Thalidomide and Dexamethasone

Indication
First line treatment or treatment of relapsed multiple myeloma in patients who are unsuitable for alternative combination treatment.

ICD-10 codes
Codes with a pre-fix C90

Regimen details

Day	Drug	Dose	Route
1-28 (continuously)	Thalidomide	50mg ON*	PO
1-4 and 15-18	Dexamethasone	20-40mg OM	PO

* Thalidomide may be increased to 100mg ON during cycle 1 if tolerated and to 200mg ON for subsequent cycles.

Cycle frequency
28 days

Number of cycles
Maximum of 6 cycles

Administration
Thalidomide is available as 50mg capsules. The capsules should be swallowed whole in the evening.

Women of child bearing potential must have a **NEGATIVE PREGNANCY TEST** within 72 hours before starting thalidomide therapy, and then before each cycle during treatment until one month after stopping treatment (every 2 weeks if irregular periods). If a woman thinks she may be pregnant she must stop taking thalidomide immediately.

Dexamethasone is available as 500microgram and 2mg tablets. The dose should be taken in the morning, with or after food.

Pre-medication
Nil

Emetogenicity
This regimen has low emetogenic potential.

Additional supportive medication
H_2 antagonist or proton pump inhibitor
Allopurinol 300mg OD (100mg OD if CrCl< 20mL/min) for patients with a high tumour burden, for the first cycle only
Bisphosphonates as per local policy
Antifungal, antiviral and PCP prophylaxis as per local policy
Laxatives if required.

Anticoagulation may also be required – risk assess patient and consider prophylactic LMWH as per local policy (unless platelet count < 30 x 10^9/L, then withhold until recovered). If patient is already taking warfarin switch to treatment dose LMWH.

Extravasation

N/A

Investigations – pre first cycle

Investigation	Validity period
FBC and film	7 days
Clotting screen	7 days
U+Es (including creatinine)	7 days
LFTs	7 days
Glucose	7 days
Calcium	7 days
HIV, hepatitis B and C status	7 days
Pregnancy test (women of childbearing potential)	3 days

Serum electrophoresis (or alternative biological measure of response if M protein not measurable)
Bone marrow aspirate and trephine

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	96 hours
U+Es (including creatinine)	7 days
LFTs	7 days
Calcium	7 days
Blood pressure	On day 1
Pregnancy test (women of child bearing potential)	3 days

Serum electrophoresis (or alternative biological measure of response if M protein not measurable)

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 70 x 10^9/L
Creatinine clearance	≥ 50mL/min
Bilirubin	< 1.5 x ULN

Dose modifications

- **Haematological toxicity**

Treatment on day 1 should only be initiated if neutrophils ≥ 1.0 x 10^9/L and platelets ≥ 70 x 10^9/L.

- **Renal impairment**

No specific dose recommendations available. Closely monitor for adverse effects in severe renal impairment.

- **Hepatic impairment**

No specific dose recommendations available. Closely monitor for adverse events in severe hepatic impairment.

- **Other toxicities**

Toxicity	Definition	Thalidomide dose
Peripheral neuropathy	Grade 3-4	Stop thalidomide (usually permanently). If symptoms resolve consider starting at 50mg for subsequent cycles (dose may be escalated in 50mg increments)
	Grade 1-2	Reduce thalidomide dose by 50% and consider discontinuing.
Sedation, constipation, rash, fatigue, tremor, oedema	Grade 3-4	Stop thalidomide for remainder of cycle. Consider restarting at 50mg for subsequent cycles (dose may be escalated in 50mg increments).

Thalidomide – MHRA alert: viral reactivation and pulmonary hypertension :
- Cases of viral reactivation have been reported in patients previously infected with varicella-zoster and Hepatitis B. Previously infected patients should be closely monitored for signs and symptoms or reactivation throughout treatment.
- Cases of pulmonary hypertension have been reported following thalidomide treatment. Patients should be closely monitored for signs and symptoms of cardiopulmonary disease.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Thromboembolism
Psychosis

- **Frequently occurring side effects**

Myelosuppression
Constipation
Nausea and vomiting
Fatigue
Peripheral neuropathy
Headache
Rash
Bradycardia
Insomnia
High blood sugars
Fluid retention

- **Other side effects**

Altered LFTs
Decreased appetite
Confusion
Depression

Significant drug interactions – for full details consult product literature/ reference texts

Thalidomide:
Hormonal contraceptives: may increase risk of thrombo-embolic disease – not recommended
Sedative medication: may enhance sedative effect

Additional comments

Thalidomide is highly teratogenic.
Women of child bearing potential must have a negative pregnancy test within 3 days prior to starting treatment. Pregnancy testing should be repeated monthly thereafter until 4 weeks after stopping thalidomide (or every 2 weeks in women with irregular menstrual cycles). If a woman taking thalidomide thinks she may be pregnant she must stop the drug immediately.

Men taking thalidomide must use a barrier method of contraception throughout treatment and for one week after stopping, if their partner is capable of bearing children.

Women of child-bearing potential must use an agreed effective method of contraception for at least 4 weeks before starting thalidomide, while on thalidomide and for 4 weeks after. (The combined oral contraceptive pill is not recommended due to the increased risk of thromboembolism).

Thalidomide is supplied through the Celgene Pregnancy Prevention Programme. All patients need to be provided with the Pregnancy Prevention Programme booklet before starting treatment.
A completed Celgene Prescription Authorisation Form must be sent to pharmacy with each prescription.

References

- Summary of Product Characteristics Thalidomide (Celgene) accessed 11 Nov 2015 via www.medicines.org.uk
- National Institute for Clinical Excellence. Technology Appraisal Guidance 311. Accessed 11 Nov 2015 via www.nice.org.uk
- Nooka A, Kastritis E, Dimopoulos M, Lonial S. Treatment options for relapsed and refractory multiple myeloma. Blood. 2015 May;125 (20):3085-3099
- MHRA alert accessed 27 July 2016 via https://www.gov.uk/drug-safety-update/letters-sent-to-healthcare-professionals-in-june-2016

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