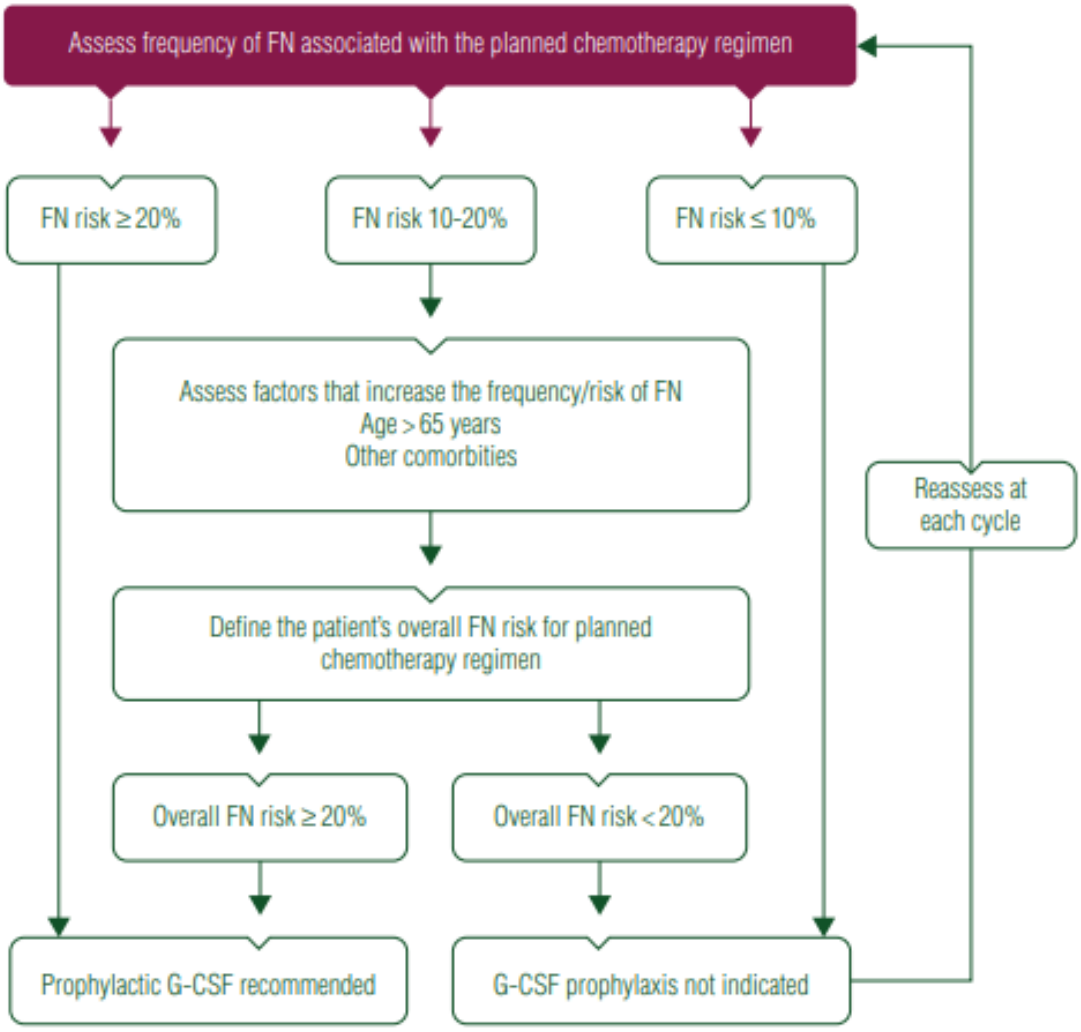
Chemotherapy induced neutropenia

Primary profylaxis

- **Why?**
  - To reduce the incidence and duration of febrile neutropenia.
  - To reduce the need for hospitalization for antibiotic therapy.
  - To avoid dose chemotherapy reductions or delay

- **When?**

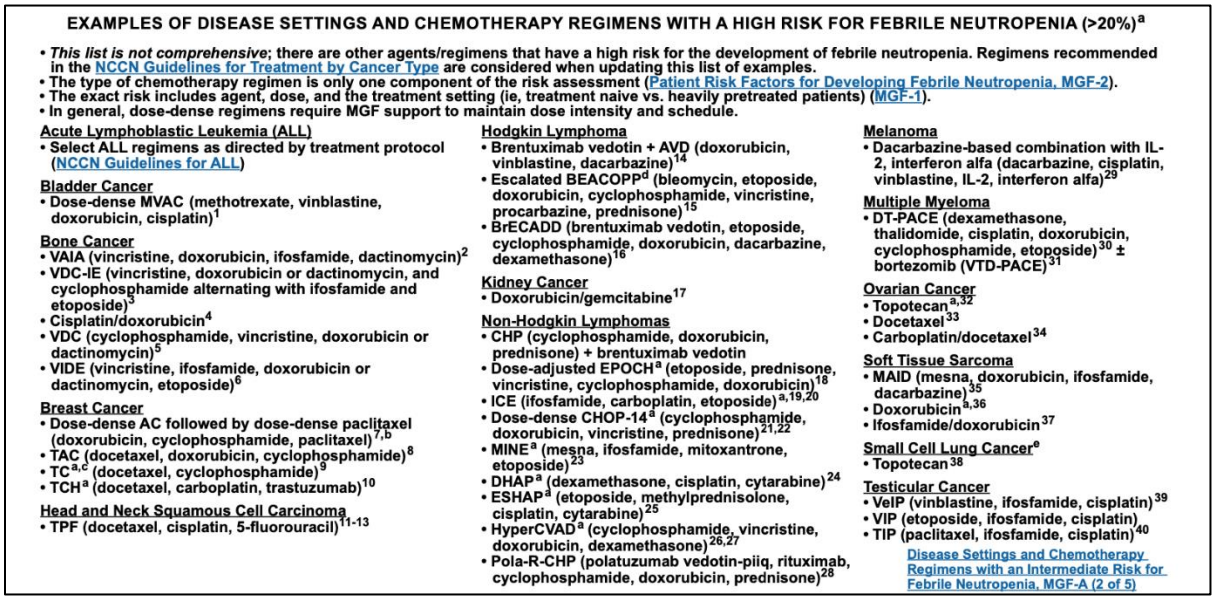


Risk factors: persistent neutropenia, bone marrow involvement, recent surgery, liver or renal dysfunction, age >65y

- **Consideration should be given to alternative, equally effective and safe chemotherapy regimens not requring CSF support when available.**

Update: January 2025

- **Risk assesment of febrile neuterapie with regard to disease settings and chemotherapy :**



EXAMPLES OF DISEASE SETTINGS AND CHEMOTHERAPY REGIMENS WITH A HIGH RISK FOR FEBRILE NEUTROPENIA (>20%)[a]

- *This list is not comprehensive*; there are other agents/regimens that have a high risk for the development of febrile neutropenia. Regimens recommended in the NCCN Guidelines for Treatment by Cancer Type are considered when updating this list of examples.
- The type of chemotherapy regimen is only one component of the risk assessment (Patient Risk Factors for Developing Febrile Neutropenia, MGF-2).
- The exact risk includes agent, dose, and the treatment setting (ie, treatment naive vs. heavily pretreated patients) (MGF-1).
- In general, dose-dense regimens require MGF support to maintain dose intensity and schedule.

Acute Lymphoblastic Leukemia (ALL)
- Select ALL regimens as directed by treatment protocol (NCCN Guidelines for ALL)

Bladder Cancer
- Dose-dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)[1]

Bone Cancer
- VAIA (vincristine, doxorubicin, ifosfamide, dactinomycin)[2]
- VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)[3]
- Cisplatin/doxorubicin[4]
- VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)[5]
- VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)[6]

Breast Cancer
- Dose-dense AC followed by dose-dense paclitaxel (doxorubicin, cyclophosphamide, paclitaxel)[7,b]
- TAC (docetaxel, doxorubicin, cyclophosphamide)[8]
- TC[a,c] (docetaxel, cyclophosphamide)[9]
- TCH[a] (docetaxel, carboplatin, trastuzumab)[10]

Head and Neck Squamous Cell Carcinoma
- TPF (docetaxel, cisplatin, 5-fluorouracil)[11-13]

Hodgkin Lymphoma
- Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)[14]
- Escalated BEACOPP[d] (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)[15]
- BrECADD (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone)[16]

Kidney Cancer
- Doxorubicin/gemcitabine[17]

Non-Hodgkin Lymphomas
- CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin
- Dose-adjusted EPOCH[a] (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)[18]
- ICE (ifosfamide, carboplatin, etoposide)[a,19,20]
- Dose-dense CHOP-14[a] (cyclophosphamide, doxorubicin, vincristine, prednisone)[21,22]
- MINE[a] (mesna, ifosfamide, mitoxantrone, etoposide)[23]
- DHAP[a] (dexamethasone, cisplatin, cytarabine)[24]
- ESHAP[a] (etoposide, methylprednisolone, cisplatin, cytarabine)[25]
- HyperCVAD[a] (cyclophosphamide, vincristine, doxorubicin, dexamethasone)[26,27]
- Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, prednisone)[28]

Melanoma
- Dacarbazine-based combination with IL-2, interferon alfa (dacarbazine, cisplatin, vinblastine, IL-2, interferon alfa)[29]

Multiple Myeloma
- DT-PACE (dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, etoposide)[30] ± bortezomib (VTD-PACE)[31]

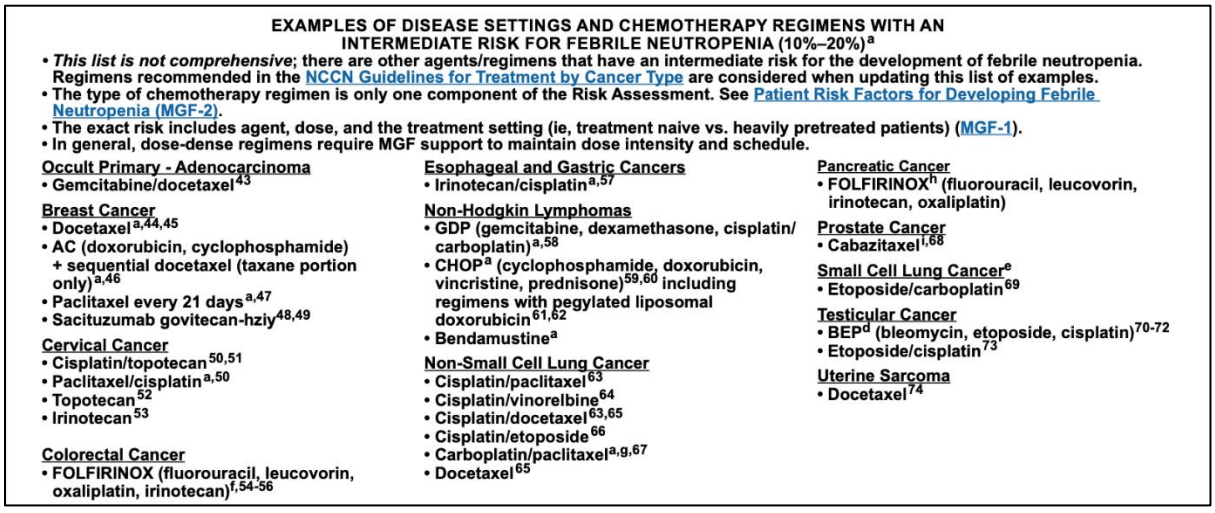
Ovarian Cancer
- Topotecan[a,32]
- Docetaxel[33]
- Carboplatin/docetaxel[34]

Soft Tissue Sarcoma
- MAID (mesna, doxorubicin, ifosfamide, dacarbazine)[35]
- Doxorubicin[a,36]
- Ifosfamide/doxorubicin[37]

Small Cell Lung Cancer[e]
- Topotecan[38]

Testicular Cancer
- VeIP (vinblastine, ifosfamide, cisplatin)[39]
- VIP (etoposide, ifosfamide, cisplatin)
- TIP (paclitaxel, ifosfamide, cisplatin)[40]

Disease Settings and Chemotherapy Regimens with an Intermediate Risk for Febrile Neutropenia, MGF-A (2 of 5)



EXAMPLES OF DISEASE SETTINGS AND CHEMOTHERAPY REGIMENS WITH AN INTERMEDIATE RISK FOR FEBRILE NEUTROPENIA (10%–20%)[a]

- *This list is not comprehensive*; there are other agents/regimens that have an intermediate risk for the development of febrile neutropenia. Regimens recommended in the NCCN Guidelines for Treatment by Cancer Type are considered when updating this list of examples.
- The type of chemotherapy regimen is only one component of the Risk Assessment. See Patient Risk Factors for Developing Febrile Neutropenia (MGF-2).
- The exact risk includes agent, dose, and the treatment setting (ie, treatment naive vs. heavily pretreated patients) (MGF-1).
- In general, dose-dense regimens require MGF support to maintain dose intensity and schedule.

Occult Primary - Adenocarcinoma
- Gemcitabine/docetaxel[43]

Breast Cancer
- Docetaxel[a,44,45]
- AC (doxorubicin, cyclophosphamide) + sequential docetaxel (taxane portion only)[a,46]
- Paclitaxel every 21 days[a,47]
- Sacituzumab govitecan-hziy[48,49]

Cervical Cancer
- Cisplatin/topotecan[50,51]
- Paclitaxel/cisplatin[a,50]
- Topotecan[52]
- Irinotecan[53]

Colorectal Cancer
- FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, irinotecan)[f,54-56]

Esophageal and Gastric Cancers
- Irinotecan/cisplatin[a,57]

Non-Hodgkin Lymphomas
- GDP (gemcitabine, dexamethasone, cisplatin/carboplatin)[a,58]
- CHOP[a] (cyclophosphamide, doxorubicin, vincristine, prednisone)[59,60] including regimens with pegylated liposomal doxorubicin[61,62]
- Bendamustine[a]

Non-Small Cell Lung Cancer
- Cisplatin/paclitaxel[63]
- Cisplatin/vinorelbine[64]
- Cisplatin/docetaxel[63,65]
- Cisplatin/etoposide[66]
- Carboplatin/paclitaxel[a,g,67]
- Docetaxel[65]

Pancreatic Cancer
- FOLFIRINOX[h] (fluorouracil, leucovorin, irinotecan, oxaliplatin)

Prostate Cancer
- Cabazitaxel[i,68]

Small Cell Lung Cancer[e]
- Etoposide/carboplatin[69]

Testicular Cancer
- BEP[d] (bleomycin, etoposide, cisplatin)[70-72]
- Etoposide/cisplatin[73]

Uterine Sarcoma
- Docetaxel[74]

- **Reimbursement of G-CSF in Belgium :**

Short-acting agents: filgrastim (Neupogen/Tevagrastim/Accofil)

- Breast cancer ≥ 65 y and treated with chemotherapy containing anthracyclines and/or taxanes in adjuvant or neo-adjuvant setting (no metastases).
- M+ gastric / GEJ cancer treated with chemo containing docetaxel, cisplatine and 5-FU

Long-acting agents: lipefilgrastim (Lonquex) en pegfilgrastim (Neulasta/Ziextenso)

- Cytotoxic treatment with risk of febrile neutropenia >= 20%.
- Cytotoxic treatment with risk of febrile neutropenia >= 10%, where underlying and/or tumor-related factors significantly increase the risk of febrile neutropenia.
- Dose-dense or dose-intense chemotherapy (if supported by efficacy data):
  - Adjuvant treatment of high-risk breast cancer
  - High dose–intensity methotrexate, vinblastine, doxorubicin, and cisplatin (HD-MVAC) in urothelial cancer

Update: January 2025

- To avoid the need for dose reduction and/or dose delay of treatment, especially in curative treatment or in first-line treatment of metastatic disease.

- **How?**:
  - Start with the first cycle and continuing through subsequent cycles of chemotherapy.
  - Avoid administration immediately before or simultaneously with chemotherapy: worsening neutropenia.

- **Filgrastim:**
  - Dose based on weight: ≤ 60 kg: 300 µg ; > 60 kg: 480 µg
  - Continue until reaching target ANC of at least 2 to 3 × 10^9/L (ASCO guidelines).
  - Administration 24–72h after the last day of chemo until sufficient post-nadir ANC recovery.

- **Pegfilgrastim**:
  - Individualized single dose of 6 mg (Equivalent dose of filgrastim is 5 µg/kg/day for ~ 10 d)
  - Administration SC 24h after chemotherapy
  - At least 12 days between the dose of pegfilgrastim and next cycle of chemotherapy.
- **NB. Avoid in patients receiving concomitant chemoradiotherapy, particularly involving the mediastinum: increased risk of bone marrow suppression.**

Secondary prophylaxis

- **Why?** To prevent dose chemotherapy reductions or delay that may compromise disease-free or overall survival or treatment outcome
- **When?** Recommended in patients who experienced from a previous cycle of chemotherapy:
  - Febrile neutropenia
  - Neutropenic complication
  - Dose-limiting neutropenic event

NB. Dose reduction or delay may be a reasonable alternative for secondary prophylaxis

Therapeutic use in neutropenic fever:

- **Why?** To prevent infection-associated complications.

- **When?** Consider in patients with fever and neutropenia who are at high-risk for infection-associated complications or who have prognostic factors that are predictive of poor clinical outcomes:
  - Expected prolonged (> 10 days) and profound (< 0.1 × 10^9/L) neutropenia.
  - Age older than 65 years.
  - Uncontrolled primary disease.
  - Pneumonia.
  - Hypotension.
  - Multiorgan dysfunction (sepsis syndrome).
  - Invasive fungal infection.

NB. No routine use for patients with neutropenia who are afebrile

NB. No routine use as adjunctive treatment with antibiotic therapy for patients with fever and neutropenia

References:

1. Klastersky J, de Naurois J, Rolston K, Rapoport B, Maschmeyer G, Aapro M, et al. Management of febrile neutropaenia: ESMO Clinical Practice Guidelines. Annals of Oncology. 2016;27:v111-v8.
2. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Hematopoietic Growth Factors. Version 1.2025.
3. ASCO: https://society.asco.org/sites/new-www.asco.org/files/content-files/practice-and-guidelines/documents/wbcgf-slide-set.pdf.
4. RIZIV: https://webappsa.riziv-inami.fgov.be/ssp/ProductSearch.