

Supplementary Material: Summary of protocol amendments

- 16/12/2007 **Substantial Amendment 1:** Amendment to protocol concerning use of 6MP in pregnancy/subjects of childbearing age, switch to matching placebo (rather than over-encapsulation) supplied by GSK and amendment to safety blood procedures.
- 18/11/2008 **Substantial Amendment 3:** Use of all Scottish district hospitals for referrals, repeat safety bloods not required at V2, clarifications to protocol: V2 \leq 7 days of V1; point 3 of inclusion criteria added.
- 15/06/2009 **Substantial Amendment 5:** Reduce number of colonoscopies and clarification in PIL/Consent the types of sample and how they are handled and stored.
- 07/07/2008 **Substantial Amendment 6:** Decision to stop study drug if subjects prescribed Allopurinol.
- 15/12/2009 **Substantial Amendment 7:** Amendment to safety assessments in protocol, prohibited medications added as appendix.
- 03/03/2010 **Substantial Amendment 8:** Isolated elevation of GGT do not represent exclusion to recruitment or withdrawal.
- 28/09/2010 **Substantial Amendment 12:** Extension to study, clarifications to protocol including amendment to exclusion criteria, retention of original signed consent forms in site files, updated policy on pharmacovigilance and protocol deviations.
- 10/02/2011 **Substantial Amendment 13:** Clarifications to the protocol
- 15/03/2012 **Substantial Amendment 17:** Protocol modified to add a secondary outcome, amend exclusion criteria error, MA holder and SmPC change, amendments to appendices 3,4,6,7.
- 03/10/2013 **Substantial Amendment 20:** Protocol modified: change of MA holder name and address, SmPc update of drug brand name, trial manager and trial statistician change, clarification of Appendix 8 on prohibited medications.

07/05/2015

Substantial Amendment 21: Protocol modified: health economics analysis plan revised, revisions to planned analysis section to bring in line with Statistical Analysis Plan, minor change to MA Holder and SmPC, removal of blank Annexes.

12/01/2016

Minor Amendment: Addition of section on processing and analysis of collected study samples.