# Tertiary/Quaternary Level Essential Drug List
# Medication Review Summary

**Medication Name:** **Thalidomide** **Date:** April 2019

**Indication:** First line therapy for transplant ineligible Multiple Myeloma

**Context:** Myeloma is a plasma-cell malignancy with incidence rate of 6.2/100000 at age 65. Based on NCR data an average of 310 new myeloma cases are diagnosed yearly in South Africa. Myeloma is incurable with currently available therapy, but survival data has improved significantly with the advent of modern therapy incorporating novel agents and autologous stem cell transplant. Median overall survival (OS) was 5.2 years in 2010, with good risk patients experiencing prolonged survival extending past 10 to 15 years. The disease follows a relapse remitting course, characterized by multiple treatment courses interspersed by periods of progression free survival (PFS). Progressive disease is associated with significant morbidity and mortality secondary to renal failure, bone destruction and bone marrow failure.

Autologous transplant adds approximately 12 months to median OS and remains the standard of care for eligible patients. Patient not eligible for transplant are treated with chemotherapy alone. The standard of care in the public sector is oral Melphalan or Cyclophosphamide plus Prednisone until best response/disease progression.
Deeper responses are associated with prolongation in PFS and OS.
There are limited therapeutic options available to myeloma patients in the public sector.

**Quality of evidence:** Data evaluated included 4 Randomised controlled trials (one placebo control) and one meta-analysis. One trial was MP vs. CTDa, the rest was MP vs. MPT. Data is evaluated to be of moderate to good quality.

**Clinical efficacy:** Addition of thalidomide to treatment regimens significantly improves response rates and depth of response.
Significant PFS and OS benefit is shown. The meta-analysis by Fayers et al 2011 of MPT vs MP trials showed a median PFS of 20.3m vs 14.9m (p<.0001), and a median OS of 39.3m vs 32.7m (p.004). Across the trials overall response rate NNT is between 3 and 4 with a complete response rate NNT between 5 and 10. 3 year OS NNT is 7.

**Safety concerns:** Thalidomide has important side effects, and these need to be monitored for and actively prevented/managed. The four most important side effects is:

1. Venous thromboembolism. Especially in combination with dexamethasone. Patients require thromboprophylaxis. Options include low dose aspirin, heparin, LMWH and warfarin. The decision on which agent to use is individualized.
2. Peripheral neuropathy. Reduction in dose and/or interruption for painful neuropathy associated with weakness is necessary
3. Teratogenicity. Risk management to prevent pregnancy exposure
4. Sedation. Patients are advised to take medication at night.

**Recommendation:** Thalidomide should be available on the EML for the treatment of newly diagnosed transplant ineligible patients.

**NEMLC recommendation:** **NEMLC accepted thalidomide for multiple myeloma, provided a fair price is attained**

**Review indicators:** Price (Reference Price: 80% reduction from Single Exit Price)

CTD: *cyclophosphamide-thalidomide-dexamethasone;* PFS*: progression free survival;* OS: *Overall survival;* CR: *complete response;* MP: *melphalan-prednisone;* MPT: *melphalan-prednisone-thalidomide*

**References**


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