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INTERCEPT® Blood System for Platelets Pathogen Reduction System

Frequently Asked Questions (FAQs)

1. What are the benefits of INTERCEPT treated platelets (INTERCEPT Platelets*)?

- **Protect Patients**
  - » INTERCEPT Platelets provide broad spectrum pathogen inactivation†, targeting not only bacteria, but also viruses and protozoan parasites, reducing the risk of transfusion-transmitted infection (TTI) and sepsis; leukocytes (T-cells) are also inactivated to prevent transfusion-associated graft vs host disease (TA-GVHD).[1]
- **Improve Availability**
  - » INTERCEPT Platelets help pandemic preparedness through proactive inactivation of certain emerging pathogens;† sustained platelet availability during outbreaks has been demonstrated with pathogen reduction (PR).[2,3]
  - » INTERCEPT Platelets are released to hospitals earlier than conventional, tested platelets (large-volume delayed sampling - LVDS) with comparable usable shelf-life.[4,5]
  - » Conventional, tested platelets (LVDS tested platelets) have a higher overall positive rate, including false positives, which may lead to product discards and associated recalls.[6-8]
- **Deliver Value**
  - » INTERCEPT Blood System offers cost offsets with the ability to replace certain tests/procedures (CMV testing, babesia tests, malaria deferrals, and irradiation).[1,9-13]

2. Is amotosalen (a type of psoralen) safe?

- Yes. Psoralens are common in nature and found in a wide variety of foods, including citrus fruits, celery, carrots, figs, and many traditional food seasonings.
- The safety of INTERCEPT Blood System has been demonstrated in several animal models, in vitro, and in vivo studies.[14-17] Animal toxicity studies have shown no risk associated with amotosalen at 10,000 times the anticipated clinical exposure[15,18,19], no adverse reproductive or developmental effects in neonatal rats[20], and no evidence of carcinogenicity at 1,200 times the routine exposure for a transfusion using INTERCEPT Platelets.[21]
- PIPER, the largest platelet transfusion study to-date, demonstrated the safety of INTERCEPT Platelets in routine clinical use, showing no difference in adverse events or mortality between PR and conventional platelets.[22]
- Over 1.2 million INTERCEPT Platelets have been monitored through multi-center[23,24] and nationally mandated hemovigilance (HV) programs,[25-29] with reduced transfusion transmitted bacterial infections (TTBIs), no sepsis-related fatalities, and no TA-GVHD cases.
- Patients with a history of hypersensitivity reaction to amatosalen or other psoralens should not use INTERCEPT Platelets. However, no cases of psoralen or amatosalen hypersensitivity reaction have been reported to Cerus.

3. What data on INTERCEPT Platelets supports safety for neonatal and pediatric patient populations?

- A seven-year, multi-center active HV program in 21 hospitals tracked transfusions in pediatric and neonatal patients. Similar rates of adverse events were observed for patients receiving INTERCEPT Platelets versus conventional platelets with no reports of any adverse events in the NICU population.[23]
- INTERCEPT Platelets showed no significant difference in number or types of transfusion reactions when assessed for safety and efficacy in NICU and pediatric populations.[30]
- INTERCEPT Platelets were evaluated on rates of transfusion and transfusion reactions in pediatric and neonatal patients and showed no significant difference compared to conventional platelets.[31]
- In a study across four centers and three countries, INTERCEPT Platelets had no difference in transfusion reaction rates when evaluated for pediatric patients.[32]

* INTERCEPT Platelets are psoralen-treated platelets treated by the INTERCEPT Blood System. † There is no pathogen inactivation process that has been shown to eliminate all pathogens. Certain non-enveloped viruses (e.g. HAV, HEV, B19, and poliovirus) and *Bacillus cereus* spores have demonstrated resistance to the INTERCEPT process.

4. What are the indicated uses for INTERCEPT Platelets*?

- INTERCEPT Platelets can be used according to US standards of care in all patient populations except patient populations with contraindications listed on the package insert.[1]

5. What are the contraindications for INTERCEPT Platelets?

- Patients with a history of hypersensitivity reaction to amotosalen or other psoralens should not use INTERCEPT Platelets.
  - » Note: No cases of psoralen or amotosalen hypersensitivity reaction have been reported to Cerus.
- INTERCEPT Platelets should not be used for neonatal patients treated with phototherapy devices that emit a peak energy wavelength less than 425 nm or have a lower bound of the emission bandwidth less than 375 nm, due to the potential for erythema resulting from interaction between ultraviolet light and amotosalen.
  - » Note: The American Academy of Pediatrics Clinical Practice Guidelines recommend a spectrum between 460 and 490 nm (visible light) for intensive phototherapy, which is outside the bounds of the INTERCEPT contraindication language. None of the neonatal phototherapy devices approved for market in the US today emit a peak wavelength below 425 nm, and/or a lower bound of the emission bandwidth less than 375 nm.[33]

6. LVDS 48hr (LVDS) tested platelets have a 7-day storage claim. Why should we use INTERCEPT Platelets, which have a shorter shelf-life?

- While LVDS tested platelets have a 7-day storage claim, they require a hold time of 60 hours prior to platelet release. Therefore, the usable shelf-life for LVDS tested platelets is not 7 days, but rather ~5 days. Studies have demonstrated greater or comparable usable shelf-life between INTERCEPT Platelets and LVDS tested platelets.[5,6]
- INTERCEPT Platelets can be released as early as day 1, meaning flexibility in managing inventory and the ability for hospitals to transfuse platelets sooner.[5,6]
- INTERCEPT Blood System allows for the transfusion of younger, fresher platelets, with recent studies showing that INTERCEPT Platelets were on average two days younger than LVDS tested platelets at time of transfusion.[5,6]

7. Do INTERCEPT Platelets have an impact on Count Increments (CIs) or Corrective Count Increments (CCIs)?

- Platelet transfusions are intended to stop bleeding, so the most direct method to measure clinical efficacy is to assess the prevention and treatment of bleeding. CI and CCI do not correlate with bleeding outcomes and are therefore a poor measure of bleeding tendency.[34-38]
- CI/CCI are dependent on a variety of variables, including a patient's underlying condition (e.g., fever, splenomegaly, etc.), platelet dose and processing, and transfusion history.[39] A low response does not necessarily indicate a lack of platelet efficacy.
- While some studies have reported a decrease in CI and CCI with INTERCEPT Platelets compared to conventional platelets,[34,40]multiple studies have shown that hemostasis, along with platelet and red blood utilization are comparable, indicating INTERCEPT Platelets are effective for bleeding control.[34,36,41-47]

8. Is there a difference in platelet and/or red blood cell (RBC) utilization and does the use of INTERCEPT Platelets increase the number or transfusions needed?

- HV studies on the large-scale, routine use of INTERCEPT Platelets demonstrated comparable findings for clinical hemostasis, platelet utilization, RBC utilization, or instance of refractory response to platelet transfusion when compared to conventional platelets.[43-45]
- Large-scale HV programs in France, Belgium, and Austria reported that routine use of INTERCEPT Platelets does not lead to increase platelet or RBC component utilization compared to conventional platelets in various patient populations.[43,45,46]
- A retrospective analysis of platelet use at a large Austrian hospital found no difference in either platelet or RBC utilization over two 21-month periods, before and after use of INTERCEPT Platelets in all patient populations.[44,46]
- A review of nine clinical trials found comparable results for clinically significant or severe bleeding, or in red cell transfusion requirements between conventional and PR platelets.[48]
- A meta-analysis of five randomized controlled trials found no difference in bleeding trends with INTERCEPT Platelets versus conventional platelets.[49]

* INTERCEPT Platelets are psoralen-treated platelets treated by the INTERCEPT Blood System.

9. Can you provide support that INTERCEPT Blood System can replace irradiation?

- Our FDA approved package insert states that the INTERCEPT Blood System is approved for use as an alternative to gamma irradiation for prevention of TA-GVHD.[1]
- AABB Standard 5.19.4.1 states: "Methods known to prevent transfusion-associated graft-vs-host disease [TA-GVHD] shall be used and include either irradiation or the use of a pathogen reduction technology that is known to inactivate residual leukocytes and is cleared or approved by the FDA or Competent Authority."[13]
- INTERCEPT cross-links RNA or DNA approximately once per 83 base pairs, which ensures greater inactivation of genes - modifying DNA >400 times more often than gamma irradiation (~1 strand-break per 37,000 base pairs).[50]
- In vitro leukocyte cytokine production was substantially reduced with INTERCEPT Platelets* compared to both conventional and gamma irradiated platelets, indicating T-cell inactivation.[51]

10. Can you provide support that the INTERCEPT Blood System can replace CMV testing?

- AABB Standard 5.19.2 states that "The BB/TS [Blood Banks/Transfusion Services] shall have a policy regarding transfusion of cellular components selected or processed to reduce the risk of cytomegalovirus (CMV) transmission."[13]
- The INTERCEPT Blood System demonstrates inactivation of CMV in platelets in PAS-3 at ≥ 4.9 $\log^{10}$ reduction.[1]

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References

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Contraindications

Contraindicated for preparation of platelet components intended for patients with a history of hypersensitivity reaction to amotosalen or other psoralens. Contraindicated for preparation of platelet components intended for neonatal patients treated with phototherapy devices that emit a peak energy wavelength less than 425 nm, or have a lower bound of the emission bandwidth <375 nm, due to the potential for erythema resulting from interaction between ultraviolet light and amotosalen.

Warnings and Precautions

Only INTERCEPT Processing Sets for platelets are approved for use with the INTERCEPT Blood System. Use only the INTERCEPT INT100 Illuminator for UVA illumination of amotosalen-treated platelet components. No other source of UVA light may be used. Please refer to the Operator's Manual for the INT100 Illuminator. Discard any platelet components not exposed to the complete INT100 illumination process.

Tubing components and container ports of the INTERCEPT Blood System contain polyvinyl chloride (PVC). Di(2-ethylhexyl)phthalate (DEHP) is known to be released from PVC medical devices, and increased leaching can occur with extended storage or increased surface area contact. Blood components will be in contact with PVC for a brief period of time (approx. 15 minutes) during processing. The risks associated with DEHP released into the blood components must be weighed against the benefits of therapeutic transfusion.

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