Title:	**Guidelines for the use of granulocyte colony stimulating factor (GSCF) in adult oncology & haematology patients with solid tumours for SACT.**			
Author(s)	Paula Scullin, Consultant Medical Oncologist, Northern Ireland Cancer Centre Fionnuala Green, Regional Lead Cancer Services Pharmacist (job share) Sonali Dasgupta, Consultant Medical Oncologist, North West Cancer Centre On behalf of the Pharmaceutical Clinical Effectiveness Programme Regional Granulocyte Colony Stimulating Factors (GCSFs) Expert Group.			
Ownership:	NICaN			
Approval by:	**NICaN CRG**		**Approval date:**	**March 2018**
Operational Date:	**May 2018**		**Next Review:**	**January 2021**
Version No.	**Version 1.3**	**Supercedes**	1	
Links to other policies				

Version control for drafts:			
Date	**Version**	**Author**	**Comments**
18/08/11	0.1	P Scullin & F Green	Initial Draft
02/09/11	0.2	P Scullin	Amended following consultation with Dr Paul Kettle & Dr Michael Quinn Consultant haematologists BHSCT
18/01/12	0.3	P Scullin & O Sheehy	Amended following consultation with NICaN SACT group, NICaN Chemotherapy Nurses group & NICaN Pharmacy group
20/05/12	0.4	P Scullin & F Green	Amended following second consultation with NICaN SACT group, NICaN Chemotherapy Nurses group & NICaN Pharmacy group
	V1		Final Version issued.
22/08/2017	1.1	S Dasgupta	Amended following publication of updated GCSF guidelines from ESMO and ASCO
26/01/2018	1.2	S Dasgupta	Amended following discussion at SACT 19/01/18
18/05/2018	1.3	S Dasgupta	Amended following consultation with SACT

1.0 INTRODUCTION / PURPOSE OF POLICY

1.1 Background

For patients receiving SACT, reduction in the risk of febrile neutropenia is an important clinical outcome that justifies the use of GCSF.
GCSF stimulates the production of neutrophils and may reduce the duration of systemic anti-cancer therapy (SACT)-induced neutropenia, reduce the incidence of associated sepsis and aid maintenance of chemotherapy dose intensity.
This document provides guidance on the rational use of GCSF to support SACT administration in patients at high risk of febrile neutropenia (primary prophylaxis) and patients who have suffered a febrile neutropenic episode with a previous cycle of SACT (secondary prophylaxis). It also discusses the use of GCSF for management of prolonged neutropenia. It does not cover the use of GCSF in clinical trials or for the purpose of peripheral blood stem cell mobilisation and transplantation.

1.2 Purpose

To ensure a safe, standardised approach to the use of GCSF in adult oncology & haematology patients.

1.3 Preparations

Short acting: Filgrastim (Neupogen®, Accofil®, Nivestim® and Zarzio®) and Lenograstim (Granocyte®).

Long acting: Pegfilgrastim (Neulasta®) and Lipegfilgrastim (Lonquex®)

These preparations should be prescribed by brand name.

2.0 DEFINITIONS/SCOPE OF THE POLICY

This document provides guidance on the rational use of GCSF to support SACT administration as primary or secondary prophylaxis and in the management of prolonged neutropenia. It does not cover the use of GCSF in clinical trials or for the purpose of peripheral blood stem cell mobilisation or for use in patients with non-malignant or non-SACT induced neutropenia.

3.0 ROLES/RESPONSIBILITIES

It is the responsibility of all those involved in the prescribing of SACT and in the management of febrile neutropenia to familiarise themselves with the content of these guidelines.

4.0 KEY POLICY PRINCIPLES

4.1.1 Primary Prophylaxis

The use of GCSF for primary prophylaxis should be **limited to SACT regimens given with curative/radical intent (including adjuvant/neo-adjuvant).** Each

disease-specific group should agree the regimens for which primary prophylaxis is appropriate as part of the agreement on SACT protocols.

GCSF support should be considered in patients who are receiving SACT regimens with a febrile neutropenia rate of >20% (published or established through robust local audit). This 20 % cut-off proposed initially in 2005, has been maintained in subsequent international reports on GCSF guidelines. The benefit is in terms of reduction in frequency of febrile neutropenia and associated hospital admissions, but not in infection related mortality.

In radically treated patients with a curative intent, GCSF support can be considered for SACT regimens with a febrile neutropenia rate of 10-20%, where at least one patient related risk factor for febrile neutropenia is satisfied , i.e.,

- Age >65
- Advanced disease
- Pre-existing neutropenia due to disease (e.g. heavy marrow infiltration, AIDS)
- Extensive prior chemotherapy
- History of recurrent febrile neutropenia during previous cycles of chemotherapy of similar or less myelotoxicity
- Conditions likely to enhance the risk of serious infection (e.g. decreased immune function, open wounds, active tissue infections, poor performance status, poor nutritional status, serious co-morbidities).

4.1.2 Dose & administration

Long acting GCSF subcutaneous injection, once only, 24-48 hours post SACT with each cycle of SACT. At clinician discretion standard (i.e. non-pegylated) GCSF may be used as an alternative.

4.2.1 Secondary Prophylaxis

The use of GCSF for secondary prophylaxis should be limited to SACT regimens given with curative/radical intent (including adjuvant/neo-adjuvant). It may be considered for use in regimens where maintenance of chemotherapy dose intensity has been shown (in clinical trials) to significantly improve outcome. Each disease-specific group should agree the regimens for which secondary prophylaxis is appropriate as part of the agreement on SACT protocols.

GCSF support should be considered in patients who experienced a neutropenic complication from a prior cycle of SACT.

4.2.2 Dose & administration

Long acting GCSF subcutaneous injection, once only, 24-48 hours post SACT with each cycle of SACT. At clinician discretion standard (i.e. non-pegylated) GCSF may be used as an alternative.

4.3 Prophylactic use of GCSF in conjunction with palliative SACT

GCSF should **NOT** be routinely used in conjunction with palliative SACT. NICE (National Institute for Health and Care Excellence) guidelines mandate avoidance of

GCSF as prophylaxis for neutropenic sepsis in chemotherapy treated cancer patients (unless GSCF is a standard part of chemotherapy regimen in order to maintain dose intensity). Alternative strategies like antibiotic prophylaxis or dose reduction of chemotherapy agent is recommended.

4.4. GCSF and concomitant chemo radiation

GCSF should not routinely be used in concomitant chemo radiation.

4.5.1 Management of Prolonged Neutropenia

There is limited evidence to support the use of GCSF in the management of patients with acute neutropenia. GSCF should **NOT** be used for afebrile neutropenic patients or for the treatment of uncomplicated febrile neutropenia.

However, GCSF may be *considered* for patients with febrile neutropenia who have a high risk of complications following infection. High risk features include;

- Profound neutropenia (ANC $<0.1x10^9$/l) expected to be prolonged (>10 days)
- Persistent fever despite appropriate antibiotics & antifungal treatment
- Evidence of invasive fungal infection
- Pneumonia
- Sepsis syndrome (hypotension & muti-organ dysfunction)
- Uncontrolled primary disease
- Haemodynamic compromise

In these situations, management with GCSF should only be initiated on instruction from an oncology/haematology consultant/registrar/associate specialist or staff grade. Short acting GCSF should NOT be given in cases where the patient has received long acting (pegylated / glycopegylated) GCSF.

4.5.2 Dose & administration

For management of prolonged neutropenia, standard (i.e. non-pegylated) GCSF should be used as a daily subcutaneous injection. Discontinue after 2 consecutive days of ANC >1x109/l.

5.0 IMPLEMENTATION OF POLICY

These guidelines will be implemented by all staff involved in prescribing GSCF in adult oncology and haematology patients.

6.0 MONITORING

The use of GCSF against these guidelines should be audited at Trust level at regular intervals, according to local policy.

7.0 EVIDENCE BASE / REFERENCES

1. Aapro et al. Position paper: EORTC Guidelines for the Use of Granulocyte-Colony Stimulating Factor to reduce the Incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphomas and solid tumours. Eur J Cancer 42 (2006): 2433 – 2453.
2. Smith et al. 2006 Update of Recommendations for the Use of White Blood Cell Growth Factors: An Evidence-Based Clinical Practice Guideline. J Clin Oncol July 1 2006; 24 (19): 3187 – 3205.
3. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (2007). Myeloid Growth Factors.
4. British Committee for Standards in Haematology. British Journal of Haematology (2003) 123:22-33
5. Smith et al. Recommendations for the Use of WBC Growth Factors: American Society of Clinical Oncology Clinical Practice Guideline Update. Journal of Clinical Oncology. 2015. 33 (28):3199-3212.
6. Klastersky et al. Management of febrile neutropaenia: ESMO Clinical Practice Guidelines. Annals of Oncology. 2016. 27 (Supplement 5): v111–v118
7. National Institute for Health and Care Excellence Guidelines on Complications of Cancer. Available at https://www.nice.org.uk/.../do-not-routinely-offer-gcsf-granulocytecolony-stimulating

8.0 CONSULTATION PROCESS

Three rounds of consultation to NICaN SACT group, NICaN Chemotherapy Nurses group & NICaN Pharmacy group

9.0 APPENDICES / ATTACHMENTS

10.0 EQUALITY STATEMENT

In line with duties under the equality legislation (Section 75 of the Northern Ireland Act 1998), Targeting Social Need Initiative, Disability discrimination and the Human Rights Act 1998, an initial screening exercise to ascertain if this policy should be subject to a full impact assessment has been carried out.
The outcome of the Equality screening for this policy is:

Major impact ☐

Minor impact ☐

No impact. ☑

SIGNATORIES

(Policy – Guidance should be signed off by the author of the policy and the identified responsible director).

_____ **Date:** _____

Name
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