

Improving Value in Specialised Services

Antifungal Stewardship Implementation Pack

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This pack provides information and guidance to support the local implementation of this Improving Value initiative. A local implementation project can use the guidance contained within this pack to guide successful implementation.

This checklist can be used to check local readiness for implementation / identify gaps in readiness to implement.

| Implementation Checklist | Y/N |
|---|------------|
| Clear rationale of need to change | |
| Local Clinical engagement in project | |
| Measurable objectives | |
| Measurable success criteria | |
| Impact assumptions have been tested and are realistic | |
| Scale and timing of impact is clear | |
| Risks have been assessed | |
| Milestones for delivering change are clear | |

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Scheme Details

| | |
|----------------------------------|--|
| Scheme Name | Antifungal Stewardship |
| Scheme Reference Number | F01181946IM |
| Related Programme of Care | Pan POC |
| Related Clinical Reference Group | Medicines Optimisation |
| Scheme Lead | Malcolm Qualie |
| Scheme Lead Contact | malcolm.qualie@nhs.net |
| Start Date for Implementation | May 2018 |
| Other Details | Other CRGs with a considerable interest in Antifungal Stewardship: Renal Services, Chemotherapy, Adult Critical Care, Blood & Marrow Transplantation, HIV, Specialised Respiratory |

Project Team

The following team developed this national initiative:

| Name | Title / Role | e-mail |
|----------------|------------------------------------|--|
| Malcolm Qualie | Chair of Project Group | malcolmqualie@nhs.net |
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| Mark Leach | Improving Value Programme Manager | markleach@nhs.net |
| | | |
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| | | |

Summary of Scheme

| | |
|--|--|
| <p>What is the scheme trying to achieve?</p> | <p>The overall aim of this project is to achieve improved value from NHS England's spend on antifungal medicines – this includes preserving the future effectiveness of antimicrobials (prevent resistance) and to improve patient outcomes, including reducing adverse effects.</p> <p>Specifically, the 3 key objectives are:</p> <ul style="list-style-type: none"> • Improved Antifungal Stewardship across the NHS in England • Greater standardisation in the use of antifungals across the NHS in England • Optimise use of generic products wherever clinical appropriate to ensure best value |
| <p>How will we know change is an improvement?</p> | <p>Greater % of treatments decided through diagnosis (less empirically) Greater standardisation of antifungal stewardship activities across NHS Hospitals Reduction in empiric versus targeted at discharge Reduced antifungal resistance Increased use of generic antifungals Reduced commissioner cost per patient treated Reduced overall commissioner expenditure on antifungal medicines Increased intravenous to oral switching Increased de-escalation of therapeutic use of antifungals</p> |
| <p>What changes will be made that will result in improvement?</p> | <p>This initiative is based around the following five improvement principles:</p> <ol style="list-style-type: none"> 1. Evidence based guidance within every NHS Trust, including a nationally standardised prophylaxis risk table 2. Antifungal Reviews by Stewardship Teams: Antifungal therapy (treatment – targeted/empiric) should be reviewed 48-72h after initiation and every 7 days thereafter by a specialist stewardship team 3. Regular audit of antifungal prescribing utilising a standardised audit proforma, with key metrics reported 4. Diagnostics Gap analysis against the British Society for Medical Mycology best practice recommendations for the diagnosis of serious fungal diseases 5. Introduce Blueteq prior-approval for the higher cost agent isavuconazole |

Case for Change – Strategic Context



Antimicrobial stewardship has overwhelmingly focused on antibiotics: A recent study established that only 11% of trusts had an antifungal stewardship programme compared to 100% with an antibiotic stewardship programme.

Antibiotic stewardship programmes have reduced inappropriate antimicrobial use, improved patient outcomes and limited the emergence of resistance. It is proposed that the implementation of antifungal stewardship will result in the same successful outcomes as antibiotic stewardship.

Whilst resistance to antifungal drugs is not as common as that seen with antibacterial drugs, it is a real clinical threat and one for which there is an opportunity to manage through the more judicious use of drugs. (Perlin 2015, Pfaffer 2012)

Invasive fungal infections (IFI) are less prevalent than bacterial infections, but their health and financial burden are substantial and increasing. As the “at-risk” population increases the use of antifungal drugs, both for treatment and prevention of infection, increases, which in turn increases the risk of resistance. Antifungal resistance has been described as a global emergency with recent outbreaks of multi-resistant *C. auris* across England and globally.

Clinical specialities associated with higher rates of use of antifungal drugs are:

- Haemato-oncology patients receiving myeloablative chemotherapy
- Bone marrow transplant patients due to significant immunosuppression from conditioning and anti-rejection drugs
- Solid organ transplant patients due to suppressed immune system from post-transplant drugs
- Intensive care patients
- Patients with chronic lung conditions such as bronchiectasis

Optimising the prevention and treatment of IFIs is particularly important due to their high attributable mortality, the challenges in diagnosis of IFI, and the complexity of the drugs and patient groups involved.

References

- Micallef C, Ashiru-Oredope D, Hansraj S, et al. An investigation of antifungal stewardship programmes in England. *Med. Microbiol.* 2017;66(11):1581-1589
- Fisher MC, Hawkins NJ, Sanglard D, et al. Worldwide emergence of resistance to antifungal drugs challenges human health and food security. *Science* 2018;360(6390):739-742

Case for Change – Strategic Context (cont.)

There is significant variation in practice across England in management and prevention of IFI. The project group audited 8 NHS Trusts Antifungal Guidelines during 2017 and found significant variation in practice particularly relating to:

- Invasive candidiasis treatment
- Treatment of IFI in haem-oncology patients
- Antifungal prophylaxis in haemato-oncology patients

Case for Change (2) – Evidence Base / Case Studies

1. Implementation of an AFS program in a London Teaching Hospital led to a 26% reduction in antifungal expenditure over its first 3 years (total antifungal expenditure reduced from £0.98 million to £0.73 million) without compromising clinical or microbiological outcomes. Following this expenditure then rose to between £1.17-1.4 million p.a.: a 20% increase compared to pre-intervention associated with a significant increase in numbers of at risk patients within the Trust. By comparison, NHS England shows that national antifungal expenditure more than doubled from £37.8 million to £79.9 million during the 5 year period 2011-16. **(Whitney L, et al. Effectiveness of an antifungal stewardship program at a London teaching hospital 2010-16. *J Antimicrob Chemother awaiting publication 2018*)**
2. Recent long- and short- term evidence from UK practice has demonstrated that drug costs can be reduced significantly along with improved clinical benefit for patients. This evidence is supported by a growing evidence base from Europe and North America where antifungal stewardship programmes have been implemented. **(Andruszko B, Ashley ED. Antifungal Stewardship: an Emerging practice in Antimicrobial Stewardship. *Current Clinical Microbiology Reports 2016;3(3):111-9*)**
3. A report from a tertiary UK centre demonstrated a crude saving of £188,000 in drug costs over a 1-year intervention period for 173 patients. **C. Micallef, S. H. Aliyu, R. Santos, et al. Introduction of an antifungal stewardship programme targeting high-cost antifungals at a tertiary hospital in Cambridge, England. *J Antimicrob Chemother. 2015;70(6):1908-11***
4. Just 11% (5/47) of English acute NHS Trusts surveyed reported having a dedicated antifungal stewardship programme, compared to 98% with an antibiotic stewardship programme. **Micallef C, Ashiru-Oredope D, Hansraj S, et al. An investigation of antifungal stewardship programmes in England. *Med. Microbiol. 2017;66(11):1581-1589***

Improvement Principles

Following evidence review, audit of current practice in a selection of NHS Trusts and using clinical and commissioning expertise, the project group has developed 5 Improvement Interventions to underpin Antifungal Stewardship.

1. Evidence based guidance within every NHS Trust, including a nationally standardised prophylaxis risk table

2. Antifungal Reviews by Stewardship Teams: Antifungal therapy (treatment – targeted/empiric) should be reviewed 48-72h after initiation and every 7 days thereafter by a specialist stewardship team

3. Regular audit of antifungal prescribing utilising a standardised audit proforma, with key metrics reported

4. Diagnostics Gap analysis against the British Society for Medical Mycology best practice recommendations for the diagnosis of serious fungal diseases

5. Standardise use of isavuconazole through Introduction of Blueteq prior-approval form for this higher cost agent.

1. Evidence based guidance

The NHS England High Cost Drugs List (Medicines not reimbursed through national prices and directly commissioned by NHS England) requires any NHS Trust prescribing high cost antifungal medicines to do so against agreed Trust prescribing guidelines.

Commissioners should expect:

- That the Trust has up to date, evidence based Antifungal Prescribing Guidelines that are reviewed for existing or develop guidelines for prophylaxis and treatment of invasive fungal infections within 2019-20.
- The guidelines should also include recommended investigations to improve diagnosis
- That the guidelines have been agreed by the relevant Trust Committee (D&T committee or Antimicrobial Stewardship Committee)
- That the guidelines have been agreed with the Antifungal Stewardship team and other key stakeholders (pharmacy, ITU physicians, haemato-oncology)
- That the guidelines should cover – prophylaxis in haemato-oncology patients, and invasive candidiasis, treatment of IFI in haemto-oncology patients.
- That a standard prophylaxis risk table should be incorporated into these guidelines

1b Evidence based guidance – Standard Prophylaxis Risk Table

| Guidance | High Risk | Low Risk |
|--|---|---|
| Infectious Diseases Society of America | <p>Allogenic HSCT - candida prophylaxis Intensive Treatment for ALL/AML - fluconazole, itraconazole, voriconazole, posaconazole, micafungin, caspofungin AML/MDS intensive chemo - posaconazole Autograft - mould active agent if prior IA, neutropenia > two weeks expected or prolonged neutropenia prior to HSCT</p> | <p>Anticipated neutropenia duration < seven days</p> |
| National Comprehensive Cancer Network | <p>Intermediate to high risk ALL – fluconazole, micafungin or AmBisome till resolution of neutropenia MDS & AML (with neutropenia) consider posaconazole, voriconazole, micafungin, fluconazole, amphotericin until resolution of neutropenia Allo –SCT – fluconazole, micafungin, voriconazole, posaconazole, Amphotericin, during neutropenia Significant GVHD – posaconazole, voriconazole, caspofungin, micafungin, amphotericin until significant GVHD resolved</p> | <p>Auto-SCT – candida prophylaxis if mucositis until neutropenia resolved</p> |
| ECIL 5 (2013) | <p>AML & MDS undergoing AML-like chemo Allogenic HSCT CML intensive chemo Mould active prophylaxis ALL – fluconazole due to interactions with vincristine</p> | <p>Myeloma – fluconazole or no prophylaxis Lymphoma (including auto HSCT) fluconazole or no prophylaxis MDS – not undergoing intensive chemo CML (treated with TKIs or conventional treatment) CLL - No prophylaxis Consider in CLL with prolonged neutropenia (>6 months), elderly, advanced and unresponsive disease</p> |

| Guidance | High Risk | Low Risk |
|--|--|--|
| <p>Höchstmann B et al. BMT 2013 Supportive care in severe and very severe aplastic anaemia</p> | <p>Severe aplastic anaemia – mould active prophylaxis. Consider prophylaxis for first months after ATG and after HSCT for as long as neutropenia and/or lymphopenia is present</p> | |
| <p>American Society of clinical Oncology</p> | | <p>Solid tumours - Profound neutropenia and mucositis expected to last for ≥ 7 days in environments with > 10% risk of invasive Candida infection; fluconazole or caspofungin/micafungin Mould active prophylaxis only for patients at substantial risk for IFI (> 6% to 10%) from regimens likely to decrease ANC to < 100/μL for ≥ 7 days.</p> |
| <p>Australia & New Zealand Guidelines</p> | <p>ALL/AML or MDS with remission induction and re-induction chemotherapy Severe GVHD: steroid dependent or refractory or grade 3 or 4 Extensive chronic GVHD Allogeneic HSCT with expected neutropenia >14 days Mould active prophylaxis Allografts to day 75 in absence of GVHD GVHD – 16 weeks or until prednisolone <10mg OD Others – neutrophil recovery High risk without recommendations for prophylaxis Neutrophils <0.1 for >3 weeks 16 or <0.5 for >5 weeks Corticosteroids >1 mg/kg prednisolone equivalent and neutrophils <1 × 10⁹ /L for >1 week Corticosteroids >2 mg/kg prednisolone equivalent >2 weeks High-dose cytarabine Fludarabine use in highly treatment-refractory patients with CLL or low-grade lymphoma Alemtuzumab use, especially in highly treatment-refractory patients with CLL or lymphoma</p> | <p>Candida prophylaxis Auto-HSCT with high risk of mucositis, or recent aggressive chemo Allo-HSCT with expected neutropenia <14 days (II, A) Lymphoma - intensive/dose-escalated therapy No prophylaxis Lymphoma - standard chemo CML Other myeloproliferative neoplasms</p> |

Consensus between national guidelines for prophylaxis risks

| High Risk - mould active prophylaxis | Low Risk - candida prophylaxis | Low Risk - no prophylaxis |
|---|---|---|
| <p>Allo-HSCT Intensive treatment for ALL, AML, MDS Significant GVHD –till resolved. CML intensive chemo Severe aplastic anaemia Duration Allografts to day 75-100 GVHD – 16 weeks or until prednisolone <10mg OD Others – neutrophil recovery</p> | <p>Auto-SCT – candida prophylaxis if mucositis or recent excessive chemo until neutropenia resolved Myeloma – fluconazole or no prophylaxis Lymphoma - intensive/dose-escalated therapy Solid tumours – if profound neutropenia and mucositis expected to last for ≥ 7 days in environments with > 10% risk of invasive Candida infection</p> | <p>MDS – not undergoing intensive chemo CML (treated with TKIs or conventional treatment) CLL No prophylaxis (consider in CLL with prolonged neutropenia (>6 months), elderly, advanced and unresponsive disease) Lymphoma - standard chemo Other myeloproliferative neoplasms</p> |

Unclear

Autograft – mould-active agent if prior IA, neutropenia >2 weeks expected or prolonged neutropenia prior to HSCT
Allo-HSCT with expected neutropenia <14 days (II, A)
Aplastic anaemia - Consider prophylaxis for first months after ATG and after HSCT for as long as neutropenia and/or lymphopenia is present
Allogeneic HSCT with expected neutropenia >14 days
 Corticosteroids >1 mg/kg prednisolone equivalent and neutrophils <1 × 10⁹ /L for >1 week
 Corticosteroids >2 mg/kg prednisolone equivalent >2 weeks
 High-dose cytarabine
 Fludarabine use in highly treatment-refractory patients with CLL or low-grade lymphoma
 Alemtuzumab use, especially in highly treatment-refractory patients with CLL or lymphoma

2. Antifungal Reviews by Stewardship Teams

The aims of antifungal stewardship (AFS) are broadly similar to those of antibiotic stewardship, namely to reduce inappropriate use and improve patient outcomes while reducing the evolution and spread of microbial resistance. As outlined in Whitney et al 2014, and Micallef et al 2015 creation of a multidisciplinary antifungal stewardship team should be a key component of an effective antifungal stewardship programme.

The role of such a stewardship team should include:

- Implementation of evidence-based guidelines/care pathways, adapted to the local setting
- Post-prescription review with feedback including:
 - cessation of unnecessary treatment
 - de-escalation
 - intravenous to oral switch
 - optimising non-drug treatment—source control, restoring immunity, or reducing immunosuppression
 - optimising drug usage—ensuring appropriate dosing taking into account PK/PD, interactions, TDM, hepatic/renal dysfunction, and managing and preventing adverse drug reactions
- Education
- Regular review of local fungal epidemiology including rates of resistance
- Optimising access to and turn-around time of fungal diagnostics
- Processes to measure and monitor antifungal use and expenditure

2. Antifungal Reviews by Stewardship Teams (Cont.)

Commissioners should expect:

- An Antifungal Stewardship (AFS) team to be in place that includes as a minimum: Consultant Microbiologist or ID physician or medical mycologist and a pharmacist
- The team to discuss antifungal treatments with senior member/s of the patients clinical team
- An antifungal therapy review to be undertaken 48-72h after initiation and every 7 days thereafter by the AFS team.
- The review to include the following:
 - Within 24h: appropriate diagnostic investigations to have been undertaken/arranged.
 - At 48-72h: review available diagnostics. stop if diagnostics favour alternative diagnosis or rule out IFI, de-escalate antifungal therapy if possible, consider IV to PO switch, advise on additional investigations required, advise on the need to perform TDM.
 - Subsequent reviews: review continued need for antifungals, consider de-escalation/IV to PO switch if not done at previous review, review TDM results and adjust treatment if outside therapeutic range, plan duration of therapy and specialist follow up, if appropriate

A standard audit proforma has been created to support these principles.

3. Regular audit of antifungal prescribing

Standardised, regular audit of antifungal prescribing can provide evidence & feedback of the extent to which effective anti-fungal stewardship is in place, and the scope for further improvement in prescribing practice. An audit proforma has been developed to support audit of antifungal prescribing.

The audits are for *“treatment of invasive candidiiasis”*, *invasive mold infections* and *“ empiric treatment of IFI in “at risk patients”*”.

Commissioners should expect that:

- The Medicines Optimisation CQUIN Trigger 5 related to Antifungal Stewardship indicator considers the clinical review of antimicrobial prescriptions of patients prescribed antifungals for treatment of invasive fungal infection who are still inpatients at 72 hours and measures the proportion of antifungal treatment prescriptions reviewed by the Antifungal Stewardship Team at 24hours, 48 to 72 hours and 7 days. The CQUIN states that Acute Trusts should undertake a local audit of a maximum of 20 patients per quarter or 30% of total patients receiving an antifungal whichever is the lower figure. The first data collection is required by quarter 4 of the first year of this CQUIN and then each quarter thereafter.
- The minimum number of patients audited relates to patients with proven/suspected invasive candidiiasis and proven/suspected invasive mold infections combined. Each set of patients are audited separately on the relevant sheet of this data collection tool. This reflects the different standards of diagnosis and treatment for each disease.
- The results of the audit will be published through the PHE Fingertips database and/or model hospital dashboard
- The reporting will allow the following KPIs to be reviewed and improvement targets to be established against baseline:

% of patients initiated on antifungal treatment have a documented AFS team review at 72 hours from decision to prescribe

% of empiric treatments where an appropriate diagnostic investigation has been arranged within 24 hours of decision to prescribe

% of empiric treatment where patients have proven or probable infection

4. Diagnostics Gap Analysis

Until recently there have been suboptimal diagnostic tools, which have driven the overuse of antifungal agents. One of the most challenging parts of antifungal stewardship to implement is de-escalation of empirical treatment, i.e. reduce treatment where there is not a definitive diagnosis. Incorporating non-culture-based tests into clinical pathways may enhance antifungal stewardship. The British Society of Medical Mycology have recently developed best practice recommendations for the diagnosis of serious fungal diseases. All 43 recommendations are auditable and should be used to ensure best diagnostic practice and improved outcomes for patients.

The lack of available diagnostic tests and the time it takes to turn around the diagnostic tests that are available have been particularly challenging.

Commissioners should expect:

- Trusts to undertake a gap analysis of current practice against the British Society of Medical Mycology recommendations
- That the gap analysis (including priorities for improvement) should be reported to the relevant Trust Committee (D&T committee or Antimicrobial Stewardship Committee) and made available to commissioners

5. Standardise use of Isavuconazole

- Isavuconazole is a high cost antifungal used to treat Invasive aspergillosis and Mucormycosis in patients for whom amphotericin B is inappropriate.
- Blueteq prior-approval is required to prescribe this drug to ensure: *Trusts are prescribing isavuconazole only when it is clinically appropriate to do so and there is no other alternative*

Commissioners should expect:

- Trusts who wish to prescribe Isavuconazole are registered with the Blueteq system
- Prescribed doses of Isavuconazole to only be reimbursed by NHS England where a Blueteq form has been completed

Logic Model for Scheme



| Input | Activities | Outputs | Outcomes |
|---|--|--|--|
| Agreement of Evidence Based guidelines, including standardised prophylaxis risk scoring | Review of current Trust guidance Implementation of standard approach to prophylaxis risk scoring | Prescribing practice in line with evidence base Standard approach to risk scoring to inform prophylaxis risk | Reduced harm from reduced unwarranted variation in prophylaxis use Reduce risk of resistance Reduced commissioner cost per patient treated |
| Antifungal Reviews by Stewardship Teams | Implementation of specialist AFS team Review of prescribing for all patients by AFS teams | Improved prescribing practice Including cessation of unnecessary treatment De-escalation where appropriate, Increased intravenous to oral switch Optimising non-drug treatments, improved Use of diagnostic measurements and education of prescribers | Improvement in access to diagnostics and reduced empirical use in a reduction in AF usage Reduced harm from reduced unwarranted variation in empirical use Improvements in diagnostics will benefit patients and result Reduced commissioner cost per patient treated Reduced overall commissioner expenditure on Antifungal medicines |
| Diagnostic Gap analysis | Each Trust to undertake review of current available diagnostics for AF against British Society for Medical Mycology best practice recommendations for the diagnosis of serious fungal diseases | Identification of priority recommendations to improve access to best practice diagnostics Transparency of gap in access to diagnostics | Improvement in access to diagnostics and reduced empirical use Reduced harm from reduced unwarranted variation in empirical use Reduce risk of resistance Reduced commissioner cost per patient treated |
| Standardise use of isavuconazole | Use of Blueteq prior approval | Isavuconazole only used as 2 nd line or where patient not suitable for alternative | Reduced commissioner cost per patient treated Reduced overall commissioner expenditure on Antifungal medicines |

Benefits

This section should contain the measures used to evidence scheme benefits for patients, providers and/or commissioners . For activity impact please provide service line specific information (e.g. HRG and NPOC codes)

| Benefit Type* | Description | Numerator | Denominator | Data Source | Service Line Detail | Code |
|---------------|--|--|---|------------------|--|----------|
| Patient | Fewer prescriptions and reduced number of treatments of potentially toxic drugs. | Number of antifungal drugs prescribed in 2019 | Number of antifungal drugs prescribed in 2018 | KPI from AF Tool | A05 - CARDIOTHORACIC SERVICES | NCBPS01c |
| Patient | More treatments decided on diagnostics rather than empiric | Number of treatments decided on diagnostics 2019 | Number of treatment decided on diagnostics 2018 | KPI from AF Tool | B02 - CHEMOTHERAPY | NCBPS01c |
| Commissioner | Reduced cost of antifungals | Cost of antifungal drugs prescribed in 2019 | Cost of antifungal drugs prescribed in 2018 | KPI from AF Tool | F01 - BLOOD AND MARROW TRANSPLANTATION | NCBPS02z |
| Provider | Number of providers completing AF audit | Number of Trusts completing an AF Tool | Number of Trusts prescribing Antifungals | KPI from AF Tool | OTHER | NCBPS01c |
| | | | | | TRANSPLANT DRUGS | NCBPS02z |

Contractual Levers

| Contractual Lever | Used to Support this Scheme | Link to document / Guidance |
|---|--|-----------------------------|
| CQUIN | Proposed | |
| Procurement | All Antifungals are awarded through regional tenders | |
| SDIP (service development improvement plan) | | |
| DQIP (data quality improvement plan) | MDS reporting | |
| Others | Blueteq | |
| | AF Tool | |

| Question | Response |
|---|--|
| Why is it important to move from empiric to diagnostic based prescribing? | Antifungals are a limited resource with potential for increased resistance if used inappropriately. There is evidence that antifungals are being over-prescribed and prescribing would be reduced if timely and appropriate diagnostic tests are utilised. |
| Why use blueteq for isavuconazole? | Isavocunozole is a high cost drug which is not routinely prescribed as a first line treatment. |
| What level of audit is required? | The audit tool has been developed to mirror current AMR audit requirements. An audit of 40 patients per quarter is suggested for larger providers and for smaller providers a target of between 10 and 20 has been set. The importance is having an audit process. There is flexibility to negotiate numbers of patients audited with commissioners. |
| How do providers find out what the implementation requirements are? | Antifungal Stewardship is supported by an NHS England Implementation pack which has been developed for commissioners. Commissioners can adapt the information for local use and share this with each provider – in the North region the lead pharmacist has developed a provider implementation pack which has been shared with each provider. |
| What if review of guidelines shows that there is an underuse of diagnostic testing? | The project group has highlighted inconsistencies in diagnostic testing. The aim is to gather evidence for where gaps in diagnostic testing is occurring. This evidence can be used to support the development of appropriate diagnostic testing. |

National Stakeholder Engagement

| Stakeholder Group | National Engagement to Date | Ongoing Engagement? |
|--|------------------------------|---------------------|
| English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) | Involvement in project group | Ongoing |
| British Society of Medical Mycologists | Involvement in project group | Ongoing |
| Public Health England | Involvement in project group | Ongoing |
| NHS England Commissioners | October 2016 | |
| | | |
| | | |
| | | |

National Project Milestones to Support Local Implementation

| Milestone | Responsible Group or Lead | Completed? | Date for Completion |
|---|---------------------------|------------|---------------------|
| Agree a governance CQUIN to support antifungal stewardship and the review of antifungal usage | MO CRG | | |
| Blueteq form for isavuconazole uploaded | Malcolm Qualie | | |
| KPI spreadsheet signed off and in use | AFS group | | |
| | | | |
| | | | |
| | | | |
| | | | |

Local Implementation Milestones

| Milestone | Responsible Group or Lead | Completed? | Date for Completion |
|--|---------------------------|------------|---------------------|
| Evidence based guidelines in place to oversee the prescribing of antifungals | | | |
| AFS team in place | | | |
| Diagnostic gap analysis undertaken | | | |
| Audits undertaken of antifungal use | | | |
| | | | |
| | | | |
| | | | |

Overall Risks and Issues



| Risk | L | I | Overall Risk Level | Mitigation | L | I | Residual Risk |
|--|---|---|--------------------|--|---|---|---------------|
| CQUIN not supported | 3 | 4 | 12 | Ensure CQUIN is supported through dialogue with key stakeholders | | | |
| CQUIN not taken up by Trusts | 3 | 4 | 12 | Given the recent statement from WHO regarding antifungal resistance there is a reasonable expectation that Trusts will take on this CQUIN. Will need to ensure local hubs are pushing the CQUIN | | | |
| Diagnostic gap analysis not undertaken | 4 | 3 | 12 | Will seek support of the BSMM | | | |
| Clinicians don't accept the scheme | 3 | 4 | 12 | The AFS programme has engaged widely across all relevant CRGs and has developed a consensus position for promoting antifungal stewardship so that the clinical integrity of antifungal usage can be maintained | | | |

| Issues | L | I | Overall Risk Level | Mitigation | L | I | Residual Risk |
|---------------------------------|---|---|--------------------|------------|---|---|---------------|
| Waiting final sign off of CQUIN | 3 | 4 | 12 | As above | | | |

| | | Risk Matrix | | Likelihood / Probability | | | | |
|--------|-------------|-------------|--|--------------------------|----------|----------|--------|----------------|
| | | | | Rare | Unlikely | Possible | Likely | Almost Certain |
| | | SCORES | | 1 | 2 | 3 | 4 | 5 |
| Impact | Major | 5 | | | | | | |
| | Significant | 4 | | | | | | |
| | Moderate | 3 | | | | | | |
| | Minor | 2 | | | | | | |
| | Negligible | 1 | | | | | | |

| |
|----------------|
| Very High Risk |
| High Risk |
| Medium Risk |
| Low Risk |
| Very Low Risk |

Quality Impact Assessment

Describe the Impact on Clinical Effectiveness:

| Risk | L | I | Overall Risk Level | Mitigation | L | I | Residual Risk |
|--|---|---|--------------------|---|---|---|---------------|
| Patients receive sub optimal treatment | 3 | 4 | 12 | The AFS programme is to ensure patients receive optimal antifungal therapy and have fewer bed days due to better management | | | |
| Evidence based guidance is not implemented | 3 | 4 | 12 | The CQUIN will incentivise Trusts to review and implement an AFS strategy to include evidence based guidance | | | |
| | | | | | | | |

Describe the Impact of Patient Safety

| Risk | L | I | Overall Risk Level | Mitigation | L | I | Residual Risk |
|---|---|---|--------------------|--|---|---|---------------|
| Patients are over treated leading to unnecessary ADRs | 3 | 4 | 12 | The AFS programme is to ensure patients receive optimal antifungal therapy | | | |
| | | | | | | | |
| | | | | | | | |

Quality Impact Assessment

Describe the Impact on Patient Experience:

| Risk | L | I | Overall Risk Level | Mitigation | L | I | Residual Risk |
|---|---|---|--------------------|---|---|---|---------------|
| Patients receive substandard antifungal treatment | 3 | 4 | 12 | The AFS programme is to ensure patients receive high quality antifungal therapy | | | |
| Patients are over treated leading to unnecessary ADRs | 3 | 4 | 12 | The AFS programme is to ensure patients receive optimal antifungal therapy | | | |
| | | | | | | | |

Describe the Impact on Equality and Diversity:

| Risk | L | I | Overall Risk Level | Mitigation | L | I | Residual Risk |
|--|---|---|--------------------|--|---|---|---------------|
| The AFS programme will ensure fair and equal access to antifungal treatments – if not implemented this access may not be equal | 3 | 4 | 12 | Ensure the AFS is delivered across the country | | | |
| | | | | | | | |

References

| Document Name | Reference for slide in attached Zip Folder |
|---|--|
| Silke Shelenz et al. 2015; British Society for Medical Mycology best practice recommendations for the diagnosis of serious fungal diseases; | 1. BSSM best practice guidance |
| Mathew C Fisher et al. 2018 Worldwide emergence of resistance to antifungal drugs challenges human health and food security; 360 : 739-742; | Slide 13 2. WHO |
| Ananda-Rajah MR, Slavin MA, Thursky KT. The case for antifungal stewardship. <i>Curr Opin Infect Dis.</i> 2012; 25 : 107-15 | Slide 6 |
| Micallef C, Ashiru-Oredope D, Hansraj S, <i>et al.</i> An investigation of antifungal stewardship programmes in England. <i>Med. Microbiol.</i> 2017; 66 : 1581-1589 | Slide 7 |
| Gutierrez F, Wall PG, Cohen J. An audit of the use of antifungal agents. <i>J Antimicrob Chemother.</i> 1996; 37 : 175-85 | Slide 8 |
| Nivoix Y, Launoy A, Lutun P, <i>et al.</i> Adherence to recommendations for the use of antifungal agents in a tertiary care hospital. <i>J Antimicrob Chemother.</i> 2012; 67 : 2506-13 | Slide 9 |
| Sutepvarnon A, Apisarnthanarak A, Camins B, <i>et al.</i> Inappropriate use of antifungal medications in a tertiary care center in thailand: A prospective study. <i>Infect control Hosp Epidemiol.</i> 2008; 29 : 370-3 | Slide 10 |
| Valerio M, Rodriguez-Gonzalez CG, Munoz P, <i>et al.</i> Evaluation of antifungal use in a tertiary care institution: Antifungal stewardship urgently needed. . <i>J Antimicrob Chemother.</i> 2014; 69 : 1993-9 | Slide 11 |
| Perlin DS, Rautemaa-Richardson R, Alastruey-Izquierdo A. The global problem of antifungal resistance: prevalence, mechanisms, and management. <i>Lancet Infect Dis.</i> 2017; 17 : 383 - 392 | Slide 12 |

References

| Document name | Reference in attached Zip Folder |
|--|----------------------------------|
| Reed EE, West JE, Keating EA, <i>et al.</i> Improving the management of candidemia through antimicrobial stewardship interventions. <i>Diagn Microbiol Infect Dis.</i> 2014; 78 :157-61 | Slide 14 |
| Mondain V, Lieutier F, Hasseine L, <i>et al.</i> A 6-year antifungal stewardship programme in a teaching hospital. . <i>Infection.</i> 2013; 42 :621-8 | Slide 15 |
| Apisarnthanarak A, Yatraser A, Mundy L. Impact of education and an antifungal stewardship program for candidiasis at a Thai tertiary care center. <i>Infect Control Hosp Epidemiol.</i> 2010; 31 :722-7 | Slide 16 |
| Alfandari S, Berthon C, Coiteux V. Antifungal stewardship: Implementation in a french teaching hospital. <i>Med Mal Infect.</i> 2014; 44 :154-8 | Slide 17 |
| López-Medrano F, San Juan R, Lizasoain M, <i>et al.</i> A non-compulsory stewardship programme for the management of antifungals in a university-affiliated hospital. <i>Clin Microbiol Infect.</i> 2013; 19 :56-61 | Slide 18 |
| Shah DN, Yau R, Weston J, <i>et al.</i> Evaluation of antifungal therapy in patients with candidaemia based on susceptibility testing results: implications for antimicrobial stewardship programmes. <i>J Antimicrob Chemother</i> 2011; 66 :2146–51 | Slide 19 |
| C. Micallef, S. H. Aliyu, R. Santos, <i>et al.</i> Introduction of an antifungal stewardship programme targetting high-cost antifungals at a tertiary hospital in Cambridge, England. <i>J Antimicrob Chemother.</i> 2015; 70 :1908-11 | Slide 20 |
| Guarascio AJ, Slain D, McKnight R, <i>et al.</i> A matched-control evaluation of an antifungal bundle in the intensive care unit at a university teaching hospital. <i>Int J Clin Pharm.</i> 2013; 35 : 145-8 | Slide 24 |
| Bienvenu AL, Argaud L, Aubrun F, <i>et al.</i> A systematic review of interventions and performance measures for antifungal stewardship programmes, <i>J of Antimicrob Chemother,</i> 2018; 73 : 297–305 | Slide 25 |

Key Documents & Guidance

| Document Name | Reference in attached Zip Folder |
|--|----------------------------------|
| British Society for Medical Mycology best practice recommendations for the diagnosis of serious fungal Diseases; Silke Shelenz et al. 2015 | 1. BSSM best practice guidelines |
| Worldwide emergence of resistance to antifungal drugs challenges human health and food security; Mathew C Fisher et al. 2018 | 2. WHO paper |
| Antifungal Stewardship monitoring tool; Laura Whitney | 3. AF Tool |
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| Further Guidance | Web Link |
| Impact of diagnostics – driven antifungal stewardship programme in a UK tertiary referral teaching hospital | Link to study |