THALIDOMIDE WITH OR WITHOUT DEXAMETHASONE

INDICATION

As initial therapy or at relapse in patients thought unsuitable for combination treatment such as CTD or MPT.

GENERAL PRE-ASSESSMENT

1. Ensure all the following staging investigations are done:
   - FBC & film
   - Clotting screen
   - U&Es
   - LFTs
   - Calcium
   - Albumin
   - Uric acid
   - CRP
   - Virology : HIV, Hepatitis B (including core antibody), and Hepatitis C
   - Calculated creatinine clearance (CrCl), urine protein/ creatinine ratioElectrophoresis and immunofixation for quantitation of serum paraprotein and immunoglobulins.
   - Serum free light chain assay (Freelite)
   - β_2 microglobulin
   - Myeloma FISH should be performed in all patients at diagnosis, and in selected patients at relapse/progression to help guide treatment decisions Samples should be sent to Wessex Regional Genetics Laboratory (address below). Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
   - Group and save
   - Imaging as per NICE/network guidance and clinical presentation
   - Bone marrow aspirate and trephine (with immunophenotyping for kappa/lambda if appropriate)

Wessex Regional Genetic Laboratory
Salisbury NHS Foundation Trust
Salisbury Disctrict Hospital
Salisbury
Wiltshire
SP2 8BJ

Additional investigation:
   - Plasma viscosity if hyperviscosity suspected

2. Fertility - all patients should be offered fertility advice, as appropriate.
3. Hydration - fluid intake of at least 3 litres /day should be attempted.
4. Counselling - all patients should receive verbal and written information on oral chemotherapy. Ensure pre-chemotherapy counselling in line with NPSA recommendation and chemotherapy measures

5. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent for the treatment including signing Celgene risk management programme forms.

REGIMEN SPECIFIC PRE- ASSESSMENT

The conditions of the Thalidomide Celgene Pregnancy Prevention Programme must be fulfilled for all male and female patients.

Clinical Assessment of thrombo-embolic risk.

DRUG REGIMEN

The optimum dose of thalidomide is unknown. 200 mg is a typical target dose (100 mg in the elderly). These doses are rarely achievable.

Thalidomide	100-200 mg po (preferably nocte). Start dosing at 50-100 mg/day, increase every 2-4 weeks dependent on side effects	Nocte
WITH OR WITHOUT		
Dexamethasone	20 mg po daily for 4 days for elderly patients	Days 1 to 4 Days 15 to 18
OR	OR	
Dexamethasone	40 mg po daily for 4 days for younger patients	Days 1 to 4 Days 12 to 15

CYCLE FREQUENCY

The cycle is repeated every 4 weeks (3 weeks in younger patients). The treatment typically continues for 4-9 months depending on response and side effects. See note above on maintenance thalidomide.

DOSE MODIFICATIONS

Myelosupression: No dose reductions are generally necessary.

Neuropathy: Thalidomide should be stopped or dose reduced if there are symptoms of progressive peripheral or autonomic neuropathy causing functional disability (grade 2 or above). Consider cautious re-introduction of thalidomide at 50 mg daily if neuropathy symptoms resolve to grade 1 or better. Alternatively consider second line treatment.

Thalidomide:

Renal	Hepatic
No dose reduction necessary	No dose reduction necessary

INVESTIGATIONS - Beginning of each cycle

- Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle
- FBC, U&Es, LFTS Ca^{++}, glucose – every 3-4 weeks.
- Ig's, paraprotein, usually monthly after first 2 months, Freelite assay if appropriate.
- Consider bone marrow assessment after four cycles for non-secretory Myeloma.

CONCURRENT MEDICATIONS

- Allopurinol 300 mg daily for 7 days for cycle 1 only. Aim to start day before chemotherapy.
- Prophylactic laxatives to be taken if needed.
- Proton pump inhibitor or H2 antagonists at clinician's discretion
- Consider prophylactic fluconazole (not appropriate for thalidomide monotherapy)
- Bone protection as per NSSG Bone Protection protocol MM.3
- Thromboprophylaxis/anticoagulation – see above.
- Prophylactic acyclovir 200 mg bd to tid (depending on renal function)

EMETIC RISK

Minimal emetic risk.

ADVERSE EFFECTS/REGIMEN SPECIFIC COMPLICATIONS

- **Drowsiness, somnolence and sedation**: Prescribe as night time dose. Thalidomide may potentiate the drowsiness caused by alcohol and other sedative medication. If affected, patients should be instructed not to drive cars, use machinery or perform hazardous tasks whilst taking thalidomide

- **Peripheral neuropathy**: Patients should be advised to report prickling, numbness and paraesthesia.

- **Venous thromboembolism (VTE)**:
  There is an increased risk of thrombosis, and some form of prophylaxis is recommended as follows:

  1. Aspirin can be appropriate for patients with no additional risk factors for thrombosis

  If additional risk factors consider:

2. Prophylactic low-molecular weight heparin OR
3. Vitamin K antagonists at a therapeutic dose, to maintain an international normalised ratio (INR) of 2–3

Additionally:

4. Can consider use of a direct oral anticoagulant eg apixaban for thromboprophylaxis or treatment dose as indicated.

Aspirin is generally not preferred for higher risk patients with additional risk factors such as immobility. If VTE occurs, thalidomide can be continued and the patient should be fully anticoagulated according to standard guidelines.

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- **Teratogenic**: A risk management programme should be observed. The concomitant use of 2 effective methods of contraception is mandatory in all female patients of childbearing potential. Male patients should also use a condom when having sexual intercourse with women of childbearing potential. **Prescribing and dispensing of thalidomide must be in line with the pregnancy prevention programme**.

- **Dizziness and orthostatic hypotension**: Patients should be advised that thalidomide may cause orthostatic hypotension and that they should sit upright for a few minutes prior to standing up from a recumbent position.

- **Skin toxicity**: in the event of toxic skin reactions such as Stevens-Johnson syndrome, thalidomide should be discontinued permanently.

- **Other warnings**: Patients should be informed not to donate blood or semen during or within 8 weeks of stopping thalidomide treatment.

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REVIEW

Name	Revision	Date	Version	Review date
Nadjoua Maouche Pharmacist	Formatting, adverse effects and pre assessment section , dose modification, contraindication section removed	May 2016	4.3	May 2018
Dr J. Kothari Consultant	VTE, Regimen specific pre assessment section included	May 2016	4.3	May 2018
Manuela Sultanova Service Coordinator	Formatting, Standardisation of general pre-assessment section, Wessex lab address and VTE	August 2017	4.4	May 2018