PAEDIATRIC HOSPITAL LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 3: BLOOD AND BLOOD FORMING ORGANS
NEMLC 8 DECEMBER 2022

MEDICINE AMENDMENTS

SECTION	MEDICINE	ADDED/DELETED/NOT ADDED
3.6 Haemophilia A and B	Prophylactic Factor VIII	Under consideration
3.10 Thrombotic Thrombocytopaenic Purpura/Haemolytic Uraemic Syndrome	Cefotaxime	Retained as deleted

3.6 Haemophilia A and B

Prophylactic Factor VIII: Under consideration

Work on evaluating the evidence and cost implications for use of prophylactic factor over on demand therapy has been evaluated in the paediatric setting.

It was however recommended that this was a consideration to be evaluated across levels of care and in both adults and paediatric. A Haemophilia treatment working group has been established to evaluate this and other recommendations around care of patients with haemophilia.

The recommendations will be retained as is while this review is undertaken.

3.10 Thrombotic thrombocytopaenic purpura/haemolytic uraemic syndrome (HUS)

Cefotaxime for the management of infections in neonates with thrombotic thrombocytopaenic purpura/HUS was previously recommended to be removed due as this condition was not common in neonates. An external comment was received indicating that HUS is possible in the neonatal period and there are some published case reports on this.

The Committee acknowledged that this comment affirmed that this is rare in the neonatal period, and retained recommendation to not include Cefotaxime for infections in neonates with thrombotic thrombocytopaenic purpura/HUS.

Changes made prior to external comment

PREVIOUS MEDICINE AMENDMENTS

SECTION	MEDICINE	ADDED/DELETED/NOT ADDED
3.1 Anaemia, Aplastic	Cefotaxime	Deleted
	Amikacin	Deleted

	Ceftriaxone	Retained
	Gentamicin	Added
	Piperacillin-tazobactam	Added
3.2 Anaemia, Haemolytic	Folic Acid	Dose not changed
3.2.2 Anaemia, Sickle Cell	Haemophilis Influenzae type B (HIB) vaccine	Added
	Meningococcal Conjugate vaccine (MCV)	Added
3.3 Anaemia, Megalobastic	Folic Acid	Dose not changed
	Vitamin B12	Dose amended
3.4 Anaemia, Iron Deficiency	Iron (elemental)	Dose not changed
3.6 Haemophilia A and B	Prophylactic Factor VIII	Under consideration
	Pain Stepwise management	Added
3.10 Thrombotic Thrombocytopaenic Purpura/Haemolytic Uraemic Syndrome	Fresh Frozen Plasma/Freeze Dried Plasma	Amended to Specialist Initiated
	Cefotaxime	Deleted

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NEMLC 25 FEBRUARY 2021

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	Amikacin	Deleted
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Approach to a child with a child with a haemotological problem

The initial section of the chapter included the various blood abnormalities and how they could be identified. This was considered to be undergraduate level knowledge and thus not applicable to this guide. This section of text was deleted.

~~**3.1 Combined/multiple abnormalities**~~
~~Bi- or pancytopaenia: systematic disease affecting bone marrow e.g. aplastic anaemia.~~

~~**3.2 Abnormalities of red blood cells**~~
~~Anaemia: haemorrhage, haemolysis, haematinic deficiencies or haematological malignancy.~~
~~Polycythaemia: compensatory mechanism in hypoxia.~~

~~**3.3 Abnormalities of white blood cells**~~
~~Leukopaenia or leukocytosis and abnormal function: infection, tumours, allergies.~~

~~**3.4 Abnormalities of platelets**~~
~~Thrombocytopaenia or thrombocytosis & abnormal function: bleeding, infections.~~

~~**3.5 Abnormalities with bleeding**~~

~~Clotting factors from intrinsic, extrinsic and/or final common pathway and platelet number and/or function abnormal.~~

~~**3.6 Abnormalities with thrombosis and embolism**~~
~~Virchow's triad: vessel/circulation/hypercoagulability - can be arterial or venous.~~

A link to the South African National Blood Services Price list was added to provide access to current pricing.

3.1 Anaemia, Aplastic

Cefotaxime: Deleted
Amikacin: Deleted
Ceftriaxone: Retained
Gentamicin: Added
Piperacillin-tazobactam: Added

The Paediatric Expert Review Committee adopted a similar approach to the management of febrile neutropenia as done in the Adult Hospital Level STGs and EML. A cephalosporin plus gentamicin is recommended if febrile neutropenia occurs within 48 hours of admission. In cases where febrile neutropenia occurs after 48 hours of admission, it is recommended that local antimicrobial resistance patterns be considered, however if these are not known, then to use piperacillin-tazobactam, and adjust based on microbiology results.

For all cases blood should be taken for cultures, and it is recommended that all suspected patients be referred.

3.2 Anaemia, haemolytic

Folic Acid: dose not changed

An external comment was received outlining that the folic acid dose of 2.5 mg/day was generally too high. The South African Medicine Formulary[1] indicates the dose of 1-2 mg/day.

The Paediatric Committee indicated that folic acid is not harmful as excreted in urine. Pragmatically it simplifies dosing if half a tablet (2.5 mg – tablet is 5 mg) can be administered, as opposed to crushing and dissolving, or making a suspension. It was recommended that the dose of 2.5 mg be retained.

3.2.2 Anaemia, Sickle Cell

[1] South African Medicines Formulary, 12th Edition. Division of Clinical Pharmaology , Faculty of Health Sciences, University of Cape Town, and Health and Medical Publishing Group. 2016.

Haemophilius Influenzae, type B (Hib) vaccine: Added
Meningococcal Conjugate Vaccine (MCV): Added

Prophylaxis against infection
Since functional asplenia is present by 1-2 years of age in patients with sickle cell anaemia, the Paediatric Expert Review Committee (ERC) recommended that prophylaxis against infection should be as recommended for post splenectomy. Thus the Hib vaccine and MCV should be added as recommended for post splenectomy.

3.3 Anaemia, megaloblastic

Folic Acid: dose not changed
As for section 3.2 Anaemia, haemolytic.

Vitamin B12: Dose Amended
An external comment was received indicating that the dose of 500 mcg per month was too high. The South African Medicine Formulary[1] and Micromedex[2] states a dose of 100 mcg per month. The Paediatric ERC recommended amending the dose in line with these recommendations. The text was amended as follows:

Vitamin B_{12} deficiency:
• Vitamin B_{12}, IM, ~~500~~ 100 mcg monthly. Should be given together with folate to prevent developmental of subacute combined degeneration of spinal cord. Prolonged treatment may be needed.

3.4 Anaemia, iron deficiency

Iron (elemental): Dose not changed

An external comment was received indicating that the dose of elemental iron was too high, as the South African Medicine Formulary recommends a prophylactic dose of 1 mg/kg/day.

The Paediatric ERC did not agree with this recommendation as the recommended dose of elemental iron for prevention of iron deficient anaemia in premature breast infants is 2-4 mg/kg/day. There was discussion on perhaps including recommendations for formula fed neonates, however it was felt that the majority of babies would be breast fed.

[2] Micromedex Solutions. Licensed subscription (TRUVEN Health).

3.6 Haemophilia A and B

Prophylactic Factor VIII: Under consideration

Currently the Paediatric STGs and EML only recommends for Factor VIII deficiency when a bleed has occurred. It has however been established that replacement therapy (prophylaxis) can prevent bleeds and joint damage, and improve quality of life for patients with haemophilia. [3,4] The concern however with replacement therapy is the cost of the factor needed. A number of pharmacoeconomic reviews have demonstrated the cost-effectiveness of prophylaxis versus on-demand treatment. [5,6,7]

The Paediatric ERC thus recommended consideration of prophylactic Factor VIII. This economic evaluation in planned with assistance from external resources.

Pain management steps added

Due to the varying degree of pain in this condition, and the potential for severe pain; it was proposed that the pain management steps for mild, moderate and severe pain be added. This is in line with the Pain Management Chapter, with the exclusion of NSAIDS.

The following was added:

Mild Pain

- Paracetamol, oral, 15 mg/kg 6 hourly.

Moderate Pain

ADD

- Tilidine, oral, 1 mg/kg/dose (1 drop per 2.5 kg 6 hourly).

Severe Pain:

- Paracetamol, oral, 15 mg/kg 6 hourly.

PLUS

- Morphine, oral [Immediate release morphine (liquid)].
  - Starting dose:
    - If 0 – 1 month of age: 0.05 mg/kg 6 hourly.
    - If > 1–12 months of age: 0.1 mg/kg/dose 4 hourly.
    - If > 12 months of age: 0.2–0.4 mg/kg/dose 4 hourly.

[3] Srivastava A. Haemophilia care – beyond the treatment guidelines. Haemophilia. 2014, 20 (4): 4-10.

[4] Wu R, Luke KH, Poon MC, Wu X, Zhang N, Zhao L, Su Y, Zhang J. Low dose secondary prophylaxis reduces joint bleeding in severe and moderate haemophilic Children: a pilot study in China. Haemophilia. 2011, 17: 70-74.

[5] Unim B, Veneziano MA, Boccia A, Ricciardi W, La Torre G. Haemophilia A: Pharmacoeconomic Review of Prophylaxis Treatment versus on-demand. The Scientific World Journal. 2015.

[6] Thorat T, Neumann PJ, Chambers JD. Hemophilia Burden of Disease: A Systematic Review of the Cost-Utility Literature of Hemophila. J Manag Care Spec Pharm. 2018, 24 (7): 632-642.

[7] Risebrough N, Oh P, Blanchette B, Curtin J, Hitzler j, Feldman BM. Cost-utility analysis of Canadian tailored prophylaxis, primary prophylaxis and on-demand therapy in young children with severe haemophilia A. Haemophilia. 2008, 14(4): 743-752.

Link to active registers were added.

3.9 Immune Thrombocytopaenic Purpura (ITP)

The following comment was added to the medicine section regarding conservative management:

Acute ITP Most cases are self-limiting and will resolve without treatment. Consider such conservative management for mild cases (in discussion with relevant specialist/subspecialist).

3.10 Thrombotic Thrombocytopaenic Purpura/Haemolytic Uraemic Syndrome (HUS)

Fresh Frozen Plasma/Freeze Dried Plasma: Amended to specialist initiated

Concern was raised that in cases of atypical HUS plasma may be harmful. It was thus recommended that the use of both FFP and FDP be specialist initiated.

Cefotaxime: Deleted

The Committee outlined that this condition was not common in neonates, and thus proposed that the recommended cephalosporin alternative in this group, cefotaxime, be removed.