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EDITORIAL

Non-medical switching: save today and pay tomorrow

The launch of anti-TNF biosimilars is expected to provide cost savings and add to the economic sustainability of the healthcare system. Consequently, some payers and formulary decision-makers in certain geographic regions are supporting practice of non-medical switching between originator products and their biosimilars.

Non-medical switching (NMS) occurs when a patient whose current therapy is effective and well tolerated is switched between therapies, such as from an originator TNF inhibitor to its biosimilar, for economic or other non-medical reasons[1]. The practice of NMS is also possible between biosimilars and in the switch back between biosimilar and originator. The evidence in pharmacoeconomics must be distinguished in: Budget Impact Model and Cost-effectiveness analysis. The first one (1) assesses the economic impact, (2) does not include health outcome, (3) evaluates the prospects for the payer, (4) evaluates only the direct costs, (5) has a short time horizon (1–3 years), and (6) measures the total expenditure. The cost-effectiveness analysis: (1) targets a good investment, (2) includes health outcome, (3) is a perspective for national health and society, (4) evaluates direct and indirect costs, (5) has a medium-long term horizon, and (6) provides measures through incremental cost-effectiveness/quality-adjusted life years (ICER/QALY).

Budget impact model studies for Infliximab and its biosimilars have shown a reduction in therapy costs. Brodszky *et al.*[2] constructed a model to assess the budget impact of Infliximab biosimilar CTP-13 in the treatment of rheumatoid arthritis over a 3-year time frame in six Eastern European countries (Bulgaria, Czech Republic, Hungary, Poland, Romania, and Slovakia). This model considered solely direct costs of drug treatment in two scenarios: the first where 65% of patients starting new biological therapy used CT-P13 and the second assuming also an interchanging rate of 80% with the reference drug. In the first scenario, estimated savings reached €15.3 million, while in the second scenario savings reached €20.8 million, considering a 25% discount over the originator price.

A similar budget impact model was built by Jha *et al.*[3] to assess CT-P13 in six immune-mediated diseases in five European countries (Germany, the UK, Italy, the Netherlands, and Belgium) over a 1-year period. Estimating a 25% switch rate and a 50% uptake in newly-treated patients, projected savings in the 10%, 20%, and 30% discount scenarios were as follows: €2.3, €4.6, and €6.9 million in RA; €2.2, €4.3, and €6.4 million in ankylosing spondylitis (AS), and €2.7, €5.3, and €8 million in psoriatic arthritis (PsA), respectively. In the model by Brodszky *et al.*[2], if budget savings were spent in the reimbursement of additional infliximab treatment, 1,205 and 1,790 additional RA patients would be treated in the first and second scenarios, respectively. In the model by Jha *et al.*[3], an additional 300, 676, and 1,158 RA patients; 139, 313, and 538 AS patients, and 186, 419, and 718 PsA patients would be treated in the 10, 20, and 30% discount scenarios, respectively.

Other budget impact models presented as abstracts show a discount from 10% to 30% and savings from 47€ to 433€ million[4]. Another study estimated that the 5-year budget impact of etanercept biosimilars in the UK would result in savings of £100–£260 million based on the assumption that the etanercept biosimilar price would range between 10–25% lower than that of Enbrel[5]. Other authors found that the actual cost saving from the introduction of the etanercept biosimilar in the first year was £23.4 million, and it reduced the overall expenditure on etanercept by 19.10%[6]. This saving, in line with the predictions of Ruff *et al.*[5], was a result of the marketing of the etanercept biosimilar Benepali at a price 36.15% lower than that of Enbrel and a price reduction of Enbrel by 14.85%.

A copy of Etanercept (Yisaipu) not submitted by the regulatory authorities to the exercise of comparability was evaluated in a model of pharmacoeconomics. Yisaipu 50 mg/week for 9 months followed by Ysaipu 25 mg/week was evaluated in the Chinese healthcare system in patients with RA and showed the greatest number of QALYs gained (nearly 11.9 and 11.3 with or without rituximab after the failure of Yisaipu, respectively). In a model based on the PRESERVE study, had an estimated ICER estimated between $18,324 and $40,333 with the best strategy, and $12,735 when the dose is reduced to 25 mg in the first 9 months[7].

The real life studies of the NMS between originator and biosimilar showed a discontinuation due to loss of efficacy or adverse events for Infliximab from 14.7% to 81.5%[8,9]. For etanercept the discontinuation after NMS is between 7% and 17%[10].

Available data show that the treatment costs for patients switching from initial treatment during the first year of follow-up were higher than for patients who did not switch (€12,710.00 vs €11,332.00), with a difference of €1,378.00. The ICER/QALY of etanercept ranges from €15,315.00 when we consider direct and indirect costs, and up to €38,639.00 for direct costs only[11]. Short-term costs associated with non-medical switch (NMS) from originator biologics to biosimilars among stable patients with autoimmune conditions in rheumatology, gastroenterology, and dermatology from a US provider's and third-party payer's perspective were evaluated. Physicians expended an extra 6 min for the NMS visit and 22 min over 3 months; NMS rates of 14.4%, 15.5%, and 17.7%; and 11.3%, 16.2%, and 33.2% of time not reimbursed

for gastroenterology, rheumatology, and dermatology, respectively. The total switching costs for payer's were $771,460 (for $n = 3,609$ patients with an NMS rate of 16.6%), mostly due to follow-up visits and additional laboratory tests/procedures. In sensitivity analyses, the NMS rate was the main cost driver. Increasing the NMS rate to 25% and 50% increased payer's total switching costs to $1.19 and $2.39 million, respectively[12].

Finally, an article by Tarallo *et al.*[13] in the *Journal of Medical Economics* estimates the cost of NMS in a stable population with RA in the UK. The percentage of patients switching and the impact of the NMS on economic red tape was assessed with a survey on 150 rheumatologists from the EU markets (France, Germany, Spain, Italy, UK). 25.2% (1,259) patients treated with etanercept originator switched to biosimilar, of which 875 (69.5%) went to SB4 and 384 (30.5%) to GP2015. In the third month, 26.3% of patients switched again, of these 8.3% returned to the originator, 3.8% to a second biosimilar, and 14.2% to another biological.

Although originator etanercept was more expensive than biosimilars, the change was more expensive than the continuous treatment of the originator in all impact scenarios. Switching treatment had higher annual costs per patient than the continuing treatment of the originator. The transition was associated with greater use of health resources[13]. Although the study presents the limitations of a model and that the real life demonstrates a lower dropout rate[10], real life and cost-effectiveness analysis will confirm if the practice of NMS in patients with stable RA will lead to a greater cost assessed not only on loss of efficacy and adverse events, but also on hospitalization costs, lost working days and absenteeism from work, and in terms of worsening QALY with an increase in ICER over time.

Transparency

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