

Z-DEX

INDICATION

An oral regimen for patients with symptomatic myeloma with neuropathy precluding use of thalidomide and bortezomib based therapies.

PRE-ASSESSMENT

1. Ensure all the following staging investigations are done:
 - FBC & film
 - Clotting screen
 - U&Es
 - LFTs
 - Calcium
 - Albumin
 - Uric acid
 - CRP
 - Baseline random blood glucose
 - Virology : HIV, Hepatitis B (including core antibody), and Hepatitis C
 - Calculated creatinine clearance (CrCl), urine protein/ creatinine ratio
 - Electrophoresis and immunofixation for quantitation of serum paraprotein and immunoglobulins.
 - Serum free light chain assay (Freelite)
 - β_2 microglobulin
 - LDH
 - 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 District Hospital
Salisbury
Wiltshire
SP2 8BJ

Additional investigations:

- Plasma viscosity if hyperviscosity suspected
 - If allogeneic transplant an option: Tissue typing of patient and siblings and CMV serology
2. 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.

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3. Counselling - all patients should receive verbal and written information on oral chemotherapy. Ensure pre-chemotherapy counselling in line with NPSA recommendation and chemotherapy measures
4. Fertility - all patients should be offered fertility advice, as appropriate.
5. Hydration - fluid intake of at least 3 litres /day should be attempted.
6. Document patient's height and weight, dose on actual body weight.
 7. Document patient's performance status.
8. Treatment must be agreed at the relevant MDT.

REGIMEN SPECIFIC PRE ASSESSMENT

Echocardiogram

DRUG REGIMEN

Days 1 to 4 **IDARUBICIN (Zavedos)** 10 mg/m² po daily

Idarubicin is available as 5mg and 10mg capsules. Different doses may be given on different days to ensure that the total idarubicin dose given over 4 days is close to the desired total of 40mg/m². (see example 1)

In addition, the total dose over 4 days (40mg/m²) should be rounded down to the nearest 5mg dose (see example 2)

Example 1: if BSA=1.75, daily dose=17.5mg, total dose over 4 days=4x17.5mg=70mg, which can be prescribed as 20mg on days 1-2 and 15mg od on days 3-4

Example 2: if the total dose over 4 days (40mg/m²) = 67.3mg, this should be rounded down to 65mg over 4 days and prescribed as: 20mg on days 1-2, 15mg on day 3 and 10mg on day 4

Days 1 to 4 **DEXAMETHASONE** 40 mg po daily , reduce dosing in frail/elderly
Consider reducing dexamethasone dose to 20mg if ≥75 years

Days 12 to 15 **DEXAMETHASONE** 40 mg po daily , reduce dosing in frail/elderly
Consider reducing dexamethasone dose to 20mg if ≥75 years

CYCLE FREQUENCY

Every 21 days. Repeat until plateau phase (paraprotein/urine light chain excretion stable for 3 months). It is unusual to require more than 6 cycles, without justification.
Maximum cumulative dose of oral idarubicin: 400 mg/m². Take into account previous anthracycline exposure.

DOSE MODIFICATIONS

Neutrophil count should be > 1.0 x 10⁹/L and platelet count > 70 x 10⁹/L before giving treatment at any stage unless low counts are thought to be due to myeloma per se.

Idarubicin:

Renal		Hepatic	
GFR 20-50	75%	Bili < 40	100%
GFR 10 - 20	75%	Bili 40 – 85	50%
GFR <10 caution	use 50 % of dose with	Bili > 85	omit

Maximum cumulative dose of oral idarubicin: 400 mg/m². Take into account previous anthracycline exposure.

INVESTIGATIONS - First Cycle

- Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
- FBC.
- U&E, Ca⁺⁺, LFT, glucose, urate.
- Others - as per staging investigations (as listed under the PRE-ASSESSMENT heading above).

INVESTIGATIONS - Subsequent Cycles

- Urine pregnancy testing for pre-menopausal women younger than 55 before each cycle.
- FBC.
- U&E, Ca⁺⁺, glucose, LFT.

ADDITIONAL INVESTIGATIONS - Alternate Cycles

- Serum electrophoresis with PP and Ig quantification.
- Serum free light chain (Freelyte) and / or repeat 24 hr urine for BJP quantification in light chain myeloma.
- Consider bone marrow assessment after four cycles for non-secretory Myeloma.

CONCURRENT MEDICATIONS

- Allopurinol: 300 mg daily for 7 days for cycle 1 only.
- Proton pump inhibitor or H₂ antagonist at clinician’s discretion.
- Consider prophylactic fluconazole
- Consider the use of GCSF (filgrastim) in selected patients at the clinician’s discretion
- Prophylactic aciclovir 200 mg TDS (consider reducing to 200mg BD if CrCl<10ml/min)
- Bone protection as per NSSG Bone Protection protocol MM.3
- Consider prophylactic co-trimoxazole 960mg OD on M/W/F if heavily pre-treated or previous autograft.

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Extravasation risk: idarubicin-vesicant

EMETIC RISK

Moderate emetic risk on days 1-4, otherwise minimal or low risk.

REFERENCES

1. Clark AD, Douglas KW, Mitchell LD, McQuaker IG, Parker AN, Tansey PJ, Franklin IM, Cook G. Dose escalation therapy in previously untreated patients with multiple myeloma following Z-Dex induction treatment. *Br J Haematol.* 2002 Jun;117(3):605-12.
2. UK Myeloma Forum Guidelines 2014
[.http://www.bcshguidelines.com/documents/MYELOMA_GUIDELINE_Feb_2014_for_BCSH.pdf](http://www.bcshguidelines.com/documents/MYELOMA_GUIDELINE_Feb_2014_for_BCSH.pdf)
3. eMC UK Summary of Product Characteristics for Idarubicin hydrochloride (Zavedos) 10mg caps, Pfizer, 10 September 2018

REVIEW

Name	Revision	Date	Version	Review date
Nadjoua Maouche Pharmacist	Formatting, dose modifications, investigations section, reference section	May 2016	4.3	May 2018
Manuela Sultanova Service Coordinator	Formatting, standardisation of general pre-assessment section and Wessex address	August 2017	4.4	May 2018
Myeloma Protocol Review 2019	Pre-assessment, cycle frequency, concurrent medications, extravasation risk and references	June 2019	4.5	June 2020
NSSG Myeloma Group	Addition of filgrastim as option in selected patients	Nov 2020	4.6	June 2021
NSSG Myeloma Group	Update to drug regimen section to clarify prescribing of idarubicin	Mar 2021	4.7	June 2021

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