National Transfusion Advisory Group (NTAG) Plan for IBTS, HSE and Hospitals in the Republic of Ireland to address Platelet Shortages

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The NTAG Plan will be considered for update Quarter one 2022.
1 Approach and Development

1.1 The National Transfusion Advisory Group (NTAG) and Clinical Lead Advisor (CLA) for Transfusion Services have engaged with the Irish Blood Transfusion Service (IBTS), HSE, Irish Haematology Society (IHS), Academy of Clinical Science and Laboratory Medicine (ACSLM) and the National Haemovigilance Special Interest Group (NHV SIG), to agree a national plan for platelet shortages.

1.2 This platelet shortage plan applies to platelet shortage from all causes. The 2020 context was preparedness planning for the sustainability and safety of the blood supply, for the WHO declared COVID-19 pandemic.

1.3 At all times all parties will work together to reduce the risk of severe platelet shortages through the management of platelet supply and demand.

1.4 This plan aims to support a continued supply of life saving components, on a national level, with consistent equity of access to patients across the country, so that platelets are available for all essential transfusions and that overall usage is minimised, to conserve stock and ensure that patients with the most urgent demand receive the available supply.

1.5 This plan operates in a similar way to the NTAG plan to address red cell shortages. The framework for ‘Hospital Emergency Blood Management’ preparedness planning should be used for the management of platelet shortages.

2 Background and context

2.1 With national platelet issues near 22,500 in 2019, the increase of 7% on 2018 returned issues to a demand seen in 2014-16. QC testing at IBTS, in 2019, showed a mean platelet count of $3.3 \times 10^{11}$ (range 3-3.8 x $10^{11}$) per apheresis platelet component in a mean volume of 240 ml (range 230-265 ml) and 3.9 x $10^{11}$ (range 3.4-4.4) for pooled platelet components in a mean volume of 300ml with minimal variance. Currently 70% of IBTS platelet components are procured by apheresis and 30% from pooling whole blood derived buffy coats with 90 ml male donor plasma, suspended in platelet additive solution, PAS. This proportion may vary during the course of a shortage. All IBTS platelet components are irradiated prior to distribution, any change to this would require a full risk assessment. Greater than 60% of platelet component orders are for CMV negative components. NTAG will work to reduce this excessive demand through a national guideline on use of CMV seronegative cellular blood components, to more appropriate demand levels. Any difficulty in provision of clinically indicated CMV negative platelet components will be discussed with the requesting hospital unless pathogen reduction is in place.

2.2 Platelet stocks are held at the National Blood Centre (NBC) and the Munster Regional Transfusion Centre (MRTC) of the IBTS. Hospital platelet stocks are only held in HSE facilities- 6 HSE level 3 Hospitals hold a single unit of platelets (Letterkenny, Sligo, Mayo, Portiuncula, Wexford and Drogheda). Additionally, 9 HSE level 4 Hospitals hold 18 units (4 x1, 3 x 2, 2 x 4 units). Platelets are distributed to other Hospitals on a demand basis. Hospital distribution of platelets as stock and availability of platelets by ABO, Rhesus D groups or HLA type will be impacted if shortage occurs.
2.3 Reorganisation of services e.g. to support COVID-19 health care delivery, should be cognisant of platelet availability on any alternative hospital site for critical platelet using services and make suitable arrangements, as appropriate, including for platelet alternatives and additions.

2.4 COVID-19 pandemic related.

While this plan applies to platelet component shortage arising from any circumstances the early 2020 context is preparedness planning for the COVID-19 pandemic.

.1 The main transfusion-associated concern in the context of the COVID-19 pandemic, is interruption and sustainability of the blood supply. Proportionate, precautionary actions to mitigate the possible risks to safety and sustainability will be undertaken by the IBTS, in real time, and reviewed with the evolution of the outbreak, in a manner consistent with governmental and public health policies. Platelet components may not have efficacious alternative therapies, are often life-saving and have limited storage possibilities.

.2 While this is primarily a respiratory virus, spread by the respiratory route, it has the potential for impacting sustainability of the blood supply, and especially short shelf life components such as platelets for which fresh supply is regularly required. Transfusion risk is theoretical-levels of detected RNA in plasma coinciding with clinical symptoms are very low- but precautionary measures are in place. Donor selection, scheduling donations and other social distancing measures can be expected to impact on procurement levels. Component processing and donor testing may be impacted by staff shortage. It is intended that leucodepletion and testing of platelets for bacteria will be maintained. Donor testing systems are not available at time of issue. The introduction of pathogen reduction technology in this context is not supported by the WHO.

.3 Recall - It can be anticipated that recall events will increase.

2.5 Shortage from all circumstances.

.1 Clinical demand will be continuously assessed. Platelet transfusion support will be required for acute life threatening haemorrhage, trauma and critical care, bone marrow failure (especially patients receiving intensive chemotherapy) and for neonates. In a recent UK audit (National Comparative Audit 2017) almost 40% of hospital platelet use was for Haematology services (80% prophylaxis). Demand relating to COVID-19 can be anticipated in patients receiving critical care, where 9% of patients are reported to receive platelet components. The Clinical Lead Advisor for Transfusion informed likely clinical demand during shortage restrictions with a survey of Hospital Transfusion laboratories which identified platelet demand by patient category during COVID-19 related restricted Health Service delivery.

.2 In circumstances of shortage/uncertainty in procurement, there is a requirement for comprehensive conservation approaches to be considered. Specifically, the prophylactic, pre-procedure and therapeutic use of platelets should be considered as one element in haemostasis and alternatives or additions to platelet transfusion should be considered (e.g. anti-fibrinolytic agents- Tranexamic acid TXA; Desmopressin; Fibrinogen), as appropriate.
2.6 Good Patient Blood Management (PBM) with single unit (therapeutic dose) transfusion will save current stock. Second component transfusion should only follow repeat platelet count and clinical assessment, other than in acute life threatening haemorrhage and DIC.

2.7 In shortage, the IBTS will communicate regularly with healthcare personnel responsible for transfusion activities and the Clinical Lead Advisor for Transfusion will act as liaison.

2.8 Distribution arrangements will be kept under review in line with supply and most especially re-organisation of (platelet using) services. There will be active and timely engagement with the HSE unit responsible for distribution in this regard.

2.9 All adverse reactions/events associated with transfusion, or this shortage plan should be reported to the National Haemovigilance Office (NHO).

3 Rationale

3.1 The framework described below is designed to ensure that all parties work in a consistent, integrated manner to manage platelet shortages.

3.2 The appropriate use of platelet components and use of appropriate alternatives and additions are important public health and clinical governance issues. This plan is designed to support actions taken by Hospitals to improve transfusion safety and adopt Patient Blood Management (PBM) principles.

4 Plan Structure

4.1 The plan is structured to provide a framework of actions in three phases. A schematic of the plan is shown in Appendix 1.

Green: Normal circumstances where supply meets demand
Amber: Reduced availability of platelet components
Red: Severe shortage of platelet components.

4.2 During the green phase, should an issue arise with the platelet supply, the IBTS will issue a precautionary notification to the Hospital Lead Haematologist for blood transfusion and Chief/Senior Medical scientist (C/SMS) transfusion laboratory, informing them of potential issues, and asking Hospitals to take appropriate action to protect the supply chain. This action is intended to prevent the requirement to move to the Amber phase. Each Hospital should integrate this platelet shortage plan into their Emergency Blood Management (EBM) planning process.

4.3 The IBTS will actively strive to minimise the risk of platelet shortages. However, if platelets fall to a pre-determined level then the IBTS may activate shortage plans and communicate a move to the Amber phase. All Hospitals should invoke this plan at the same time, ensuring best response to the shortage. Hospital stock holding will be re-organised by the IBTS. Decision making to reduce usage by categorising patient demand is supported by Appendix 2 “Categorisation of Patient Types”. Category 3 patients are the lowest priority and should be the first to have
NTAG Plan to minimise health impact of platelet shortage (including COVID-19 Pandemic)

platelet transfusions reduced/withheld. There will be increased monitoring and movement of the national stock to ensure platelets are distributed, by residual shelf life and groupings, to minimise wastage.

4.4 Should the IBTS identify a severe imminent threat to platelet supply, then the IBTS may communicate and move directly to the red phase and request that only patients in category 1 are treated and hospital stock holding will be discontinued – see Appendix 2.

4.5 Hospitals are required to have emergency blood management (EBM) plans in place in order to respond to such notifications from the IBTS.

5 IBTS Actions

National platelet stock is monitored daily and production levels amended, where possible, to keep to a pre-set target level. Supply threats e.g. COVID-19, may impact on the feasibility of normal remedial actions. A structured review process is in place for such threats and was activated for the COVID-19 emergency and will be activated for other emergencies/threats.

6 Hospital Emergency Blood Management (EBM) Plans

6.1 The Hospital platelet shortage plan should be integrated into the Hospital Emergency Blood Management (EBM) plan - see Hospital Emergency Blood Management (EBM) plan for Managing Shortages of Blood Components.

6.2 The proposed generic actions for Hospitals at Green, Amber and Red phases are outlined in Appendix 3.

6.3 Once the arrangements have been formulated, they should be managed by the Hospital Transfusion Team and be enforced, when required, by Senior Clinical Staff representing the main clinical users of platelets.

6.4 Should national shortage occur, the IBTS will activate their emergency plan and notify Lead Haematologists for Transfusion and C/SMS transfusion laboratories to implement the Hospital EBM plan. The IBTS will communicate with Lead Haematologists for Transfusion and C/SMS for the duration of the shortage. The Clinical Lead Advisor for Transfusion will act as liaison.

The integration of the platelet shortage plan with the EBM plan should have the support of the Chief Executive/Hospital Manager and Clinical Lead. Clinical staff should be aware of their existence and be willing to accept that a decision making process, however difficult, is necessary when the supply of platelets is limited.

7 Indications for Platelet Transfusion

7.1 The indications for transfusion of platelets are available at each Hospital and should be based on published Guidelines or Randomised Controlled trials (British Society for Haematology ‘Guidelines for the use of Platelet transfusion’ 2016 and ‘Guidelines on transfusion for fetuses, neonates and older children’ 2016: PlaNeT2, Randomised Trial of Platelet Transfusion Threshold in Neonates : NICE Coronavirus (COVID-19) Guidance www.nice.org.uk/guidance/ng24/chapter/recommendations).
7.2 Practice should be evidence based with a therapeutic dose (single platelet component) transfused. Only consider giving more than a single dose of platelets in a transfusion for patients with severe thrombocytopenia and bleeding in a critical site. Reassess the patient’s clinical condition and check their platelet count after each platelet transfusion, and give further doses if needed.

7.3 Compression, Radiological guidance and thrombogels/fibrin sealants should be used, as appropriate.

7.4 Alternatives or additions to platelet transfusions should be considered such as –

- Tranexamic acid TXA for trauma, anticipated surgical bleeding (>500 mls) and short term for patients with chronic thrombocytopenia and bleeding;
- Desmopressin may be appropriate in specific circumstances – seek Haematologist advice;
- Fibrinogen to maintain fibrinogen level at 1.5-2 g/L in the case of trauma, obstetric or surgical bleeding. Where possible, anaemia should be corrected.

7.5 Prophylactic platelet transfusion is standard of care in patients receiving intensive chemotherapy or post allogeneic Bone Marrow Transplantation with platelet count threshold of 10x10^9/L

7.6 Platelet count thresholds are as indicated below for common presentations but see BSH Guidelines for comprehensive guidance.

7.6.1 Adults and older children

<table>
<thead>
<tr>
<th>Therapeutic –</th>
<th>Prophylactic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>Not bleeding</td>
</tr>
<tr>
<td>WHO Grade 2</td>
<td>transfuse where platelet count &lt;10 x10^9/L (exclude Ch BMF, ITP, HIT, TTP)</td>
</tr>
<tr>
<td>WHO Grade 3,4/critical site</td>
<td>20-50 x10^9/L ( &lt;20 x 10^9/L CVC non-tunneled, &lt;40 prior to LP)</td>
</tr>
<tr>
<td>up to 100 x10^9/L</td>
<td>where high risk of bleeding 50-75 x10^9/L</td>
</tr>
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</table>

7.6.2. Neonates and preterm infants

- Where no evidence of major haemorrhage in previous 72 hours - transfuse with platelet count threshold 25 x10^9/L (Major haemorrhage for this purpose is defined as grade III/IV intraventricular haemorrhage or pulmonary haemorrhage necessitating ventilatory change)
- Bleeding, current coagulopathy, before surgery – transfuse with platelet count < 50 x10^9/L
- Major bleeding, pre major surgery - transfuse with platelet count <100 x 10^9/L
- Discuss NAIT with Haematologist

NTAG Plan to minimise health impact of platelet shortage (including COVID-19 Pandemic)
8 Operation of the Plan

8.1 Green Phase

8.1.1 Hospitals should integrate this platelet shortage plan with their emergency blood management plan. This should show how a reduction in usage will be achieved.

8.1.2 The IBTS and the Clinical lead Advisor for Transfusion will develop communications to support Hospitals as effectively as possible during shortage.

8.1.3 The IBTS monitors platelet stock daily and amends procurement/processing accordingly. In the context of COVID-19 opportunity for increasing procurement may be limited. There is on-going monitoring of platelet Hospital distribution and wastage. A structured review process is in place for the COVID-19 emergency.

8.1.4 Clinical audit should be undertaken against agreed guidelines to establish the fate of all platelet components. Patient Blood Management (PBM) principles should be adopted to support appropriate use and minimise wastage. Every request for transfusion should clearly state the indication and the agreed protocol/transfusion threshold should be implemented. Demand for CMV screened negative blood components should be clinically indicated.

8.1.5 It is acceptable to use ABO-incompatible platelets, negative for high titre agglutinins, in the management of patients with major haemorrhage (BSH Major haemorrhage addendum, March 2017)

8.2 Amber Phase

8.2.1. If national stocks fall to a pre-determined level the IBTS will communicate with Hospitals and move to the Amber phase.

8.2.2. Information from the IBTS about platelet shortages will be communicated to the Hospital by a number of channels. This will include the nature of the shortage and the actions for Hospitals to undertake as part of their Emergency Blood Management (EBM) Plan.

8.2.3 All Hospitals should activate their emergency blood management (EBM) plan.

8.2.4. Hospital stock holding of platelets will be immediately restricted. Hospital orders will be for specific identified requirements for platelet transfusion or as required to cover procedures/Services. During this phase the residual platelet shelf life may be significantly reduced.

8.2.5. Additional measures that may be required at each Hospital include restriction of platelet transfusion as identified by categories of patients -see Appendix 2.
In the Amber phase all requests for platelet components from the Hospital transfusion
laboratory should be as authorised by the Consultant Haematologist/designee and usage restricted to patients in Category I and II (including HLA/HPA matched platelets).
Platelets transfusion for prophylaxis should be restricted.
Platelet residual shelf life may be reduced.
Platelets of alternate ABO group are more likely to be made available (but in line with BCSH adult and paediatric guidelines).
Availability of CMV negative platelets may be limited. Demand should be clinically indicated.
Rh D negative platelets will be prioritised for Rh D negative females of childbearing potential and patients less than 18 years. Rh D Positive platelets may be issued for Rh D negative patients (this can be supported by anti-D immunoglobulin administration- 250 iu anti-D Ig provides cover for five adult units of platelets). Where possible, optimise pre-operative preparation of patients and consider alternatives or additions to platelet transfusions.

8.2.6. The IBTS may be required to take further action, over and above that of the Green Phase, to maximise the supply of available platelets. Suspension of bacterial screening may be considered. In the context of COVID-19, it is not expected that suspension of bacterial screening will be required to bring platelets into stock earlier (WHO). Such change, without a pathogen reduction process in place, will be notified to the HPRA. This will become irrelevant should the IBTS introduce a pathogen reduction process for platelet components.

8.2.7. The IBTS will monitor demand from Hospitals ongoingly.

8.2.8. When platelet stocks return to a sustainable level, the IBTS will communicate to Hospitals that the Amber phase no longer applies and that orders can return to normal. However, should stocks continue to fall, the IBTS may communicate that a greater reduction in usage is required, necessitating the declaration of a Red phase.

8.3 Red Phase

8.3.1 The IBTS will declare a Red phase shortage if there is severe shortage of platelets or if an imminent threat to the supply of platelets is identified.

8.3.2 The IBTS will communicate with Hospitals as in the Amber Phase. Information will include the nature of the shortage and the actions that need to be taken by Hospitals as part of their EBM plan. This includes further reduction in usage over the Amber phase and restriction of platelet usage to patients in category 1 - see Appendix 2.

8.3.3 Requests for platelet components must be made by a Consultant Haematologist/designee and will be referred to the IBTS Medical team. Such requests should include the patient identifiers, the indication for transfusion, the requesting Consultant’s name and contact details, the patient category and the patient blood group.
8.3.4 During the red phase, the IBTS will track platelet distribution and Hospitals will be requested to establish the fate of each unit delivered to them, with feedback to the IBTS. Any platelet components not used should be made available for re-routing to an alternative Hospital, to minimise any wastage of platelets and support urgent cases. Timely communication with the HSE and IBTS is essential to maximise potential for alternative use.

9 Impact and Monitoring of Shortages

9.1 The uncertainty of blood supply through the COVID-19 pandemic is a reminder to all, of the requirement for attention to ensure appropriate use of platelets at all times.

9.2 A declared shortage scenario will need to be accompanied by a reduction in Hospital use of platelet components.

9.3 Hospitals should report adverse incidents in patients or with the operation of this plan, through local governance systems, the IBTS complaints system and the NHO.

10 Recovery from Shortages

10.1 The IBTS will contact the Transfusion Laboratories to let them know that stocks have risen to a level where hospitals can move to Amber or Green phase.

10.2 The Lead Consultant Haematologist for Transfusion /designee and Chief/Senior Medical Scientist Transfusion Laboratory will disseminate the information as above. The EBM group should convene to review the effect of the platelet shortage and identify any enhancements to local arrangements. Any recommendations should be fed back to the Hospital Transfusion Committee.
Appendix 1: Schematic of Platelet Shortage Plan

**GREEN**
- Actions to ensure appropriate use of platelets and alternatives and additions
- Ensure EBM plan current
- Stock holding Hospitals to assess current stockholding

**AMBER**
- Action Amber EBM plan
- Stock holding Hospitals to restrict stock holding
- Maximise use of stock
- Make available unused platelets for other Hospitals

**RED**
- Action Red EBM plan
- Reduce usage further to category 1 patients
- Provide data set for all requests
- Discuss with IBTS medical team

**IBTS**
- Manage national stocks
- Develop shortage plans
- Develop communications

- IBTS communicates Amber shortage to hospitals and required actions

- IBTS communicates return to Green if shortage is concluded

- IBTS communicates further usage reduction required if shortage continues

- IBTS communicates return to Amber if shortage becomes less severe

- IBTS communicates Red shortage if further usage reduction required

- IBTS communicates return to Green if shortage is concluded
Appendix 2: Categorisation of Patient Types

The following table provides general guidance for the use of platelet transfusions in the context of reduced availability of all platelet groups. Maximise use of available platelet components by following recommendations in Appendix 3 (Amber alert section). The use of platelets should be considered as one element in the overall management of these patients. Use should be guided by the clinical condition of the patient and laboratory/near patient testing.

Table X Platelet Transfusion in times of Shortage (BSH, 2016)

<table>
<thead>
<tr>
<th>Category 1</th>
<th>Category 2</th>
<th>Category 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>These patients have the greatest clinical need for platelet support and should be given priority-Patients to be treated in Red Phase</td>
<td>Patients to be treated in Red and Amber Phases</td>
<td>These patients are the lowest priority, the first to have platelet transfusion withheld - will not be transfused in the Amber phase</td>
</tr>
</tbody>
</table>

**Massive haemorrhage & Critical care**
Massive transfusion for any condition, including obstetrics, emergency surgery and trauma, with on-going bleeding, maintain platelet count > 50 x 10^9/L.

Multiple trauma or CNS trauma, aim for platelet count >100 x 10^9/L. Bleeding in the presence of sepsis/acute DIC, maintain platelet count >50x 10^9/L.

**Critical care**
Patients resuscitated following massive transfusion with no on-going active bleeding, maintain platelet count > 50 x 10^9/L.

**Surgery**
Planned Elective, non-urgent surgery likely to require platelet support for thrombocytopenia or congenital/ acquired platelet defects

**Bone marrow failure**
Active bleeding associated with severe thrombocytopenia or functional platelet defects

**Immune thrombocytopenia**
if serious/life-threatening bleeding

**Bone marrow failure**
All other indications except those in category 1 or 3

*Bone marrow failure*
- Prophylactic transfusion of stable patients following autologous stem cell transplant.

**Neonates**
For preterm neonates with very severe thrombocytopenia (platelet count below 25 x 10^9/L) platelet transfusions should be administered in addition to treating the underlying cause of the thrombocytopenia. Suggested threshold counts for platelet transfusions in other situations are given in the BSH guidelines.

*prophylactic transfusion category should include WHO grade 1 bleeding (as in TOPPS trial). Exclusions – previous WHO > grade 3 bleed, inherited haemostatic or thrombotic disorder, requirement for therapeutic doses of anticoagulation, acute promyelocytic leukaemia, prior to surgery/invasive procedure

- 43 patients required treatment with prophylactic transfusions to prevent 1 patient from bleeding in a 30 day period Vs 5 patients for Chemotherapy/allogenic stem cell transplants (Stanworth et al, 2013)
Appendix 3: Proposed Generic Actions for Hospitals at each Phase

**Green Phase** – Secure arrangements for the appropriate use of platelet components

- Each Hospital should have guidelines, training and audit to support safe and appropriate prophylactic, pre-procedure and therapeutic use of all platelet components and alternatives and additions to platelet transfusion.
- Wherever possible drugs affecting platelet function should be discontinued pre-operatively in a timely manner.
- A Hospital Emergency Blood Management (EBM) plan should include management of platelet shortage to ensure consistent, appropriate use of platelets.
- Hospitals should ensure that every request for transfusion clearly states the indication.
- All relevant Hospital staff should be aware of the emergency blood management (EBM) plan.
- Hospitals should engage in local/regional re-routing of platelet components in a manner that enables the receiving Hospital to utilise the transferred components.
- Hospitals should establish local protocols to empower blood transfusion laboratory staff to ensure that appropriate clinical information is provided with request for platelet transfusion and to query clinicians about the appropriateness of request for platelets against local guidelines.

**Amber Phase** – Secure arrangements to reduce usage

- Hospital stock holding of platelet components will be restricted and restructured.
- Hospitals should maximise the use of available platelets through accepting platelets procured by apheresis or pooled, shorter residual shelf life platelets, more frequent variations in ABO group, Rhesus D positive platelets for D negative patients (with anti-D Ig administration), and reduction of CMV negative components.
- Alternatives for HLA/HPA matched platelets may have to be considered.
- Hospitals should ensure that all requests are by Senior Clinical Staff.
- All possible alternatives and additives to transfusion of platelets should be considered.
- Patient outcomes post transfusion should be monitored to inform further transfusion support

**Red Phase** – Restrict supply to category 1 patients only

- Hospitals will manage platelet supply as per Amber Phase and in addition restrict transfusion to Category I patients only.
- Clinical Haematologists/designee will provide individual patient requirements for discussion with the IBTS Medical team.
- Chief/Senior Medical Scientists should provide information to IBTS to assist with tracking/transfer of platelet components.

**References**

Curley A et al for Pia Ne T2 MATISSE Collaborators, Randomised Trial of Platelet Transfusion Threshold in Neonates. NEJM, 2019;380: 242-51