely. Patients who have known liver disease should not receive more than 1000mg daily. A few cases of pancreatitis have been reported.
- Photosensitivity. Erythematous and maculo-papular rashes, pruritus, bullous dermatoses, exfoliative dermatitis and skin discolouration have occurred occasionally but serious skin reactions are rare.
- Headache, dizziness, visual disturbances and rarely impaired hearing have been reported with tetracyclines
- Bulging fontanelles in infants and benign intracranial hypertension in juveniles and adults have been reported.
- There have been isolated cases of myasthenia.
- As with all antibiotics, overgrowth of resistant organisms may cause candidiasis, pseudomembranous colitis (*Clostridium difficile* overgrowth) glossitis, stomatitis, vaginitis, or staphylococcal enterocolitis.
- Hypersensitivity reactions including urticaria, Stevens-Johnson syndrome, angioneurotic oedema, anaphylaxis, anaphylactoid purpura, pericarditis and exacerbation of systemic lupus erythematosus (SLE) may occur.
- Renal dysfunction, especially in patients with pre-existing renal impairment, and rarely, acute renal failure or nephritis, have been reported with tetracyclines.
- Reversible nephrogenic diabetes insipidus occurs (as an intended consequence of treatment).
- Haemolytic anaemia, thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia and eosinophilia have been reported rarely.

Common drug interactions

Demeclocycline is a tetracycline, so concurrent prescribing of tetracycline antibiotics eg. doxycycline should be avoided.

The following interactions relate to tetracyclines generally:

- Tetracyclines depress plasma prothrombin activity and reduced doses of concomitant anti-coagulants such as coumarins and phenindione may be required.
- Absorption is impaired by the concomitant administration of milk and dairy products, food, iron, calcium, zinc, magnesium and particularly aluminium salts commonly used as antacids. Absorption of tetracyclines is possibly reduced by kaolin, quinapril tablets (quinapril tablets contain magnesium carbonate), strontium ranelate, sucralfate.
- The concomitant use of tetracyclines may result in failure of oral contraceptives; an increased incidence of breakthrough bleeding may also be experienced.
- There is a possible increased risk of benign intracranial hypertension with concomitant use of tetracyclines and retinoids, eg. acitretin, isotretinoin, tretinoin.
- There is increased risk of ergotism when tetracyclines given with ergotamine and methysergide.
- Typhoid vaccine (oral): antibacterials inactivate oral typhoid vaccine and therefore should be avoided for 3 days before and after oral typhoid vaccine.

Communication

For any queries relating to this patient's treatment with demeclocycline, please contact the specialist named at the top of this document. Contact details for oncology or endocrinology services and clinical chemists may also be obtained through the main hospital switch boards.

This information is not inclusive of all prescribing information and potential adverse effects.
Please refer to full prescribing data in the SPC or the BNF

Date prepared: June 2017

Date of review: June 2020