Guidelines for the Use of G-CSF Following Chemotherapy

These guidelines are based upon the 2015 update of the ASCO guidelines and 2010 EORTC guidelines.
The use of G-CSF as a priming agent (e.g. in FLAG), in PBSCM, or in treatment of MDS is not considered here.
Reason(s) for giving G-CSF should be documented in the patient's records.

St Luke's Alliance definition of febrile neutropenia: neutrophils < 1.0 x 10^9/l, with fever or clinical signs of sepsis

Primary Prophylaxis - i.e. starting with first cycle of chemotherapy

a) Should be used routinely in patients who are receiving chemotherapy regimens with a febrile neutropenia (FN) rate of > 20%.
For those regimens where the risk of FN is known to be > 20%, routine use of primary G-CSF will be specified within the chemotherapy protocol e.g. ESHAP, regimens for AML, FEC-T

b) Should be considered in patients receiving regimens with a FN rate of 10 – 20%, and who also have patient-related risk factors* which may increase the FN risk to > 20%.
Regimens with a known FN rate of 10-20% include:
Carboplatin & Etoposide; CAV; ECX; EOX; Folfiri; R-CHOP; Topotecan; Vinorelbine & Cisplatin

*The risk factors which may elevate the risk of FN are: age > 65 years, a previous episode of FN whilst receiving earlier chemotherapy, poor performance status, pre-existing neutropenia or bone marrow involvement, poor nutritional status, extensive prior chemotherapy, previous irradiation to large volume of bone marrow, open wounds or active infections, multiple comorbid conditions, HIV infection

Apart from high grade lymphoma, there is insufficient evidence to support primary G-CSF with any other regimen in this group based solely on age – additional risk factors should also be considered when deciding to use G-CSF in the elderly.
There is however no valid model or formula for calculating the risk of FN. If in doubt, discuss with Consultant.

c) Primary G-CSF should be routinely administered to all patients with diffuse aggressive lymphoma **aged > 65** and being treated with curative CHOP or R-CHOP.

Secondary Prophylaxis - for patients who experienced a neutropenic complication from a previous cycle

Secondary prophylaxis is indicated where treatment is being given with curative intent, or in the adjuvant setting, and where a dose reduction would compromise disease-free or overall survival, or treatment outcome.

Dose reduction, or the use of a less myelosuppressive regimen, are the primary therapeutic options for patients receiving palliative chemotherapy.

In Established Febrile Neutropenia

In order to reduce the period of neutropenia, and the period of hospitalisation, G-CSF should be initiated in febrile solid tumour or lymphoma patients with neutrophils < 0.5 x 10^9/l, ***or*** neutrophils < 1.0 x 10^9/l with any signs of severe sepsis.

Afebrile patients

Growth factors should not be routinely used for afebrile neutropenic patients (unless recommended within the relevant chemotherapy protocol, in order to minimise any further delay in treatment)

Reason for Update: guidance for patients with FN amended; Aria cut-off for primary lenograstim and filgrastim for larger patients reviewed; biosimilars statement added; SLCA definition for FN	Approved by Chair of Alliance Chemotherapy Group: Dr J De Vos
Version: 4	Date: 21.3.16
Supersedes: Version 3	Review Date: April 2018
Prepared by: S Taylor	Checked by: C Tucker

Clinical Trial Patients

Use of G-CSF should follow the trial protocol, irrespective of exclusions stated above.

Progenitor Cell Mobilisation

Use of G-CSF should follow the protocol provided by the transplant centre.

Choice and Dose of G-CSF

Filgrastim: 5mcg/kg once daily by subcutaneous injection.

Doses should be rounded up or down to the most appropriate syringe size (300mcg or 480mcg).
It is common practice for a daily dose of 300mcg to be given. However, patients with weight ≥ 90kg may be given the 480mcg vial/syringe either initially* or if they have an inadequate response to the standard dose.
*The initial dose used in Aria regimens which include primary prophylaxis will be 480mcg for patients ≥ 90kg.

Lenograstim: 150mcg/m^2 once daily by subcutaneous injection.

Doses should be rounded up or down to the most appropriate vial / syringe size (105mcg and 263mcg).
It is common practice for a daily dose of 263mcg to be given, but patients with BSA > 1.8m^2 may be given an additional 105 micrograms (i.e. 368 micrograms total) daily, either initially* or if they have an inadequate response to the standard daily dose.
*The initial dose used in Aria regimens which include primary prophylaxis will be 368mcg for patients with BSA ≥ 1.85m^2.

Peg-filgrastim: Pegfilgrastim usage is not funded.

Biosimilar Products:

For chemotherapy support, biosimilar filgrastim is an appropriate choice, and currently the most cost-effective option. The choice of biosimilar is a local decision.
Biosimilar filgrastim products are also now licensed for mobilisation of peripheral blood progenitor cells, however they may not yet be accepted for use in autologous stem cell mobilisation at our local tertiary centres (at the time of this update, RMH still use lenograstim for mobilisation). If in doubt, please check.

Duration & Timing of G-CSF

G-CSF is not recommended within 24 hours of chemotherapy.

A reasonable starting point for lenograstim and filgrastim is to start not less than 24 hours and not more than 72 hours after cytotoxic treatment is completed.

G-CSF injections should continue until the neutrophil count has recovered to > 1.0 x 10^9/L on two consecutive days. This will normally require a minimum of 5 days of treatment, although consideration should be given to a minimum of 7 days for more myelosuppressive regimens – studies looking at NHL patients receiving myelosuppressive chemotherapy showed that patients receiving 5 doses of G-CSF had about 3 times the risk of febrile neutropenia and hospitalization than those who received a 10 day course[1, 2].

References: Smith, TJ et al; JCO 2015; published on-line July 13th (ASCO guidelines)
Aapro, M et al; Eur J Cancer 2011; 47: 8 – 32 (EORTC guidelines)
[1]Scott, SD et al; J Manag Care Pharm 2003; 9: 15 – 21
[2]Weycker, D et al; Proc ASCO 2004; 23: 613 Abstract 6731