Whittington Health NHS

Antifungal Guideline for Invasive Fungal Infections in Adults

Subject:	Antifungals for Invasive Fungal Infections in Adults
Policy Number	[IPC/Micro]
Ratified By:	Clinical Guidelines Committee
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Policy Executive Owner:	Dr Michael Kelsey, Consultant Microbiologist
Designation of Author:	Ai-Nee Lim, Lead Antimicrobial Pharmacist
Name of Assurance Committee:	Drugs & Therapeutics Committee
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Target Audience:	All clinical staff involved in prescribing, dispensing and administering antifungals. Doctors, nurses, midwives and pharmacists
Key Words:	Antifungal, fungal, yeast, mould, candida, aspergillus, pneumocystis, PCP, fluconazole, amphotericin, voriconazole, caspofungin, itraconazole

Version Control Sheet

Version	Date	Author	Status	Comment
1.0	Sept 2009	Ai-Nee Lim	In-active	First version
1.0	Jan 2012	Ai-Nee Lim	In-active	Date revision
2.0	Sept 2015	Ai-Nee Lim	Active	Transfer on to new template. Section on pneumocystis jirovieci (carinii) pneumonia and crytococcal meningitis has been updated to reflect national and international guidelines.

➢ Criteria for use

Invasive fungal infection

Invasive fungal infections are seen mostly in:

1. Intensive care patients, who are not necessarily neutropenic, but are compromised due to:
    - breaches in their integument e.g. extensive abdominal surgery,
    - presence of long-term intravascular lines,
    - receiving parenteral nutrition (PN),
    - severe systemic illness or burns, or
    - prolonged broad-spectrum antibiotic therapy.

2. Patients with prolonged neutropenia or sustained immunosuppression following intensive chemotherapy, bone marrow transplant or solid organ transplantation.

3. Patients immunocompromised due to HIV-infection.

Definitions

Proven infection:
Positive blood cultures or culture from a sterile site with clinical or radiological abnormality OR histology/cytochemistry showing yeasts/hyphae from a biopsy with evidence of tissue damage.

Probable and Possible infection:
Combinations of host factors (fever, neutropenia and resistance of fever of unknown origin to broad-spectrum antibacterials) plus clinical, microbiological and radiological criteria.

This purpose of this guideline is to provide guidance on the selection of antifungal therapy for serious, invasive fungal infections. It is based upon current published evidence at the time of writing. It is not intended to be a comprehensive clinical pathway or a substitute for consultation with Microbiology.

➢ Clinical indications

HIGH RISK INTENSIVE CARE UNIT and SURGICAL PATIENTS

Patients who are pyrexial (temperature > 38ºC) despite being on antibacterials for 48 hours and have had gastric/duodenal/pancreatic/hepatic/complex abdominal surgery - consider antifungals. Septic screen crucial.

1st line:	**Fluconazole** 400mg IV OD (initial loading dose: 800mg stat).
2nd line:	**Anidulafungin** 200mg IV on first day then 100mg IV OD.

NB: Review treatment after 5 – 7 days against culture and sensitivity results. Discuss with Microbiology.

HAEMATOLOGY / ONCOLOGY

EMPIRICAL THERAPY

Febrile neutropenic patients (<1.0 x 10^9/L) unresponsive to broad-spectrum antibacterials for 96 hours.

1st line:	**Ambisome** 3mg/kg IV OD (initial test dose: 1mg over 10 minutes). Max. period of treatment 42 days.
2nd line:	**Voriconazole** 6 mg/kg IV every 12 hours for 2 doses then 4mg/kg IV every 12 hours.

NB: Continue until afebrile for 72 hours. If high resolution CT scan of chest, CT scan of upper abdomen and X-ray of sinuses are normal and no other clinical suspicion of invasive fungal infection, discontinue antifungal therapy.

PROBABLE OR PROVEN INFECTION

1st line:	Treat according to tissue cultures and biopsies, supplemented by radiological findings. Discuss with Microbiology.

PRIMARY PROPHYLAXIS

High risk patients (e.g. allogeneic stem cell transplant‡, AML chemotherapy, adult ALL chemotherapy*, high-dose steroid / cytarabine / fludarabine regimens, chronic graft-versus-host disease, graft rejection/failure):

‡ If conditioning contains cyclophosphamide, itraconazole should start 48 hours AFTER the end of chemotherapy. * Avoid using itraconazole, posaconazole and voriconazole with vinca alkaloid containing regimen i.e. vinblastine or vincristinedue to increased risk of neurotoxicity.

1st line:	**Itraconazole** 200mg PO BD

For patients receiving vinca alkaloids i.e. vinblastine and vincristine containing regimens:

Alternative:	**Ambisome** 2mg/kg IV Mon/Wed/Fri

NB: Continue until unsupported neutrophil count > 1 x 10^9/L. Allograft patients will continue longer in presence of GvHD or therapy with corticosteroids.

SECONDARY PROPHYLAXIS

Patients presenting with neutropenia or graft-versus-host disease, who have had previous probable or proven invasive fungal infection but is currently regarded as inactive:

1st line:	**Itraconazole** 200mg PO BD

Patients whose previous infection broke through itraconazole prophylaxis/unresponsive to itraconazole:

Alternative:	**Voriconazole** 400mg PO every 12 hourly for 2 doses then 200mg PO BD (half both the loading and maintenance dose if body-weight under 40kg) *or* **Ambisome** 2mg/kg IV Mon/Wed/Fri (if patient receiving vinca alkaloids)

NB: Continue until unsupported neutrophil count > 1 x 10^9/L. Allograft patients will continue longer in presence of GvHD or therapy with corticosteroids.

CANDIDIASIS:

Candida is a commensal in the oropharynx and the bowel. *Candida albicans* is the commonest species, but others include *C. glabrata, C. tropicalis, C. krusei*, *C. parasilosis*. Following are the groups likely to need treatment for candidosis:

- High risk ITU patients:

  Long term central venous catheters, diabetes, abdominal surgery, exposure to broad spectrum antibacterials (>7 days), steroid use, immunosuppression, PN, renal failure, prolonged ITU stay (>15 days), *candida* colonisation (≥ 3 sites) or mechanical ventilation. Evidence shows increase in the number of *non-albicans candida* in ITU.
- High risk Haematopoietic Stem Cell Transplantation (HSCT) patients:

  First 3 weeks of Intensive conditioning for HSCT, AML induction, high dose cytarabine, severe mucositis or colonisation by yeasts at > 1 site during neutropenia.
- HIV patients
- Intravenous drug users

Definition of candidaemia: presence of positive blood cultures with *candida sp..*

TREATMENT FOR CANDIDAEMIA / CANDIDIASIS

1. Non-neutropenic patients and ITU patients

1st line:	**Fluconazole** 400mg IV OD (initial loading dose: 800mg stat).

In patients with previous azole exposure, severe infection (hemodynamic instability) or if organism confirmed to be *C. glabrata or C. krusei :*

Alternative:	**Anidulafungin** 200mg IV on first day then 100mg IV OD

NB: Treat for 14 days after first negative blood culture. Removal of all intravascular devices if possible. Opthalmological examination and ECHO recommended.

2. Neutropenic patients

1st line:	**Anidulafungin** 200mg IV on first day then 100mg IV OD
Alternative:	**Ambisome** 3mg/kg IV OD (initial test dose: 1mg over 10 minutes) *or* **Voriconazole** 400mg PO every 12 hours for 2 doses then 200mg PO every 12 hours (half both the loading and maintenance dose if body-weight under 40kg)

NB: Above regimens will be altered according to further microbiological identification and sensitivities.

3. Candida osteomyelitis/septic arthritis/endocarditis/endophthalmitis/central nervous infection

1st line:	Discuss all suspected cases with microbiology Team

PROPHYLAXIS IN HIGH RISK GROUPS

Repeated gastrointestinal perforations and anastomotic leaks, liver and pancreatic transplant:

1st line:	**Fluconazole** 400mg IV OD (initial loading dose: 800mg stat).

NB: Review treatment after 5 – 7 days against culture and sensitivity results. Discuss with Microbiology.

ASPERGILLOSIS:

Risk factors for Invasive Aspergillosis:

- Allogenic HSCT with steroid dependent GVHD or graft failure.
- Intensive chemotherapy for AML, and ALL or advanced myelodysplastic syndrome with prolonged.
- Neutropenia (> 21 days).
- Previous mould infection during previous neutropenia
- Exposure to high levels of environmental spores during neutropenia.

TREATMENT OF ACUTE INVASIVE ASPERGILLOSIS

Surgical interventions crucial in management of sinonasal, paranasal granuloma, osteomyelitis, cerebral and endocarditis.

1st line:	**Voriconazole** 6 mg/kg IV every 12 hours for 2 doses then 4mg/kg IV every 12 hours (reduce to 3mg/kg IV BD if not tolerated). Max: 6 months.
2nd line:	**Ambisome** 3 – 5 mg/kg IV OD (initial test dose: 1mg over 10 minutes)

NB: Minimum 2 week treatment for Acute Invasive Aspergillosis.

PNEUMOCYSTIS JIROVECI (CARINII) PNEUMONIA:

Risk factors for PCP including:

- HIV patients with CD4 < 200 cells/μL
- Neutropenic patient
- Other immunosuppressed groups

Treatment should be started in all suspected cases. Do NOT wait for the results of the HIV screen to be available.

Definition:

Moderate to Severe	Oxygen PaO_2 room air, at rest ≤ 9.3kPa (≤ 70mmHg) or SpO_2 at rest on air < 92%
Mild to Moderate	Oxygen PaO_2 room air, at rest > 9.3kPa (> 70mmHg)

PCP will need subsequent referral to the Chest team for bronchoscopy, in order to confirm PCP on BAL.

In G6PD deficiency, caution use of Co-trimoxazole, Primaquine and Dapsone. If an individual develops haemolysis, is confirmed to be G6PD-deficient or has high risk of significant G6PD deficiency, discuss treatment options with a haematologist.

The decision to switch from one therapy to another due to suspected treatment failure should only be considered after at least 5 days of anti-PCP therapy.

PNEUMOCYSTIS JIROVECI (CARINII) PNEUMONIA *(*PCP) TREATMENT – MODERATE to SEVERE

1st line:	**Co-trimoxazole** 30mg/kg IV **QDS** for **3 DAYS** then reduce to **Co-trimoxazole** 30mg/kg IV/PO **TDS** for a further **18 DAYS.** (Dose according to Actual Body Weight. Round up to a convenient dose drawn from the 96mg/ml ampoule). ***PLUS*** *(ideally started at the same time as the anti-PCP therapy and certainly within 72 hours of starting anti-PCP therapy):* **Prednisolone** Day 1 – 5 (for 5 days): 40mg PO BD Day 6 – 10 (for 5 days): 40mg PO OD Day 11 – 21 (for 11 days): 20mg PO OD ***OR*** *(if unable to take oral preparation):* **Methylprednisolone** IV at 75% of the respective prednisolone dose.
2nd line:	**Clindamycin** 600mg IV QDS (*or* 450mg PO QDS) for 21 days ***PLUS*** **Primaquine** 15 – 30mg PO OD for 21 days ***PLUS*** *(ideally started at the same time as the anti-PCP therapy and certainly within 72 hours of starting anti-PCP therapy):* **Prednisolone** Day 1 – 5 (for 5 days): 40mg PO BD Day 6 – 10 (for 5 days): 40mg PO OD Day 11 – 21 (for 11 days): 20mg PO OD ***OR*** *(if unable to take oral preparation):* **Methylprednisolone** IV at 75% of the respective prednisolone dose.

PNEUMOCYSTIS JIROVECI (CARINII) PNEUMONIA *(*PCP) TREATMENT
– MODERATE to SEVERE (continue)

3rd line: **Pentamidine isethionate** 4mg/kg IV OD for 21 days

(Dosed according to Ideal Body Weight (IBW) if obese i.e. > 15% over IBW.
IBW = 50kg [male] or 45.5kg [female] + (0.91 x every cm over 152.4cm).

PLUS *(ideally started at the same time as the anti-PCP therapy and certainly within 72 hours of starting anti-PCP therapy):*

Prednisolone

Day 1 – 5 (for 5 days): 40mg PO BD

Day 6 – 10 (for 5 days): 40mg PO OD

Day 11 – 21 (for 11 days): 20mg PO OD

OR *(if unable to take oral preparation):* **Methylprednisolone** IV at 75% of the respective prednisolone dose.

PNEUMOCYSTIS JIROVECI (CARINII) PNEUMONIA *(*PCP) TREATMENT
– MILD to MODERATE

1st line: **Co-trimoxazole** 1920mg PO TDS (*or* 30mg/kg IV/PO TDS) for 21 days

(NB: Dose according to Actual Body Weight).

2nd line: **Trimethoprim** 5mg/kg PO QDS ***PLUS*** **Dapsone** 100mg PO OD for 21 days

(NB: Dose according to Actual Body Weight).

3rd line: **Atovaquone** 750mg PO BD for 21 days

(NB: Take with food, particularly high fat, to improve bioavailability).

PNEUMOCYSTIS JIROVECI (CARINII) PNEUMONIA (PCP)
– PROPHYLAXIS REGIMENS

Prophylaxis for HIV patients with persistent CD4 < 200 cells/µL, previous PCP or other AIDS-defining illness:

1st line: **Co-trimoxazole** 480mg PO OD

2nd line: **Dapsone** 50mg PO OD

PLUS **Pyrimethamine** 50mg PO ONCE WEEKLY (to protect against toxoplasmosis)

(NB: If issues with compliance, consider Dapsone 200mg PO *PLUS* Pyrimethamine 75mg PO both given ONCE WEEKLY as an alternative)

CRYPTOCOCCOSIS

1. Cryptococcal meningitis in HIV positive patients:

1st line:	**Ambisome** 3 mg/kg IV OD (initial test dose: 1mg over 10 minutes) for 2 weeks *PLUS* **Flucytosine** 25 mg/kg IV/PO QDS for 2 weeks *FOLLOWED BY* **Fluconazole** 400mg PO OD for 8 weeks *MAINTAINENCE THERAPY:* **Fluconazole** 200mg PO OD long term for at least 12 months and until HIV controlled by antiretroviral therapy (i.e. undetectable HIV viral load and CD4 > 100 cells/μL on two occasions 6 months apart).

If bone marrow suppression with Flucytosine:

Alternative:	**Ambisome** 3 mg/kg IV OD (initial test dose: 1mg over 10 minutes) for 2 weeks *PLUS* **Fluconazole** 800 mg PO OD for 2 weeks *FOLLOWED BY* **Fluconazole** 400 mg PO OD for 8 weeks *MAINTAINENCE THERAPY:* **Fluconazole** 200mg PO OD long term for at least 12 months and until HIV controlled by antiretroviral therapy (i.e. undetectable HIV viral load and CD4 > 100 cells/μL on two occasions 6 months apart).

If Ambisome contraindicated / not appropriate:

Alternative:	**Fluconazole** 800 mg PO OD for 6 weeks *PLUS* **Flucytosine** 25 mg/kg IV/PO QDS for 6 weeks *MAINTAINENCE THERAPY:* **Fluconazole** 200mg PO OD long term for at least 12 months and until HIV controlled by antiretroviral therapy (i.e. undetectable HIV viral load and CD4 > 100 cells/μL on two occasions 6 months apart).

2. Cryptococcal meningitis in non–HIV positive patients:

1st line:	**Ambisome** 3 mg/kg IV OD (initial test dose: 1mg over 10 minutes) for 2 weeks *PLUS* **Flucytosine** 25mg/kg IV QDS for 2 weeks (NB: Consider a longer course of induction therapy of 4 – 6 weeks in those with high risk therapeutic failure e.g. uncontrolled underlying disease, inadequate clinical response to initial 2-week induction therapy or neurological complications) *FOLLOWED BY* **Fluconazole** 400mg PO OD for 8 weeks *MAINTAINENCE THERAPY:* **Fluconazole** 200mg PO OD long term for at 6 – 12 months.

If bone marrow suppression with Flucytosine:

Alternative:	**Ambisome** 3 mg/kg IV OD for 6 – 10 weeks.

OTHER MOULD INFECTIONS

CONTACT MICROBIOLOGY

3. Antifungal Agents

	FLUCONAZOLE	ITRACONAZOLE	AMBISOME (LIPOSOMAL AMPHOTHERICIN B)	VORICONAZOLE	ANIDULAFUNGIN	FLUCYTOSINE
Formulary status	General use	Restricted antifungal - Microbiology approval required	Restricted antifungal - Microbiology approval required	Restricted antifungal - Microbiology approval required	Restricted antifungal - Microbiology approval required	Restricted antifungal - Microbiology approval required
Dosage	IV / PO	IV / PO	IV	IV / PO	IV	IV
Oral bioavailability	> 90%	55%	N/A	> 95%	N/A	N/A
Activity	Fungistatic	Fungistatic	Fungicidal	Fungicidal against *Aspergillus* spp. Fungistatic against *Candida* spp.	Fungicidal against *Candida* spp. Fungistatic against *Aspergillus fumigatus*	Fungicidal
CSF penetration	Excellent (~ 80%)	Poor (< 10%)	Poor (< 2.5%)	Good (40 – 60%)	Unknown	Good (60 – 75%)
Elimination route	Renal	Hepatic	Unknown	Hepatic	Hepatic	Renal
Renal dose adjustment	Yes	No Avoid use of IV formulation in CrCl<30ml/min. Accumulation of cyclodextrin component	No	No Caution use of IV formulation in CrCl<50ml/min. Accumulation of cyclodextrin component	No	Yes
Hepatic dose adjustment	No	Yes	No	Yes	No	No
Toxicities	Hepatotoxicity (high doses and prolonged therapy)	GI Hepatotoxicity Negative inotropic effect	Nephrotoxicity Infusion related reactions Electrolyte abnormalities	Visual disturbances Hepatotoxicity Rash Hallucinations	Hypokalaemia GI Rash Elevated liver enzymes	Bone marrow suppression GI Rash Hepatotoxicity
Potential drug interaction	+	+++	-	+++	-	-

➢ Appendix 1

This table is a guide to clinical susceptibility of fungi and should be used to guide empirical treatment of suspected fungal infections in the absence of laboratory confirmation. It is not intended to substitute specialist advice or laboratory data.

Organism	Azoles			Echinocandins	Polyenes	Others
	Fluconazole	Itraconazole	Voriconazole	Anidulafungin	Ambisome	Flucytosine
Yeasts						
Candida albicans	S	S	S	S	S	S
Candida glabrata				S		S
Candida krusei			S	S		
Candida lusitaniae	S	S	S	S		S
Candida parapsilosis	S	S	S		S	S
Candida tropicalis	S	S	S	S	S	S
Cryptococcus neoformans			S		S	S
Dimorphic fungi						
Histoplasma capsulatum		S	S		S	
Moulds						
Aspergillus spp.			S	S	S	
Scedosporium apiospermum			S			
Fusarium spp.						
Zygomycetes						
Absidia, Apophysomyces					S	
Mucor					S	
Rhizomucor, Rhizopus					S	

S	Susceptible
	Susceptibility dependent on achieving the maximal blood concentration of antifungal agent
	Variable susceptibility
	Resistant
	No data available

➢ Contacts (inside and outside the Trust including out-of-hours contacts)

During working hours (Monday to Friday, 09:00 – 17:00)

ST Doctor in Microbiology	ext. 5085 or bleep 3069
Dr Michael Kelsey (Consultant Microbiologist)	ext. 5082
Dr Julie Andrews (Consultant Microbiologist)	ext. 3894
Lead Pharmacist, Antimicrobials	ext. 3732 or bleep 3138
Medicines Information	ext. 5021

Out of hours

On-call SpR in Microbiology	aircall via Whittington switchboard
On-call pharmacist	aircall Via Whittington switchboard

➢ References

1. BRITISH COMMITTEE FOR STANDARDS IN HAEMATOLOGY (2008) Guidelines on the management of invasive fungal infection during therapy for haematological malignancy. Available at: http://www.bcshguidelines.com. Accessed on 5th May 2009.

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3. WALSH, T. J., ANAISSIE, E. J., DENNING, D. W. et al (2008) Treatment of Aspergillosis: Clinical practice guidelines of the Infectious Disease Society of America. *Clinical Infectious Diseases*, vol 46 (18) pp 327 – 360.

4. PERFECT, J. R., DISMUKES, W. E. et al (2010) Clinical practice guideline for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*, vol 50 (3) pp 291 – 322. Available at: http://cid.oxfordjournals.org/content/50/3/291.full.pdf+html

5. British HIV Association (2011) British HIV Association and British Infection Association Guidelines for the treatment of opportunistic infection in HIV-seropositive individuals 2011. *HIV Medicine*, vol 12 (Suppl. 2) pp1 – 5. Available at: http://www.bhiva.org/documents/guidelines/oi/hiv_v12_is2_iss2press_text.pdf

6. FLÜCKIGER, U., MARCHETTI, O., BILLE, J. et al (2006) Treatment options of invasive fungal infections in adults. *Swiss Medical* Weekly, vol 136 (26) pp 447 – 463.

7. A joint collaboration between the Royal Free Hospital, University College Hospital and the North London Cancer Network (2005) Antifungal Strategy for Patients with Haematological Malignancies. *NLCN*

➢ Compliance with this guideline

Tool to Develop Monitoring Arrangements for Policies and guidelines

What key element(s) need(s) monitoring as per local approved policy or guidance?	Who will lead on this aspect of monitoring? Name the lead and what is the role of the multidisciplinary team or others if any.	What tool will be used to monitor/check/observe/Assess/inspect/ authenticate that everything is working according to this key element from the approved policy?	How often is the need to monitor each element? How often is the need complete a report? How often is the need to share the report?	What committee will the completed report go to?
Element to be monitored	**Lead**	**Tool**	**Frequency**	**Reporting arrangements**
Compliance with antifungal treatment guideline. Appropriate dosing and duration of treatment of antifungal agents.	Respective speciality team supported by the Microbiology & Pharmacy Department.	In-house audit tool	Ad hoc as issues arises.	Respective departmental meeting.

To be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval

		Yes/No	Comments
1.	**Does the procedural document affect one group less or more favourably than another on the basis of:**		
	• Race	No	
	• Ethnic origins (including gypsies and travellers)	No	
	• Nationality	No	
	• Gender	No	
	• Culture	No	
	• Religion or belief	No	
	• Sexual orientation including lesbian, gay and bisexual people	No	
	• Age	No	
	• Disability - learning disabilities, physical disability, sensory impairment and mental health problems	No	
2.	**Is there any evidence that some groups are affected differently?**	No	
3.	**If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?**	No	
4.	**Is the impact of the procedural document likely to be negative?**	No	
5.	**If so can the impact be avoided?**	N/A	
6.	**What alternatives are there to achieving the procedural document without the impact?**	N/A	
7.	**Can we reduce the impact by taking different action?**	N/A	

If you have identified a potential discriminatory impact of this procedural document, please refer it to the Director of Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact the Director of Human Resources.

Checklist for the Review and Approval of Procedural Document

To be completed and attached to any procedural document when submitted to the relevant committee for consideration and approval.

	Title of document being reviewed:	Yes/No	Comments
1.	**Title**		
	Is the title clear and unambiguous?	Yes	
	Is it clear whether the document is a guideline, policy, protocol or standard?	Yes	
2.	**Rationale**		
	Are reasons for development of the document stated?	Yes	
3.	**Development Process**		
	Is it clear that the relevant people/groups have been involved in the development of the document?	Yes	
	Are people involved in the development?	Yes	
	Is there evidence of consultation with stakeholders and users?	Yes	
4.	**Content**		
	Is the objective of the document clear?	Yes	
	Is the target population clear and unambiguous?	Yes	
	Are the intended outcomes described?	Yes	
5.	**Evidence Base**		
	Are key references cited in full?	N/A	
	Are supporting documents referenced?	N/A	
6.	**Approval**		
	Does the document identify which committee/ group will approve it?	Yes	
7.	**Dissemination and Implementation**		
	Is there an outline/plan to identify how this will be done?	Yes	
8.	**Document Control**		
	Does the document identify where it will be held?	Yes	
9.	**Process to Monitor Compliance and**		

	Title of document being reviewed:	Yes/No	Comments
	Effectiveness		
	Are there measurable standards or KPIs to support the monitoring of compliance with and effectiveness of the document?	Yes	
	Is there a plan to review or audit compliance with the document?	Yes	
10.	**Review Date**		
	Is the review date identified?	Yes	
	Is the frequency of review identified? If so is it acceptable?	Yes	
11.	**Overall Responsibility for the Document**		
	Is it clear who will be responsible for co-ordinating the dissemination, implementation and review of the document?	Yes	

Executive Sponsor Approval			
If you approve the document, please sign and date it and forward to the author. Procedural documents will not be forwarded for ratification without Executive Sponsor Approval			
Name		Date	
Signature			
Relevant Committee Approval			
The Director of Nursing and Patient Experience's signature below confirms that this procedural document was ratified by the appropriate Governance Committee.			
Name		Date	
Signature			
Responsible Committee Approval – only applies to reviewed procedural documents with minor changes			
The Committee Chair's signature below confirms that this procedural document was ratified by the responsible Committee			
Name		Date	
Name of Committee		Name & role of Committee Chair	
Signature			