Reimbursement of Targeted Cancer Therapies Within 3 Different European Health Care Systems

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ABSTRACT

Purpose: Targeted cancer therapies (TCTs) are drugs that specifically act on molecular targets within the cancer cell, causing its regression and/or destruction. Although TCTs offer clinically important gains in survival in one of the most challenging therapeutic areas, these gains are followed by considerable increases in health care expenditures. The aim of this study was to identify differences in the recommendations for TCTs in 3 European health care systems (Serbian, Scottish, and Dutch) and to examine the role of pharmacoeconomic (PE) assessments in such recommendations.

Methods: A list of currently approved TCTs cited from the European Medicines Agency was cross-referenced with drug reimbursement reports issued by the National Health Insurance Fund for Serbia, the Scottish Medicines Consortium for Scotland, and the National Health Institute for the Netherlands. The following key variables were gathered from the reports: drug indication, registration status, reimbursement status, and outcome of the PE evaluation.

Findings: There were 41 TCTs approved by the European Medicines Agency for 70 cancer indications. Of the total number of TCT indications, 20 were reimbursed in Serbia, and 25 are still without a decision from the national agency. The remaining TCT indications (n = 25) are not registered in Serbia. None of the submissions or the PE analyses were publicly available. The Scottish Medicines Consortium positively assessed 26 TCT indications and rejected 30. All appraisals were published, and the majority contained full PE assessments. Finally, the Dutch agency accepted 60 TCT indications and disapproved the use of 1. The majority of reimbursed drugs were exempted from PE evaluation in accordance with 2 recent policies regarding expensive hospital drugs.

Implications: In the 3 examined health care systems, the reimbursement status of the TCTs differed significantly. Level of PE application within the TCT evaluation procedures seemed to largely affect the final reimbursement decisions. Although, there are special policies in the Netherlands that enabled fast access for 98% of the TCTs that applied for reimbursement, a clear definition of cost-effectiveness threshold and strict requirements for full cost utility assessments in Scotland led to acceptance of only 46% of the TCT submissions. More precise PE guidelines must still be designed for TCT reimbursement in Serbia. Guidelines must account for specific epidemic and economic conditions of the country and could build on the experiences of Scotland and the Netherlands. (*Clin Ther.* 2015;37:474–480)

Key words: health care policy, Europe, pharmacoeconomics, reimbursement, Serbia, targeted cancer therapy.

INTRODUCTION

Targeted cancer therapies (TCTs) are drugs that interfere with specific predefined molecular targets involved in cancer cell growth and survival. These targets, however, must be clearly identified, either

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quantitatively or qualitatively, and a correlation exists between their presence and the clinical effectiveness of the TCT.[1] Selectiveness for processes within the cancer cells is what distinguishes TCTs from traditional chemotherapies. This selectiveness provides TCTs with the potential for improved effectiveness, with fewer severe adverse events, than conventional chemotherapy regimens.

Dozens of TCTs have been licensed worldwide since the first market authorization of rituximab that occurred in the late 1990s.[2] The total number of TCTs in 2010 was 22; only 4 years later, 44 registered targeted therapies have been issued for oncologic indications by the European Medicines Agency (EMA) and/or the US Food and Drug Administration.[3–5] By revenue, these drugs comprise the biggest and fastest growing part of oncologic therapeutics, which is the most dominant therapeutic group on the global pharmaceutical market.[3,6]

Although TCTs produce clinically important gains in survival and/or quality of life within the indications that had not seen any improvements previously, they also come at considerable cost.[7] Different policies in drug pricing and reimbursement among European countries that were applied to address this issue resulted in significant imbalances in access to the TCTs. In particular, cost utility analysis (CUA) seemed to be an influential element in the assessments of new oncologic drugs.[8] To illustrate the variety of approaches and its effect on TCT reimbursement, the present study examined 3 distinctive health care systems in Europe (Serbian, Scottish, and Dutch).

The main principles for drug reimbursement in Serbia are defined within the rule book issued by the government and incorporated into practice by the National Health Insurance Fund (in Serbian, Republički fond za zdravstveno osiguranje [RFZO]).[9] In accordance with this regulation, assessments are performed by the RFZO committees, and all drugs that attain a positive decision can be placed on the 5 reimbursement lists, which mostly differ in dispensability, level of patients' copayment, and potential prescription restrictions. Together with the common requests for clinical efficacy, the CUA and budget impact analysis (BIA) are obligatory parts of a submission process. However, other than basic definitions of the CUA and BIA, more details of what they should include or specification of a cost-effectiveness threshold were not provided. Furthermore, the RFZO does not consider TCTs, or any other therapeutic group, separately from the general policy. Decisions are made publicly and are available from the reimbursement lists,[10] but they do not contain submission files or respective evaluations.

In Scotland, drug assessments are performed by the Scottish Medicines Consortium (SMC), a committee that advises local boards of the National Health Service on the use and reimbursement of newly licensed drugs.[11] A standard SMC assessment examines a drug's clinical efficacy and cost-effectiveness and can engage the manufacturer, clinical experts, and patient groups within the process. Consequently, detailed reports are produced and published at the SMC site. A drug is generally considered cost-effective if its incremental cost-effectiveness ratio (ICER) is below £20,000 per quality-adjusted life-year (QALY) and not cost-effective if the ratio is over the threshold of £30,000/QALY.[12] Drugs with the ICER between 2 cited values can be regarded as cost-effective if they offer significant benefit compared with the standard treatment. Although there are no exemptions from the regular procedure for a particular therapeutic group or patient population, the SMC recognizes certain decision modifiers that can enable a positive recommendation despite relatively high and otherwise unacceptable cost-effectiveness ratios.[13] Decision modifiers potentially ascribed to TCTs are: substantial improvement in the survival or quality of life, absence of any therapeutic alternative, and additional benefit for specific subgroups of patients.

Finally, in the Netherlands, the National Health Institute (in Dutch, Zorginstituut Nederland [ZiNL]; formerly known as College voor Zorgverzekeringen [CvZ]) conducts assessments of drugs and suggests their reimbursement status to the Ministry of Health, which generally follows the advice. In deciding on a manufacturer's submission, CvZ/ZiNL evaluates a drug's clinical value, cost-effectiveness, and budget impact.[14] Although a cost-effectiveness threshold is not predetermined, a pharmacoeconomic (PE) assessment can influence the final reimbursement decision. In addition to the general reimbursement procedure, 2 recent policies with several updated versions may be applied to the TCT reimbursement. As of 2002, the Policy Rule for Expensive Hospital and Orphan Drugs (PREHO) supports supplemental financing of hospitals