Lymphadenopathy and Lymphadenitis in 0 – 18 year olds

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Guideline History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
<th>Approved By</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 2019</td>
<td>First ratified</td>
<td>Dr Groves</td>
</tr>
<tr>
<td>July 2021</td>
<td>Reviewed</td>
<td>Dr Mitchell</td>
</tr>
</tbody>
</table>
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Lymphadenopathy

Introduction

"Lymphadenopathy" refers to enlargement of the lymph nodes.

“Lymphadenitis” (see page 10) refers to enlarged, tender and inflamed lymph nodes.

“Pathological lymphadenopathy” is defined as the enlargement of a lymph node (LN) >1.5 cm in the inguinal region or >1 cm in other areas. Other criteria to consider whether lymphadenopathy is pathological are location, LN characteristics and systemic associated symptoms.

Nearly all children will get lymphadenopathy at some time, usually associated with viral or bacterial infection (45-57% of healthy children may have palpable LNs at any one time). In these cases, it usually occurs near the source of the infection. It is important to take a thorough history and examination in order to identify potential causes of the lymphadenopathy and to direct investigations.

The most common cause of lymphadenopathy is a reaction to viral infections, followed by bacterial infections.

The risk of malignancy is increased if the LN is >2 cm. An unexplained LN of this size warrants investigations (see figure 1).

Red Flags:

- LN size >2cm
- Supraclavicular LN - generally associated with malignancy in children.
- CXR changes suggestive of mediastinal lymphadenopathy or intra-abdominal LNs
- Fixed to muscular layers with no inflammatory signs
- Associated hepatomegaly with no signs of viral infection.
- Severe pallor, jaundice, unexplained bruising/bleeding
- Prolonged fever > 7 days and/or weight loss
- Quick progression
- Persistency > 4-6 weeks
- Presentation in the context of sepsis
- B symptoms from history (fever, night sweats, weight loss)

If the history, examination and basic investigations are highly suggestive of malignancy, urgent discussion with the on call consultant and paediatric oncology team is required for advice regarding further investigations and initial management.
Child with lymph node >1cm (or >1.5cm in inguinal region)

Are there any red flag or concerns for malignancy?
- LN size >2cm
- Supraclavicular LN - generally associated with malignancy in children.
- CXR changes suggestive of mediastinal lymphadenopathy or intra-abdominal LNs
- Fixed to muscular layers with no inflammatory signs
- Associated hepatomegaly with no signs of viral infection.
- Severe pallor, jaundice, unexplained bruising/bleeding
- Prolonged fever > 7 days and/or weight loss
- Quick progression
- Persistency > 4-6 weeks
- Presentation in the context of sepsis
- B symptoms from history (fever, night sweats, weight loss)

Urgent referral to SGH PID (review within 7 days)
Investigations:
- FBC, blood film, U&Es, LFTs, CRP, ESR, LDH, save sample.
- CXR
Discuss with surgical team re excision biopsy.
Discuss with RMH oncology if high suspicion / evidence of malignancy.

No
Duration < 2 weeks?
Yes

Acute lymphadenopathy
Management according to the history/exam

Subacute / chronic lymphadenopathy
Management according to the history / exam

Discuss with paediatric consultant.
Consider Investigations:
- FBC, blood film, U&Es, LFTs, CRP, ESR, LDH.
- Serology (EBV, CMV, toxoplasma, others based on exposure).
- CXR, lymph node ultrasound
- TST/IGRA
- +/- biopsy (refer to surgeons)
Consider discussion with SGH PID.

Viral aetiology
Supportive / symptomatic treatment

Bacterial aetiology
Fluctuant
Yes
Discuss with surgical SpR on call and SGH PID.

Antibiotics: refer to MicroGuide.
Review in 3-4 weeks.

No
Lymphadenopathy not resolved

Figure 1: Flow chart on the investigation and initial management of pathological lymphadenopathy.
(Adapted from St George’s guidelines (6))
Aetiology

The possible causes of lymphadenopathy in children are summarised below in table 1:

**TABLE 1. LYMPHADENOPATHY AETIOLOGY (6)**

**INFECTION:**
- Bacterial Infection: *S. aureus*; Group A *Streptococcus; Bartonella spp*; brucellosis; tularemia (*F. tularensis*); leptospirosis; *Mycobacteria spp* (TB and NTM); spirochete (Syphilis, Lyme disease)
- Viral infection: EBV; CMV; Herpes simplex virus; VZV; Adenovirus; Measles; HIV; Rhinovirus; Influenza; RSV
- Parasitic: Toxoplasmosis; Leishmaniasis; Malaria
- Fungal: Coccidioidomycosis; blastomycosis; histoplasmosis; aspergillosis

**AUTOIMMUNE:**
- SLE; JIA; Kawasaki Disease; sarcoidosis; Kikuchi-Fujimoto Disease

**METABOLIC STORAGE DISORDERS:**
- Gaucher Disease; Niemann-Pick Disease

**IMMUNODEFICIENCY:**
- Chronic Granulomatous Disease (CGD); Leukocyte Adhesion Deficiency

**DRUG RELATED:**
- Phenytoin; Isoniazid; Pyrimethamine; Allopurinol; Phenylbutazone

**VACCINES:**
- MMR, VZV, BCG, DTPa

**MALIGNANCY:**
- Hodgkin lymphoma; Non-Hodgkin lymphoma; Leukemia; histiocytosis; metastatic disease

**IMITATORS:**
- Thyroglossal cyst, thyroid mass, salivary gland enlargement, mumps

Assessment of lymphadenopathy

**Timeframe**
- Acute <2 weeks
- Subacute 2-6 weeks
- Chronic >6 weeks

**Diagnosis**

Diagnosis is based on clinical history, examination and targeted investigations.

**a. History**
- **Duration and progression.** Symptoms associated to the start of the lymphadenopathy.
- **Background of recent infections:** ENT symptoms: (recent gum/tooth infection, mouth ulcers); respiratory symptoms: (stridor/SOB/orthopnea, recent URTI).
- **Background of recent vaccinations** (i.e. BCG, DTPa)
- **Medications**
- **Contact with animals,** especially cats, dogs, birds.
- **Insect bites,** injuries.
- **Travel history** (*Rickettsia, Borrelia, Malaria, Histoplasma, etc.*)
- Contact with tuberculosis (TB)
- **Systematic review:** Fever – constant or periodic, weight loss, fatigue, bone/joint pain, night sweats, rash.
- **Previous antibiotic treatment:** lack of improvement can be related to abscess, viral or MT/NTM aetiology.
- **Previous similar episodes:** if recurrent episodes might be important to evaluate immunodeficiency.
- **Family history:** malignancy, TB, immunodeficiency (including HIV).

**b. Examination**

**General**

- Height, weight, state of health
  - Malnutrition or poor growth suggests chronic disease such as TB, malignancy or immunodeficiency
- Rashes
- ENT
- Abdominal examination: masses / organomegaly

**Lymph node/s - Examine all LN groups** (cervical, supraclavicular, axillary and inguinal)

- **Consistency:** Fluctuant (suggestive of infection), hard (previous inflammation/malignancy), firm and rubbery (malignancy/infection).
- **Fixation:** normal lymph nodes are freely movable in the subcutaneous space. Abnormal nodes can become fixed to adjacent tissues.
- **Tenderness:** typically occurs with inflammatory processes, but it also can occur because of haemorrhage into a node, immunologic stimulation, and malignancy. Thus, tenderness is not particularly helpful in discriminating between infectious and non-infectious causes of lymphadenopathy.
- **Location:** see tables 3 & appendix 1 for possible causes and their associated pattern of lymphadenopathy.
- **Supraclavicular nodes** of any size should be regarded with high index of suspicion.
- **Number:** Higher number of peripheral lymphadenopathy at different sites, including those outside the head and neck, correlated with an increased risk of malignancy.

Symptoms and signs of specific conditions are summarised in Appendix 1.
c. Investigations

For directed investigations please see flow chart above. As a guide for generalised unexplained lymphadenopathy the following investigations are suggested:

**First line:**

- Blood tests: FBC, blood film, LFTs, CRP, ESR, LDH
- Serology for EBV, CMV, toxoplasma (others to be included based on history, i.e. *Bartonella Quintana* and *Bartonella henselae*)
- Throat swab – bacterial (SGA)
- Mantoux test. If TB investigations are required, then please discuss with PID at St George’s Hospital.
- Chest x-ray – mediastinal LNs/mass, hilar lymphadenopathy
- US lymph node depending on clinical history and examination
Second line:

- Serology: Based on exposure: *Borrelia*, *Brucella*, *Bartonella*, *Leishmania*, *HIV*, *Histoplasma*, coccidiomycosis, Syphilis, and other viruses as indicated by clinical features.
- QuantIFERON.
- Autoimmune screening: ANA, RF
- Biopsy/FNA. **Histopathology will depend on clinical presentation and joint discussion with PID/paediatric oncology/surgeons.** Indications for biopsy within four weeks: see Nield and Kamat criteria in box.

**Management of lymphadenopathy**

**Acute Lymphadenopathy (≤ 2 weeks)**

See table 4.

If no response to treatment, further investigations are required and fine needle aspiration/biopsy should be considered.

**TABLE 4. MANAGEMENT OF ACUTE LYMPHADENOPATHY**

<table>
<thead>
<tr>
<th>Likely viral aetiology</th>
<th>NSAID, supportive care, no specific treatment is required.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Likely bacterial aetiology</td>
<td>Fluctuant Requires confirmation with US. Discussion with Surgeons/PID and treatment with antibiotics (as per MicroGuide).</td>
</tr>
<tr>
<td></td>
<td>• Admission and IV treatment: if moderate/severe systemic symptoms, drainage required.</td>
</tr>
<tr>
<td></td>
<td>• Ambulatory management and oral treatment if afebrile and mild systemic symptoms: Re-evaluation in 48-72 h is required.</td>
</tr>
<tr>
<td>Non-fluctuant</td>
<td>Antibiotics (as per MicroGuide). Should be followed up in 3-4 weeks. If severe symptoms – admission required.</td>
</tr>
<tr>
<td>High suspicion of TB aetiology</td>
<td>Discuss with Dr Bhatti / Dr Groves +/- SGH PID for further management.</td>
</tr>
<tr>
<td>Confirmation of SGA aetiology</td>
<td>Penicillin V for 10d</td>
</tr>
<tr>
<td>Drug related LN</td>
<td>Discontinuation of causative drug.</td>
</tr>
</tbody>
</table>

**Nield and Kamat Criteria:** Indications for biopsy within 4 weeks

- Size >2cm
- Increasing size over 2 weeks
- No decrease in size after 4-6wks/not responsive to treatment after 4 weeks
- Abnormal CXR
- Supraclavicular node, or lower cervical region
- Systemic signs and symptoms, rendering to suspicion of malignancy.
Subacute/chronic LN (>2 weeks)
See table 5.

TABLE 5. MANAGEMENT OF SUBACUTE/ CHRONIC LN

<table>
<thead>
<tr>
<th>Positive serology/microbiological confirmation</th>
<th>Treat the specific condition if required (see appendix 1). Discuss with on-call consultant +/- PID for further management.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculin Skin Test ≥ 5 mm</td>
<td>Perform QuantiFERON and further work up to define tuberculosis LN or NTM. Discuss with on-call consultant +/- PID for further investigations and management.</td>
</tr>
<tr>
<td>Negative investigations</td>
<td>Discuss with on-call consultant and consider FNA ± Biopsy.</td>
</tr>
</tbody>
</table>

Referrals
- Discuss with Consultant on call or Dr Bhatti / Dr Mitchell
  Consider referral to:
  - Royal Marsden Hospital if malignancy suspected – Cases are discussed in MDT in RMH.
  - ENT for persistent cervical lymphadenopathy for lymph node biopsy.
  - Infectious diseases team at SGH if infectious cause is suspected. (SGH PID SpR on call #b6124)
  - Paediatric surgeons if persistent inguinal lymphadenopathy or lymphadenopathy at unusual site. (surgical SHO on call #5943)
Cervical Lymphadenitis

Cervical lymphadenitis is enlarged (>1 cm), inflamed and tender lymph nodes of the neck. Acute means the lymphadenitis develops over days but may persist for months. Subacute means the lymphadenitis develops over weeks to months.

Key points to consider in the history include a travel history, TB (past history, family history or contacts) and animal exposure.

Common Infective Pathogens
- Respiratory Viral infections
- Group A Streptococcus (Strep pyogenes)
- Staphylococcus aureus
- EBV
- Anaerobic bacteria (with dental disease)
- Mycobacterium tuberculosis
- Mycobacterium avium complex
- Cat scratch disease (Bartonella henselae)
- Toxoplasmosis
- CMV

Investigations
- Blood investigations are not routinely required unless needing IV antibiotic therapy
  - FBC, blood film, U&E, LFT, CRP, ESR
  - Serology based on history & evaluation
  - Blood culture
- USS is not required in acute lymphadenitis unless worsening despite IV antibiotic therapy or suspected collection requiring drainage
- Fluid/pus for MC&S if incision and drainage performed or spontaneous rupture of abscess

Management

<table>
<thead>
<tr>
<th>Well Appearing</th>
<th>Oral antibiotics for 10 days &amp; Safety-net to return if not improving. Refer to MicroGuide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimally tender</td>
<td></td>
</tr>
<tr>
<td>Not fluctuant</td>
<td></td>
</tr>
<tr>
<td>No red flag symptoms</td>
<td></td>
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</table>

| Neonates or Unwell or         | IV Antibiotics Refer to MicroGuide                                                              |
| Unwell or No improvement with oral antibiotics And not fluctuant |                                                                                               |

| Fluctuant                    | Incision and drainage (but contraindicated in suspected Mycobacterium as may result in sinus formation) |

Red Flags:
- Size >2cm (>1cm in neonate)
- Supraclavicular nodes
- Fixed to underlying structures
- Progressive enlargement
- Weight loss >10%
- Drenching night sweats
- Persistent fever
- Rising ESR/CRP despite antibiotics

Neonates or Unwell or No improvement with oral antibiotics And not fluctuant
## Appendices

### Appendix 1. Summary specific management of LN by aetiology (alternative regimes not included). (6)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Treatment</th>
<th>Comments</th>
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<tbody>
<tr>
<td><strong>Group A</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Streptococcus</td>
<td>Penicillin V</td>
<td>Treatment for 10 days. Refer to BNFc for dosing.</td>
</tr>
<tr>
<td><strong>Bartonella spp.</strong></td>
<td>Azithromycin</td>
<td>Treatment for 5 days. In immunocompetent host, self-limited regional lymphadenitis, treatment normally not required. Discuss with PID. Specially related to contact with young cats.</td>
</tr>
<tr>
<td><strong>Brucellosis</strong></td>
<td>Combination therapy depending on age and organ involvement</td>
<td>Ingestion of unpasteurised milk or undercooked meat. Fever, night sweats, malaise, weight loss, arthralgia, myalgia. Discuss with PID.</td>
</tr>
<tr>
<td><strong>Tularaemia</strong></td>
<td>Aminoglycosides</td>
<td>Fever, skin ulcers, exposure to rabbits/rodents/biting flies/mosquitoes, ingestion of undercooked meats. Discuss with PID.</td>
</tr>
<tr>
<td><strong>TB LN</strong></td>
<td>Quadruple therapy plus pyridoxin.</td>
<td>Referrer to local guidelines on paediatric tuberculosis. Discuss with PID.</td>
</tr>
<tr>
<td><strong>Non-Tuberculosis Mycobacteria</strong></td>
<td>Surgical/medical</td>
<td>Discuss the approach with PID/Surgeons. Young children, less than 5 years. Submandibular are the commonest location. Violaceus discoloration and fluctuation is common. Observation, surgical or medical treatments should be discussed based on individual cases.</td>
</tr>
<tr>
<td><strong>Toxoplasmosis</strong></td>
<td></td>
<td>In immunocompetent host, self-limited regional lymphadenitis, treatment normally not required. Exposure to cats. May have fever, malaise, myalgia.</td>
</tr>
<tr>
<td><strong>Leishmaniasis</strong></td>
<td>Liposomal amphotericin B</td>
<td>Exposure to sand-flies. Important geographic distribution. Visceral leishmaniasis, fever, cutaneous lesions, organomegaly, pancytopenia. Discuss with PID, different treatment regimes.</td>
</tr>
<tr>
<td><strong>Malaria</strong></td>
<td></td>
<td>See Malaria protocol (Pinckney guidelines 2018)</td>
</tr>
<tr>
<td><strong>Lyme disease</strong></td>
<td>Amoxicillin or doxycycline depending on age and organ involvement.</td>
<td>3-week course antibiotics. See Lyme disease protocol (Pinckney guidelines 2018) Discuss with PID.</td>
</tr>
<tr>
<td><strong>Kawasaki Disease</strong></td>
<td>IVIG + aspirin ± Steroids</td>
<td>Fever&gt;5 days, red eyes, peeling skin of hands and feet, red lips, strawberry tongue, miserable. See KD protocol (Pinckney guidelines 2018)</td>
</tr>
</tbody>
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| Section 1 Organisational Policy | Current Version is held on the Intranet | First ratified: July 2019 | Review date: July 2024 | Issue 2 | Page 11 of 17 |
Glossary

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>EBV</td>
<td>Epstein-barr virus</td>
</tr>
<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>TST</td>
<td>Tuberculin skin test</td>
</tr>
<tr>
<td>IGRA</td>
<td>Interferon gamma release assay</td>
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<tr>
<td>NTM</td>
<td>Non tuberculosis mycobacterium</td>
</tr>
<tr>
<td>MT</td>
<td>Mycoplasma tuberculosis</td>
</tr>
<tr>
<td>KD</td>
<td>Kawasaki disease</td>
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<tr>
<td>CSD</td>
<td>Cat scratch disease</td>
</tr>
<tr>
<td>SGA</td>
<td>Streptococcus group A</td>
</tr>
<tr>
<td>RF</td>
<td>Rheumatoid Factor</td>
</tr>
</tbody>
</table>

Supporting References


6. Cervical Lymphadenopathy Guideline, St George’s Hospital.

Supporting relevant trust guidelines

| Section 1 Organisational Policy | Current Version is held on the Intranet | First ratified: July 2019 | Review date: July 2024 | Issue 2 | Page 12 of 17 |
Guideline Governance

a. Scope
This guideline is relevant to all staff caring for all children from 0-18 years old across the emergency department, inpatient ward and outpatient department.

b. Purpose
i. This guidelines aims to facilitate a common approach to the management of children. At times deviation from the guideline may be necessary, this should be documented and is the responsibility of the attending consultant.

ii. This guideline is subject to regular review to ensure ongoing evidence based practice.

c. Duties and Responsibilities
All healthcare professionals responsible for the care of all children 0-18 years should be aware of practice according to this guideline.

d. Approval and Ratification
This guideline will be approved and ratified by the Paediatric Guidelines Group.

e. Dissemination and Implementation
i. This guideline will be uploaded to the trust intranet ‘Paediatric Guidelines’ page and thus available for common use.

ii. This guideline will be shared as part of ongoing education within the Paediatric Department for both medical and nursing staff.

iii. All members of staff are invited to attend and give comments on the guideline as part of the ratification process.

f. Review and Revision Arrangements
a. This policy will be reviewed on a 3 yearly basis by the appropriate persons.

b. If new information comes to light prior to the review date, an earlier review will be prompted.

c. Amendments to the document shall be clearly marked on the document control sheet and the updated version uploaded to the intranet. Minor amendments will be ratified through the Paediatric Guidelines Group. A minor amendment would consist of no major change in process, and includes but is not limited to, amendments to documents within the appendices.
### g. Equality Impact Assessment

#### Background
- Who was involved in the Equality Impact Assessment
- Author and the supervising consultants.

#### Methodology
- A brief account of how the likely effects of the policy was assessed (to include race and ethnic origin, disability, gender, culture, religion or belief, sexual orientation, age)
- The data sources and any other information used
- The consultation that was carried out (who, why and how?)

All groups of staff and patients were taken into consideration and there is no bias towards or against any particular group.

#### Key Findings
- Describe the results of the assessment
- Identify if there is adverse or a potentially adverse impacts for any equalities groups

There is no evidence of discrimination.

#### Conclusion
- Provide a summary of the overall conclusions

There is no evidence of discrimination.

#### Recommendations
- State recommended changes to the proposed policy as a result of the impact assessment
- Where it has not been possible to amend the policy, provide the detail of any actions that have been identified
- Describe the plans for reviewing the assessment

This guideline is appropriate for use.
h. Document Checklist

To be completed (electronically) and attached to any document which guides practice when submitted to the appropriate committee for approval or ratification.

**Title of the document:** Lymphadenopathy and Lymphadenitis

**Policy (document) Author:** Dr Sophie Dowsett (FY1)  
Dr Claire Mitchell (Paediatric Consultant)

**Executive Director:** N/A

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<td><strong>Title</strong></td>
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<td>Is it clear whether the document is a guideline, policy, protocol or standard?</td>
<td>Yes</td>
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<td><strong>2.</strong></td>
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<td><strong>3.</strong></td>
<td><strong>Development Process</strong></td>
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<td>Is there evidence of engagement with stakeholders and users?</td>
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<td>Who was engaged in a review of the document (list committees/ individuals)?</td>
<td>Paediatric Guidelines Committee</td>
<td></td>
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<td>Has the policy template been followed (i.e. is the format correct)?</td>
<td>Yes</td>
<td></td>
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<td><strong>4.</strong></td>
<td><strong>Evidence Base</strong></td>
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<td>Is the type of evidence to support the document identified explicitly?</td>
<td>Yes</td>
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<td>Are local/organisational supporting documents referenced?</td>
<td>Yes</td>
</tr>
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<td>5.</td>
<td>Approval</td>
<td>Does the document identify which committee/group will approve/ratify it?</td>
<td>Yes</td>
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<td>If appropriate, have the joint human resources/staff side committee (or equivalent) approved the document?</td>
<td>N/A</td>
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| 6. | Dissemination and Implementation | Is there an outline/plan to identify how this will be done? | Yes  
On Intranet |
|   |   | Does the plan include the necessary training/support to ensure compliance? | N/A |
| 7. | Process for Monitoring Compliance | Are there measurable standards or KPIs to support monitoring compliance of the document? | N/A |
| 8. | Review Date | Is the review date identified and is this acceptable? | Yes |
| 9. | Overall Responsibility for the Document | Is it clear who will be responsible for coordinating the dissemination, implementation and review of the documentation? | Yes |
| 10. | Equality Impact Assessment (EIA) | Has a suitable EIA been completed? | Yes |
Committee Approval (Paediatric Guidelines Group)

If the committee is happy to approve this document, please complete the section below, date it and return it to the Policy (document) Owner

<table>
<thead>
<tr>
<th>Name of Chair</th>
<th>Date</th>
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</table>

Ratification by Management Executive (if appropriate)

If the Management Executive is happy to ratify this document, please complete the date of ratification below and advise the Policy (document) Owner

Date: n/a