LENALIDOMIDE for MDS

For the treatment of patients with transfusion-dependent anaemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality, when other therapeutic options are insufficient or inadequate – NICE approved Sept 2014

Drugs/Doses:	**Lenalidomide**	10mg* po once daily on Days 1 – 21, followed by 7 days rest *or according to renal function
Other drugs:	Consider allopurinol - dose according to renal function - for the first four weeks Laxative as required for lenalidomide-induced constipation. Consider thromboprophylaxis, particularly in patients with any additional risk factors	
Administration:	Lenalidomide is available as 2.5mg, 5mg, 7.5mg and 10mg capsules. The daily dose should be swallowed whole with water, with or without food, at the same time of day each day.	
Frequency:	28 day cycle with lenalidomide taken on Days 1 – 21, followed by a 7-day rest. Treatment may continue if tolerated and responding. Patients **without** at least a minor erythroid response within 4 months of therapy initiation, demonstrated by at least a 50% reduction in transfusion requirements or, if not transfused, a 1g/dl rise in haemoglobin, should discontinue lenalidomide treatment. If the patient is still receiving treatment after 26 cycles (normally 2 years), all further lenalidomide drug costs after that time will be met by the manufacturer. (Pharmacy to ensure that a claim is made with the manufacturer)	
Main Toxicities:	teratogenicity (see Comments); myelosuppression; muscle cramps; constipation or diarrhoea; rash; increased risk of thromboembolic events;	
Regular Investigations:	FBC	every week for the 1st 8 weeks, then monthly
	LFTs	every week for the 1st 8 weeks, then monthly
	U&Es	every month
	Pregnancy test	every month for women of child bearing potential

Comments:

Lenalidomide is structurally related to thalidomide, so is expected to be teratogenic. Women of child bearing potential must have a negative pregnancy test within 3 days prior to starting treatment, and within 3 days of each prescription. Pregnancy testing should be repeated monthly thereafter until one month after stopping lenalidomide (or every 2 weeks in women with irregular menstrual cycles). If a woman taking lenalidomide thinks she may be pregnant she must stop the drug immediately.

Women of child-bearing potential must use one agreed effective method of contraception for at least 4 weeks before starting lenalidomide, while on lenalidomide and for one month after. (The combined oral contraceptive pill is not recommended due to the increased risk of thromboembolism.) Men taking lenalidomide must use a barrier method of contraception throughout treatment and for one week after stopping, if their partner is capable of bearing children.

Lenalidomide is supplied through a Pregnancy Prevention Programme. All aspects of the programme should be followed, including completion of an authorisation form by both doctor and pharmacist with every cycle.

Reason for Update: CDF indication removed; FOC supply after 26 cycles added	Approved by Chair of Alliance TSSG: Dr A Laurie
Version: 4	Date: 8.11.16
Supersedes: Version 3	Review Date: Nov 2019
Prepared by: S Taylor	Checked by: C Tucker

Dose Modifications

Haematological Toxicity:

Cycle 1: If neutrophils < 0.5 x 10^9/L or platelets < 25 x 10^9/L, do not start treatment.

At weekly FBC for 1st 8 weeks, and before subsequent cycles:

FBC	Action
Neutrophils < 0.5 x 10^9/l and / or Platelets < 25 x 10^9/l	Interrupt lenalidomide treatment
Neutrophils return to ≥ 0.5 x 10^9/l and Platelets return to ≥ 25 x 10^9/l - < 50 x 10^9/l on at least 2 occasions for ≥ 7 days *or* Platelet count recovers to ≥ 50 x 10^9/l at any time	Resume lenalidomide at next lower dose level – see below

Dose reduction steps

Starting Dose	10 mg once daily on days 1-21 every 28 days	5 mg once daily on days 1-21 every 28 days	2.5 mg once daily* on days 1-21 every 28 days
Dose Level -1	5 mg once daily on days **1-28** of 28 day cycle	2.5mg once daily* on Days **1-28** of 28 day cycle	2.5mg on alternate days on Days **1-28** of 28 day cycle
Dose Level -2	2.5 mg once daily* on Day **1-28** of 28 day cycle	2.5mg on alternate days on Days **1-28**	2.5mg twice weekly on Days 1-28 of 28 day cycle
Dose Level -3	2.5 mg on alternate days on Days **1-28**	-	-

*or lenalidomide 5mg on alternate days may be considered *(unlicensed scheduling, but a significantly cheaper option if preferred by patient or clinician)*

Other Toxicities:

For other grade 3 or 4 toxicities judged to be related to lenalidomide, stop treatment and, if appropriate to continue, restart at next lower dose level when toxicity has resolved to ≤ grade 2.
Lenalidomide interruption or discontinuation should be considered for grade 2 or 3 skin rash. Lenalidomide must be permanently discontinued for angioedema, grade 4 rash, exfoliative or bullous rash, or if Stevens-Johnson syndrome or toxic epidermal necrolysis is suspected.

Renal Impairment:

CrCl (ml/min)	Lenalidomide Dose
30 - 49	5mg once daily for 21 days
< 30 (whether requiring dialysis or not)	2.5mg once daily for 21 days

Hepatic Impairment:

Lenalidomide has not formally been studied in patients with impaired hepatic function and there are no specific dose recommendations.
Consider the possibility of lenalidomide-induced liver injury in patients with unexplained deterioration of liver function. If associated, liver function generally recovers when lenalidomide is stopped.

Patient Information:

No Macmillan leaflet currently for Lenalidomide in MDS