Kent and Medway Cancer Collaborative

Guidelines for use of G-CSF in adult haematology and oncology patients

Pathway of Care

Core Network Team

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1.0 Introduction

G-CSF guidelines have been developed in order to have a degree of consistency across the Kent and Medway Cancer Collaborative (K&MCC). In addition, there is a need to better define those patients who are most likely to benefit from G-CSF support. A reduction in febrile neutropenia (FN) is an important clinical outcome that justifies the use of G-CSF in the following indications. This guidance does not cover the use of G-CSF in clinical trials, or for the purpose of peripheral blood stem cell mobilization.

This guidance does not cover the use of G-CSF in children and young persons with cancer.

2.0 Prophylactic use of G-CSF in conjunction with chemotherapy given with curative intent

2.1 Primary Prophylaxis (i.e. use with first course of chemotherapy onwards)

- G-CSF is not recommended with most first line therapies.
- G-CSF should not be used to increase dose intensity outside of a clinical trial setting
- It is recommended that G-CSF primary prophylaxis is only given when chemotherapy is administered with curative intent (adjuvant / neo-adjuvant treatment). However, there may be instances where because of a high rate of febrile neutropenia (published or established through robust local audit) it is appropriate to give G-CSF as primary prophylaxis to patients receiving palliative chemotherapy.

Table 1: Recommendations for G-CSF primary prophylaxis

1.	Where the incidence of FN associated with treatment is > 20%. It should be noted that wherever possible, regimens of equal efficacy but with a lower risk of FN should be used. *	Examples of haematology regimens	DHAP ESHAP Hyper C-VAD CAIP (R)-ICE CODOX- M / IVAC ICE (R) CHOP 14 Minibeam
		Examples of oncology regimens	FEC-T (breast) FEC100 EC-Accelerated Paclitaxel EC TPF (H&N) **TP(H&N)** Etoposide/ Platinum containing regimens (germ cell) Etoposide/ platinum regimens (small cell cancers) Docetaxel (2nd line NSCLC) Nintedanib & Docetaxel (NSCLC) Folfirinox (upper GI)
2.	In patients with acute leukaemia in accordance with the guidelines below (see section 4.0)		

3.	Primary prophylaxis may also be considered when used with regimens with febrile neutropenia rate of 10-20% in patients with one or more of the following risk factors; • Extensive prior treatment • Older patients (>65yrs) • The presence of open wounds or recent surgery • Advanced disease stage • Poor performance status where the use of chemotherapy is justified • Previous episodes of FN requiring admission • Cytopenias due to bone marrow involvement or pre-existing marrow insufficiency (including previous irradiation to large volume of bone marrow) • Poor nutritional status • Active infections including HIV • Serious co-morbidities	Haematology regimens (examples) Oncology regimens (examples)	FCR (like regimens) (R)-CHOP (like regimens) Salvage regimens for lymphoma Docetaxel / Capecitabine CAV

* NB While published rates of febrile neutropenia with platinum / etoposide combinations may not always exceed 20%, local experience has shown a high level of admission due to febrile neutropenia with these regimens. Local audit has shown rates of febrile neutropenia following docetaxel for 2nd line NSCLC exceed 20%.

See Appendix A for a decision making algorithm for primary GCSF prophylaxis

2.2 Secondary Prophylaxis (i.e. use after episode of FN or severe neutropenia (grade 4) in preceding course)

- Use of G-CSF to maintain dose intensity is not recommended in preference to dose reduction after prolonged neutropenia or an episode of neutropenic sepsis, except when chemotherapy is given with curative intent.

3.0 Prophylactic use of G-CSF in conjunction with palliative chemotherapy

- G-CSF should not routinely be used in this indication (see section 2.1)

4.0 Therapeutic use of G-CSF

G-CSF must not be routinely prescribed for the treatment of patients with uncomplicated FN (duration of fever <10 days) or afebrile neutropenia.

G-C SF may be prescribed for the supportive treatment of patients with a high risk of infection-associated complications or severe FN (ANC <0.1 x 10^9/l). G-CSF should continue until ANC >1.0 x 10^9/l for 2 consecutive days and the expected neutrophil nadir has passed. High risk features include:

- Uncontrolled primary disease
- Pneumonia
- Clinically unwell with signs such as hypotension or organ dysfunction indicating potential risk of septic shock
- Expected prolonged duration of neutropenia (>10 days)
- Proven or suspected invasive fungal infection
- Age >65 yrs old
- Being hospitalised at the time of developing fever

5.0 The use of G-CSF in specific haematological indications

Table 2

Indication	Recommendations	Initiation and duration of G-CSF
AML	G-CSF should not be used for priming of leukaemia cells (except with FLAG chemotherapy)	-
	G-CSF may be used following induction and for patients in remission following consolidation chemotherapy	From day 8 of chemotherapy until ANC >1.0 for 2 consecutive days NB Pegylated G-CSF should not be used in this group of patients
MDS (high risk)	G-CSF should only be considered for intermittent use in patients with severe neutropenia who experience recurrent infection Prolonged or continuous treatment with G-CSF is not recommended	Start when ANC <0.1.Stop when ANC >1.0 for 2 consecutive days
MDS (low risk)	G-CSF use in combination with epoetin should only be used following discussion within MDT	Three times a week
ALL	G-CSF should only be used where there is delayed recovery or infection following first few days of chemotherapy of initial induction or first post remission course of chemotherapy G-CSF should not be used for refractory or relapsed ALL	From day 5-8 post chemotherapy until ANC >1.0 for 2 consecutive days
Aplastic anaemia/ inherited BM failure	Use of G-CSF is not recommended	-

6.0 Choice and doses of G-CSF

- This guidance does not provide any recommendation on the formulation of G-CSF to be used. Pegylated G-CSF is considerably more expensive and may only be used following a successful application for funding.
- The usual dose of G-CSF in adult patients is 300 micrograms subcutaneously each day. A dose of 480 micrograms may be considered if the patient is >80kg.

7.0 Duration and timing of therapy with G-CSF

- The data is too sparse to be absolutely specific about the most appropriate time to start G-CSF and the optimum duration of treatment. Reference should be made to the chemotherapy prescription within the cancer electronic prescribing system and the associated KMCC protocol if available.

- G-CSF should not usually be administered within 24 hours of cytotoxic chemotherapy and is usually started 1-3 days after administration of myelotoxic chemotherapy. However, in some cases G-CSF may need to start while cytotoxics are being administered, particularly where the drug concerned is not the myelosuppressive component of the regimen. Administration of G-CSF daily for 3 to 5 days is usually adequate.

8.0 In clinical trial patients

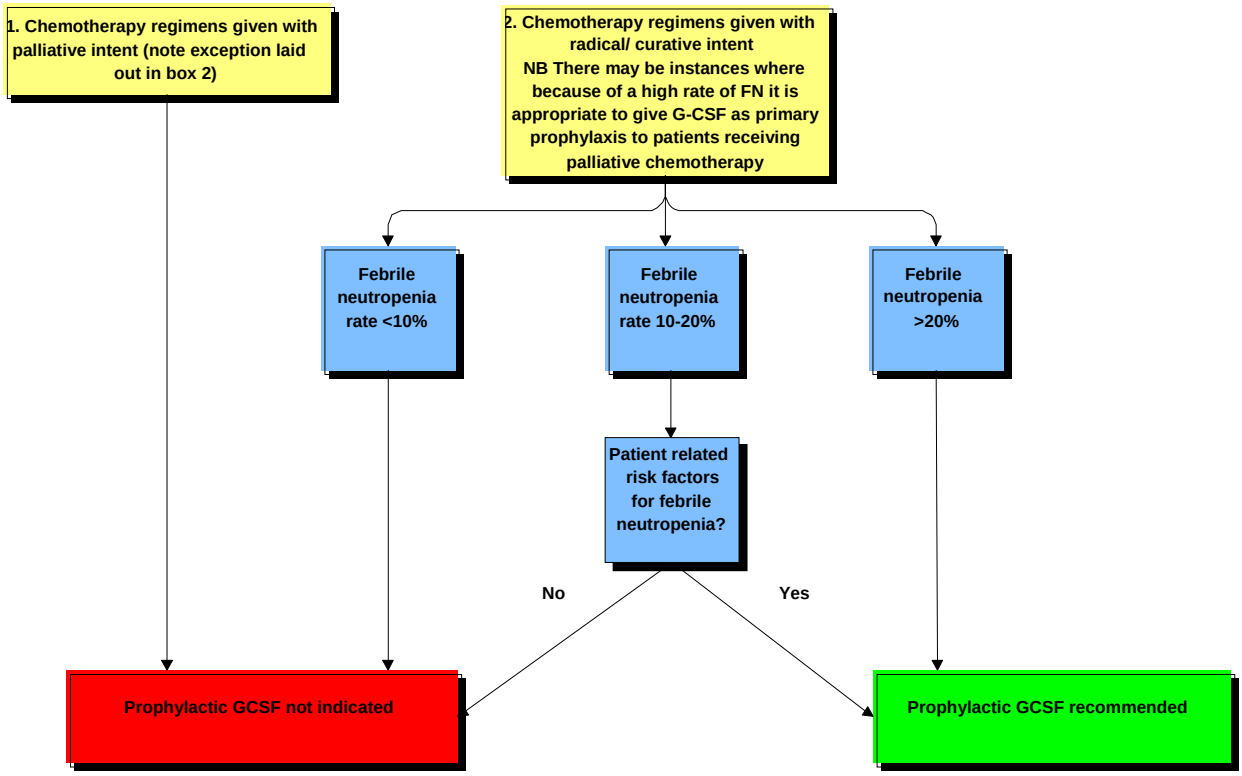
- Use of G-CSF should follow the trial protocol, irrespective of local policy.

9.0 Approved prescriber

- Oncology and haematology consultants and SpR’s should initiate treatment. SHOs should only prescribe under the instruction of a consultant or SpR.

10.0 Appendix A: Decision making Algorithm for Primary GCSF Prophylaxis

Decision making algorithm for primary GCSF prophylaxis



This decision making algorithm has been reproduced with kind permission from the London Cancer New Drugs Group.

11.0 Bibliography

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  2006 Update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline
  J Clin Oncol (2006) 24 (19) 3187-3205

- London Cancer New Drugs Group (January 2010)
  Guidance on the use of prophylactic granulocyte colony stimulating factor (GCSF) to support chemotherapy administration

- Information on file Amgen issued March 2010

- Smith et al 2015. Recommendations for the use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update.
J Clin Oncol (2015) 33 (28) 3199-3212

12.0 Personnel and Contact Information

A comprehensive, up to date list of MDM contact details can be found on the KMCC website.

13.0 Glossary

Acronyms in common usage throughout KMCC documentation

CNB	Cancer Network Board
CYP	Children & Young People (in relation to the IOG)
DCCAG	Diagnostic Cross Cutting Advisory Group
DOG	Disease Orientated Group (NSSG/TSSG/TWG)
DVH	Darent Valley Hospital
EK	East Kent
EKHUFT	East Kent Hospitals University Foundation Trust
HoP	High Level Operational Policy
IOSC	Improving Outcomes: A Strategy for Cancer
K&C	Kent & Canterbury Hospital, Canterbury, (EKHUFT)
KMCC	Kent & Medway Cancer Collaborative
KMCRN	Kent & Medway Cancer Research Network
LSESN	London & South East Sarcoma Network
MFT	Medway Foundation Trust
MTW	Maidstone & Tunbridge Wells NHS Trust
NOG	Non Surgical Oncology Group

	(Permanent oncologist sub group of the DOGs with a specific responsibility for chemo/rad pathways and advice to the DOG, Network and GEOGRAPHICAL LOCATIONs on new drugs)
PoC	Pathway of Care *(Network agreed disease site specific clinical guidelines)*
QEQM	Queen Elizabeth the Queen Mother Hospital, Margate (EKHUFT)
QoL	Quality of life
RAT	Research and Trial Group *(Permanent sub-group of the DOGs with a specific responsibility for taking forward the clinical trials agenda)*
RMH	Royal Marsden Hospital
RNOH	Royal National Orthopaedic Hospital
QVH	Queen Victoria Foundation Trust Hospital East Grinstead
UCLH	University College Hospital London
WHH	William Harvey Hospital, Ashford (EKHUFT)
WK	West Kent

14.0 Document Administration

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Principal author	Kate Miller
Co-author(s)	Caroline Waters / KMCC Chemo Group
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Revision History			
Date of revision	New Version Number	Nature of Revision	Confirmation of Accuracy by
03/2006	001	Updated in accordance with ASCO 2006 guidelines	Wasifa Webb
20/03/08	002	Comments from HOG meeting of 24/04/08 incorporated	Drs Harper-Wynne and Rassam / Caroline Waters
15/05/08	003	Comments from HOG meeting of 29/05/08 incorporated	C Waters
29/05/08	004	Comments from Care Group relating to primary prophylaxis	C Waters
12/06/08	005		C Waters
12/06/08	1	Changes to section 1.0, table 1, section 5.0 (now section 6) and the addition of appendix 1	C Waters

01/03/10	1.1	Changes made to section 2.1 & 5.0 following HOG	C Waters
30/04/10	1.2	Changes made to section 3.10, 7.0 and appendix A following NCG	C Waters
June 2010	1.3	Final changes to section 4.0 following last consultation (e-mail)	C Waters
June 2010	1.4		C Waters
June 2010	2		C Waters
October-December 2012	2.1-2.3	Updated in accordance with ASCO 2006 guidelines	C Waters
January 2013	3		C Waters
May 2018	4	Updated in accordance with ASCO 2015 guidelines	K Miller
June 2018	4.1	Nintedanib & docetaxel and EC added to point 1 Table 1	C Waters
June 2018	5	Published following consultation with KMCC Chemotherapy Groups (circulated via email)	