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| PRE-DEFINED SUSPECTED GRADE 3 or 4 DRUG TOXICITY |

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| *The medicines being used in PB-SAM are licensed drugs with a known profile of adverse reactions. Assessment of safety will therefore focus on severe and causally related events. Clinical or laboratory toxicity will be reported if Grade 3 or 4 according to the Division of AIDS table for grading severity of adverse events:* [*http://rsc.techres.com/Document/safetyandpharmacovigilance/DAIDS\_AE\_Grading\_Table\_v2\_NOV2014.pdf*](http://rsc.techres.com/Document/safetyandpharmacovigilance/DAIDS_AE_Grading_Table_v2_NOV2014.pdf)  *If abnormalities are known to be already present at enrolment, or are due to other identifiable factors, this need not be reported as a causally-related toxicity. Only record new events whilst the child is receiving study drugs.*  *Always act in the best interests of the child. When possible, discuss any decisions* *regarding stopping study drugs because of suspected toxicity with the PB-SAM PI, clinical lead, designee or local safety monitor. They can also prove information on other aspect of management of adverse reactions.*  *A grade 3 or 4 toxicity event may also constitute an SAE, and should also be reported on an SAE CRF.* |

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| 1. **STUDY MEDICATION DETAILS** | |
| * 1. **Which study drugs  is the child receiving?**  1. **Pancreatic Enzymes/Placebo**    1. Date and time of start    2. How many doses have been given? | 🞏 **Pancreatic Enzymes/Placebo**  \_\_ \_\_ / \_\_ \_\_ / \_\_ \_\_ \_\_ \_\_ \_\_ \_\_ : \_\_ \_\_ *24h Clock*  ***D D / M M / Y Y Y Y***  *h h m m*  \_\_\_ \_\_\_ doses |
| 1. **Bile Acids/Placebo**    1. Date and time of start    2. How many doses have been given? | 🞏 **Bile Acids/Placebo**  \_\_ \_\_ / \_\_ \_\_ / \_\_ \_\_ \_\_ \_\_ \_\_ \_\_ : \_\_ \_\_ *24h Clock*  ***D D / M M / Y Y Y Y***  *h h m m*  \_\_\_ \_\_\_ doses |

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| *tick all that apply* | 1. SUSPECTED GRADE 3 or 4 TOXICITY Definition |
| * 1. Allergic & Cutaneous | **🞏 Not applicable**  🞏 Generalized urticaria Clinical diagnosis  🞏 Angioedema with intervention indicated Clinical diagnosis  🞏 Symptoms of mild bronchospasm Clinical diagnosis  🞏 Acute anaphylaxis Clinical diagnosis  🞏 Life-threatening bronchospasm Clinical diagnosis  🞏 Laryngeal oedema Clinical diagnosis |
| * 1. Diarrhoea | **🞏 Not applicable**  🞏 Increase of ≥ 7 stools per 24-hour period  🞏 IV fluid replacement indicated  🞏 Life-threatening consequences (e.g., hypotensive shock) |
| * 1. Hepatic | **🞏 Not applicable**  🞏 Abnormal liver function ALT 5.0 to < 10.0 x ULN  🞏 Abnormal liver function Total bilirubin 2.6 to <5.0 x ULN  🞏 Abnormal liver function ALT > 10.0 x ULN  🞏 Abnormal liver function Total bilirubin >5.0 x ULN |

***Write details in the description box on the next page; ULN, upper limit of normal based on local laboratory reference values***

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| * 1. **Was the study drug stopped?** | ⬜ Y\* ⬜ N | If Y, Date:  \_\_ \_\_ / \_\_ \_\_ / \_\_ \_\_ \_\_ \_\_  ***D D / M M / Y Y Y Y*** | Time:  \_\_\_ \_\_\_: \_\_\_ \_\_\_ |

***\* if Y, also complete the drug discontinuation section in the Study Conclusion CRF***

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| * 1. **Description** *including concurrent medication, management undertaken and outcome* | | | |
| 1. **Toxicity CRF completed by** *initials* | \_\_ \_\_ \_\_ | Date  \_\_ \_\_ / \_\_ \_\_ / \_\_ \_\_ \_\_ \_\_  ***D D / M M / Y Y Y Y*** | Time  \_\_\_ \_\_\_: \_\_\_ \_\_\_ |
| 1. **Toxicity CRF Reviewed by** *initials* | \_\_ \_\_ \_\_ | Date  \_\_ \_\_ / \_\_ \_\_ / \_\_ \_\_ \_\_ \_\_  ***D D / M M / Y Y Y Y*** | Time  \_\_\_ \_\_\_: \_\_\_ \_\_\_ |