Tertiary/Quaternary Level Essential Drug List
Medication Review Summary

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

Indication: First line therapy for transplant eligible Multiple Myeloma

Context: Myeloma is a plasma-cell malignancy with incidence rate of 6.2/100000 at age 65. Based on NCR data from 2014, an 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.

Patients that are transplant eligible are induced with multi-agent therapy followed by stem cell collection, high dose chemotherapy and autologous stem cell transplant. Stem cell transplant is not curable but adds an additional 12 months to median overall survival. Inability to attain a partial response (>50% reduction in tumour burden) precludes the performance of an autotransplant.
There are limited induction treatment options available for myeloma patients in the public sector.

Quality of evidence: Data evaluated included three Randomised Controlled Trials and one retrospective matched case control analysis. There is a general paucity of data comparing the different chemotherapy/novel agent combinations. Data is evaluated to be of moderate to good quality.

Clinical efficacy: The addition of thalidomide to treatment regimens improves objective response rates and depth of response. Deeper responses will lead to more patients undergoing transplants and are associated with longer PFS and OS. Morgan et al. compared CTD vs CVAD as induction prior to autotransplant. Response rates were 82.5% for CTD vs 71.2% for CVAD ($p<0.0001$). Post-transplant CR was 50% for CTD vs 37.2% for CVAD ($p=0.00052$). Autotransplant objective response rate NNT ranges from 5 to 9. NNT for attaining a post-transplant CR is 8. There is evidence for a benefit in PFS and OS but it is noted that the availability of salvage therapy with newer novel agents including lenalidomide and bortezomib impacted OS in these trials.

Safety concerns: Thalidomide has important adverse effects which need to be monitored for and actively managed. The four most important adverse effects include:

1. Venous thromboembolism. Especially in combination with corticosteroids. Patients require active 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.

Further considerations: Effective oral thalidomide based regimens allow outpatient induction therapy before transplant.

Recommendation: Thalidomide should be available on the EML for the treatment of newly diagnosed transplant eligible 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;* CVAD: *cyclophosphamide-vincristine-doxorubicin-dexamethasone;* PFS*: progression free survival;* OS: *Overall survival; CR: Complete response*

References

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