Since the late eighties the availability of recombinant human erythropoietin (rHuEPO) has markedly improved the management of anaemia. Today, erythropoiesis stimulating agents (ESA) are the main tool for anaemia correction in patients with chronic kidney disease, virtually eliminating the need for blood transfusions. Currently, the patents for some ESA have expired or are approaching expiration and a number of biosimilars manufacturers are aiming to share the market with “branded” ESA. This will probably lead overall to reduced treatment costs. However, a number of issues about bioequivalence and safety are still to be completely addressed. In particular these molecules need careful pharmacovigilance of possible occurrence of pure red cell aplasia. This is a serious adverse event related to ESA therapy when administered subcutaneously. In this disease, epoetin-induced antibodies neutralize all the exogenous rHuEPO and cross-react with endogenous EPO. A sharp increase and subsequent drop in the incidence of this rare disease has occurred in the last decade, mainly related to change in formulation of epoetin alfa produced outside the United States.