GUIDANCE ON INITIAL ANTIBIOTIC MANAGEMENT OF NEUTROPENIC SEPSIS / FEBRILE NEUTROPENIA IN ADULT CANCER PATIENTS (including HAEMATO-ONCOLOGY)

This guidance has been developed for local adaptation to reflect local resistance rates. In addition previous microbiology results should be reviewed for resistance on an individual patient basis.

FEVER: Pyrexia OR Hypothermia (temperature > 38°C OR < 36°C)

SIRS (systemic inflammatory response) - sweats, chills, rigors, malaise, tachypnoea >20/minute, tachycardia >90bpm, hypotension (Patients may appear well perfused despite hypotension)

SEPSIS: EVIDENCE OF INFECTION (including SIRS) + ORGAN DYSFUNCTION i.e. ≥ 2 of hypotension, confusion or tachypnoea (Resp Rate ≥22/minute)

SEPTIC SHOCK: Sepsis induced hypotension requiring inotropic support or hypotension that is unresponsive (within 1hr) to adequate fluid resuscitation i.e. systolic BP <90mmHg or a reduction of >40mmHg from baseline

NEUTROPENIC SEPSIS OR FEBRILE NEUTROPENIA
Neutrophil count < 0.5, or < 1 if recent chemotherapy (usually within 10 days but can persist for up to 21 days)
PLUS FEVER/HYPOTHERMIA or SIRS or SEPSIS/SEPTIC SHOCK

OTHER PATIENT GROUPS INCLUDED:
Cancer patients who are clinically unwell with undifferentiated infection with normal Neutrophil count but known to be immunocompromised e.g. recent stem cell transplant, high dose corticosteroid therapy

In line with current standards for management of sepsis all patients with suspected neutropenic sepsis should be assessed within 15 minutes of presentation to hospital and resuscitation should be commenced following the 'Sepsis 6' care bundle. Sepsis severity should be assessed using an National Early Warning Score (NEWS) and patients assigned as STANDARD RISK or HIGH RISK based on the following criteria:

STANDARD RISK PATIENTS: NEUTROPENIC SEPSIS OR FEBRILE NEUTROPENIA plus NEWS ≤ 6
HIGH RISK PATIENTS: SEPTIC SHOCK or NEWS ≥ 7 plus ALL PATIENTS WITH ACUTE LEUKAEMIA OR ALLOGENEIC TRANSPLANT

STANDARD RISK PATIENTS
NEWS SCORE ≤6

PENICILLIN / beta-lactam ALLERGIC
(Confirm type and severity of previous reaction e.g. rash, anaphylaxis)

NO ↓

Start IV piperacillin/tazobactam 4.5g every 6 hours
Note: No routine IV gentamicin.

YES ↓

Start IV vancomycin (following local guidelines)
Plus either IV ciprofloxacin 400mg every 12 hours or IV aztreonam 2g every 6 hours (contraindicated if previous severe beta-lactam allergy)
Note ciprofloxacin not recommended if used as prophylaxis

Consider addition of IV gentamicin (if local epidemiology dictates and following local guidelines). Note increased risk of nephrotoxicity when used with vancomycin

N.B. ALWAYS TAKE BLOOD CULTURES (BEFORE GIVING ANTIBIOTICS) AND OTHER CULTURES AS APPROPRIATE

ADMINISTER FIRST ANTIBIOTIC DOSE WITHIN ONE HOUR + COVER SPECIFIC INFECTION RISKS*

HIGH RISK PATIENTS
SEPTIC SHOCK or NEWS SCORE ≥7
OR Acute Leukaemia or Allogeneic transplant

PENICILLIN / beta-lactam ALLERGIC
(Confirm type and severity of previous reaction e.g. rash, anaphylaxis)

NO ↓

Start IV piperacillin/tazobactam 4.5g every 6 hours
Plus IV gentamicin (if local epidemiology dictates and following local guidelines)

In Acute Leukaemia or Allogeneic stem cell transplant patients with sepsis requiring inotropic support or septic shock consider using **IV meropenem 1g eight hourly plus an aminoglycoside** (following local guidelines)

YES ↓

Start IV vancomycin (following local guidelines)
Plus either IV ciprofloxacin 400mg every 12 hours or IV aztreonam 2g every 6 hours (contraindicated if previous severe beta-lactam allergy)
Note ciprofloxacin not recommended if used as prophylaxis
Plus IV gentamicin (if local epidemiology dictates and following local guidelines). Note increased risk of nephrotoxicity when used with vancomycin

REVIEW IV THERAPY DAILY - CONSIDER IVOST (as per local guidance) AND STOP IF INFECTION EXCLUDED - MAXIMUM GENTAMICIN DURATION WITHOUT REVIEW 3 DAYS

***Antimicrobial cover for specific additional infection risks:**

1. **IV vancomycin** (following local guidelines) if recent infection with MRSA, MRSA colonised (current or previous), suspected central line infection or signs of skin/soft tissue infection.
2. **IV clarithromycin** 500mg 12 hourly if Community Acquired Pneumonia suspected and atypical cover required (check drug interactions)
3. **Previous ESBL** infection or known ESBL carrier use a carbapenem in place of piperacillin/ tazobactam. Check previous microbiology results for resistance.
4. In high risk patients add an aminoglycoside (depending on local sensitivities)

Notes:

1. Suggested antibiotic dosage is based on normal renal function
2. If using gentamicin in combination with vancomycin be alert to potential for additive adverse effects on renal function and monitor closely
3. Seek early appropriate senior specialist advice and refer to specialist unit e.g. haemato-oncology or stem cell transplant unit
4. Seek senior specialist advice before using gentamicin in myeloma patients due to the risk of renal toxicity

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Guidance developed by the Scottish Antimicrobial Prescribing Group in collaboration with the regional cancer networks and the Scottish Microbiology and Virology Network.

Healthcare Improvement Scotland
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