Switching to a Biosimilar

Physicians may have concerns regarding switching patients on stable, long-term therapy from a reference biologic to a biosimilar. The possibility of increased immunogenicity following switching from a reference product to a biosimilar is a concern for many physicians and patients. The table below includes trials supporting the switch between biosimilar and reference product. It is important to note that while multiple switches between biosimilars and their reference products are not expected, the increasing number of biosimilars entering the market could trigger these scenarios.

REFERENCE PRODUCT	BIOSIMILAR	TRIALS SUPPORTING THE SWITCH
REMICADE (INFLIXIMAB)	Inflectra (infliximab-dyyb)	Long-term efficacy and safety of biosimilar infliximab (CT-P13) after switching from originator infliximab: Open-label extension of the NOR-SWITCH trial[1] · A 26 week extension study (NOR-X) was performed to assess the efficacy, safety, and immunogenicity in patients maintained with Inflectra versus patients switching from Remicade to Inflectra · This study included 380 patients who had Crohn's Disease (127; 33%), Ulcerative Colitis (80, 21%), Spondyloarthritis (67,18%), Rheumatoid Arthritis (55, 15%), Psoriatic Arthritis (20, 5%), and Chronic Plaque Psoriasis (31, 8%) · **Study results showed no difference in safety and efficacy in patients maintained on Inflectra and those switched from Remicade to Inflectra**
		Switching from originator infliximab to the biosimilar CT-P13 in 313 patients with inflammatory bowel disease[2] · In a prospective observational cohort study, all adult IBD patients (195 Crohn's Disease, 118 Ulcerative Colitis) on Remicade treatment, at four hospitals, were switched to Inflectra · **Study results showed no significant changes in clinical disease activity, drug trough levels, patient QOL, or proportion of patients in remission**
	Renflexis (infliximab-abda)	Safety, immunogenicity and efficacy after switching from reference infliximab to biosimilar SB2 compared with continuing reference infliximab and SB2 in patients with rheumatoid arthritis: results of a randomized, double-blind, phase III transition study.[3] · This study followed 584 patients that: a) started on Renflexis and continued on Renflexis, b) started on Remicade and continued on Remicade, and c) started on Remicade and switched to Renflexis at week 54 · **Study results showed that efficacy, safety and immunogenicity profiles remained comparable in all treatment groups up to week 78**

Switching to a Biosimilar

REFERENCE PRODUCT	BIOSIMILAR	TRIALS SUPPORTING THE SWITCH
EPOGEN/PROCRIT (EPOETIN ALFA)	Retacrit (epoetin alfa-epbx)	Switching from Epoetin Alfa (Epogen®) to Epoetin Alfa-Epbx (RetacritTM) Using a Specified Dosing Algorithm: A Randomized, Non-Inferiority Study in Adults on Hemodialysis[4] • 434 patients with anemia and chronic kidney disease undergoing maintenance hemodialysis and receiving routine intravenous (IV) Epogen® were randomized 1: 1 to switch to IV Retacrit or continue standard-of-care (Epogen®) for 24 weeks, using analogous versions of the FMCNA ESA-dosing algorithm • **The study concluded switching to Retacrit was non-inferior to continuing -Epogen in maintaining hemoglobin levels in patients receiving hemodialysis, when both ESAs were dosed using a specified algorithm**
NEULASTA (PEGFILGRASTIM)	Udenyca (pegfilgrastim-cbqv)	No Studies Available*
	Fulphila (pegfilgrastim-jmdb)	Safe Switch of Treatment From the Reference Product to RGB-02, a Proposed Biosimilar Pegfilgrastim: Analysis of the Results of Three Clinical Trials[5] • Efficacy, safety and PD data of two PK/PD studies (enrolling 110 and 150 healthy volunteers, respectively) and a comparative efficacy and safety study (enrolling 239 breast cancer patients) were analyzed in order to assess whether treatment switch from Neulasta® to RGB-02 has any impact on the PD response, efficacy or safety. • Patients in the reference arm of the comparative efficacy and safety study were switched to RGB-02 treatment following the first two chemotherapy cycles. • **The mean duration of severe neutropenia (DSN) values after the therapy switch were similar to the values prior to the switch and the switched arm did not show decreased efficacy compared to the arm received RGB-02 from the first cycle. Safety results, including immunogenicity of the studies did not reveal any negative impact of the treatment switch.**
NEUPOGEN (FILGRASTIM)	Zarxio (filgrastim-sndz)	Safety and efficacy of alternating treatment with EP2006, a filgrastim biosimilar, and reference filgrastim: a phase III, randomised, double-blind clinical study in the prevention of severe neutropenia in patients with breast cancer receiving myelosuppressive chemotherapy.[6] • This study evaluated 109 patients who completed the study after randomization to receive only one product (biosimilar or reference) and two arms received alternating treatments every other cycle (biosimilar then reference or vice versa over six cycles). • **The study found non-inferiority after switching between reference product and biosimilar and there were no clinically meaningful results after switching regarding efficacy, safety or immunogenicity.**

Switching to a Biosimilar

REFERENCE PRODUCT	BIOSIMILAR	TRIALS SUPPORTING THE SWITCH
	Nivestym (filgrastim-aafi)	No Studies Available*
AVASTIN (BEVACIZUMAB)	Mvasi (bevacizumab-awwb)	No Studies Available*[7]
	Zirabev (bevacizumab-bvzr)	No Studies Available*
HERCEPTIN (TRASTUZUMAB)	Ogrivi (trastuzumab-dkst)	No Studies Available*

**At the time of the literature search, there were no studies available including the biosimilar switching to the reference product*

[1] Goll GL, Jørgensen KK, Sexton J, et al. Long-term efficacy and safety of biosimilar infliximab (CT-P13) after switching from originator infliximab: open-label extension of the NOR-SWITCH trial. J Intern Med. 2019;285(6):653–669. doi:10.1111/joim.12880

[2] Bergqvist V, Kadivar M, Molin D, et al. Switching from originator infliximab to the biosimilar CT-P13 in 313 patients with inflammatory bowel disease. *Therap Adv Gastroenterol*. 2018;11:1756284818801244. Published 2018 Oct 11. doi:10.1177/1756284818801244

[3] Smolen JS, Choe JY, Prodanovic N, et al. Safety, immunogenicity and efficacy after switching from reference infliximab to biosimilar SB2 compared with continuing reference infliximab and SB2 in patients with rheumatoid arthritis: results of a randomised, double-blind, phase III transition study. *Ann Rheum Dis*. 2018;77(2):234–240. doi:10.1136/annrheumdis-2017-211741

[4] Thadhani R, Guilatco R, Hymes J, Maddux FW, Ahuja A. Switching from Epoetin Alfa (Epogen®) to Epoetin Alfa-Epbx (RetacritTM) Using a Specified Dosing Algorithm: A Randomized, Non-Inferiority Study in Adults on Hemodialysis. *Am J Nephrol*. 2018;48(3):214–224. doi:10.1159/000492621

[5] Illes A, Perjesi L, Horvat-Karajz K, et al. Safe switch of treatment from the reference product to RGB-02, a proposed biosimilar pegfilgrastim: Analysis of the results of three clinical trials. *Ann Oncol*. 2018;29 Suppl 8:viii608–viii609. doi:10.1093/annonc/mdy300.017

[6] Blackwell K, Gascon P, Krendyukov A, Gattu S, Li Y, Harbeck N. Safety and efficacy of alternating treatment with EP2006, a filgrastim biosimilar, and reference filgrastim: a phase III, randomised, double-blind clinical study in the prevention of severe neutropenia in patients with breast cancer receiving myelosuppressive chemotherapy. *Ann Oncol*. 2018;29(1):244–249. doi:10.1093/annonc/mdx638

[7] Switching from Avastin or other Bevacizumab Biosimilars to Biosimilar Mvasi: Clinical Effectiveness. Ottawa: CADTH; 2018 Nov. (CADTH rapid response report: reference list)