BNSSG Health Community's Traffic Light System
Shared Care Guidance

Please complete all sections.
Type in the grey shaded areas (deleting the prompts for information in each section).

Section 1: Heading

Trust: North Bristol NHS Trust

Specialty / Department: Renal

Drug:penicillamine for treatment of cystinuria

Section 2: Treatment schedule

The aim of treatment is to reduce stone recurrence rate in patients with cystinuria who continue to form stones at an unacceptable rate despite advice on fluid intake and urinary alkalinisation. Penicillamine works by forming cross links with free cystine in the urine, forming a soluble compound in place of cystine, which is relatively insoluble.
Penicillamine is available in 125mg and 250mg tablets. The typical dose starting dose is 500 mg/day in four divided doses, increasing by 125mg each month to a maximum of 3g/day, adjusted according to regular measurements of urine cystine concentration (usually on 24h urine samples split into daytime and nighttime collections). Higher initial doses may be used when dissolution of existing stones is required to avoid surgery.
Patients should also be prescribed pyridoxine 25mg daily (as penicillamine appears to antagonise the effects of vitamin B6)

Section 3: Monitoring

Baseline FBC, U&E, Creatinine, LFTs and urinalysis will be performed prior to treatment by the Renal Unit.
During the first 8 weeks, FBC and urinalyisis (for blood and protein) should be carried out every 1 - 2 weeks, and a week after each dose increase.
Subsequently FBC and urinalysis should be carried out monthly for 6 months, then 3 monthly thereafter.

Section 4: Side-effects

Nausea, anorexia, fever - usually transient in early stages of treatment but a dose reduction may be required. Stop if persistent

Rash - Urticarial reactions may be controlled by antihistamines or steroids. If symptoms are severe, stop penicillamine and discuss with the Renal Unit. A late rash may develop after several months or years of therapy and may require a dose reduction. Sometimes a rash will not recur if Penicillamine is stopped and then restarted at very low dose followed by progressive increases in dose over time. Penicillamine can occasionally cause an SLE-like syndrome, and an autoantibody screen should be sent if the patient develops a photosensitive rash.

Loss of taste - reversible, and therefore treatment should be continued.

Thrombocytopenia (common) and leucopenia (less commonly) - can occur at any time during treatment and are usually reversible. Any reports of rash, oral ulceration, abnormal bruising or sore throat should prompt an urgent FBC.
Withdrawal of treatment should be considered if:
- platelet count falls below 120
- white blood cell count falls below 2.5
- or if three successive falls are noted within the normal range.

Treatment may be restarted at a reduced dose when counts return to normal, but should be permanently withdrawn on recurrence of leucopenia or thrombocytopenia.

Date approved: September 2012 Date to be reviewed: September 2014

Proteinuria (occurs in 30% of patients) and haematuria (rarely) - if trace or greater protein shown on a dipstick test then send urine sample to Biochemistry in a plain container to Biochemistry for an albumin:creatinine ratio (ACR). If ACR > 5 mg/mmol, discuss with the Renal Unit. Worsening proteinuria may results from penicillamine-induced membranous nephropathy and is an indication to stop the drug, as the condition will worsen with continued exposure but resolve after drug withdrawal. Isolated haematuria is not an indication to stop penicillamine but penicillamine should be discontinued if haematuria recurs.

Breast enlargement has been reported as a rare complication of penicillamine therapy in both women and men. Danazol has been used successfully to treat breast enlargement which does not regress on drug discontinuation.

See Summary of Product Characteristics accessed via www.emc.medicines.org.uk for full listing of adverse effects .

Section 5: Drug interactions

Penicillamine should not be given with other drugs capable of causing similar serious haematological or renal adverse effects, for example gold salts, chloroquine, clozapine or hydroxychloroquine, or immunosuppressive drugs.

Patients who are allergic to penicillin may react similarly to penicillamine, but cross-sensitivity appears to be rare.

Concomitant use of NSAIDs and other nephrotoxic drugs may increase the risk of renal damage.

Penicillamine should be used with caution in patients who have previously had adverse reactions to gold and concomitant treatment with gold should be avoided.

Penicillamine absorption is reduced by antacids (in particular those containing aluminium and magnesium), oral iron and zinc and if indicated these should not be given within 2 hours of penicillamine.

Concomitant digoxin should not be given within 2 hours of taking penicillamine as oral absorption of digoxin may be reduced.

Coadministration with levodopa may result in elevated levodopa levels.

Section 6: Cautions and special recommendations

The safety of penicillamine during pregnancy has not been established therefore any patients with a positive pregancy test should be advised to stop treatment and consult their renal consultant.

It has been suggested that doses of penicillamine should be reduced to 250 mg daily for 6 weeks prior to elective surgery because of possible effects of penicillamine on collagen and elastin (and thereby on wound healing).

Chicken pox/shingles infection - stop and commence aciclovir.

Patients should avoid contact with people who have active chickenpox or shingles and report any contact to their GP and hospital specialist. If immunosuppressed patients are exposed to chickenpox or shingles, they will need to be assessed for susceptibility and the need for aciclovir post exposure prophylaxis, see: UKHSA guidance: Guidelines on post-exposure prophylaxis (PEP) for varicella/shingles (https://www.gov.uk/government/publications/post-exposure-prophylaxis-for-chickenpox-and-shingles) and the Green Book Chapter 34

(https://www.gov.uk/government/publications/varicella-the-green-book-chapter-34).

Section 7: Advice to the patient

Patients will be asked to report any symptoms suggesting myelosupression (unexplained fever, bruising, purpura, sore throats, fever, malaise, mouth ulcers or rashes) to their GP or renal consultant.

Patients should be advised to maintain an adequate fluid intake - this will be discussed by the Renal Unit on initiation of penicillamine.

Section 8: Responsibilities for Secondary Care

The Renal Unit will undertake all baseline monitoring, patient counselling and initiation of penicillamine. Prescribing responsibility will remain with the Renal Unit until for 3 months.The consultant initiating the prescription of penicillamine will contact the patient's GP to explain the rationale for prescribing, the monitoring which will be required and the most appropriate way of communicating test results. The patient will be reviewed by their consultant at least every 6 months.

Section 9: Responsibilities for Primary Care

During the initiation period, primary care may be asked to undertake monitoring for the patient's convenience. Blood tests and urinalysis should be carried out as above and communicated to the Renal Unit as requested. When the patient's dose remains stable for 3 months full responsibility for supply and monitoring may be transferred to primary care.

Section 10: Contact details

Name	Organisation	Telephone number	Fax number	E-mail address
Dr C Tomson	North Bristol NHS Trust	0117 323 5224	0117 950 8677	Charlie.Tomson@nbt.nhs.uk

Section 11: Document details

Date prepared:	27th April 2010, reviewed August 2012
Prepared by:	Katy Hunter – Renal Pharmacist (North Bristol NHS Trust)
Date for next review:	August 2014
Reviewed by:	Katy Vincent – Renal Pharmacist (North Bristol NHS Trust) Dr Charlie Tomson – Renal consultant (North Bristol NHS Trust)

Section 12: Collaboration

Specialists in any one discipline are encouraged to collaborate across the BNSSG health community in preparing shared care guidance. Please give details.
Not applicable.
Change to information about PEP for varicella/shingles February 2023 added by BNSSG Formulary Team.

Section 13: References

Summary of Product Characteristics (Distamine 125mg) accessed via www.emc.medicines.org.uk last updated 17/04/12
Martindale. The Complete Drug Reference accessed via www.medicinescomplete.com