INTERIM HEALTH TECHNOLOGIES ASSESSMENT (HTA) IN ROMANIA. A proposal for a better transition to full HTA

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1. INTRODUCTION
Health Technology Assessment (HTA) is a multidisciplinary process that aims to use multiple approaches and techniques in order to provide health policy makers with a broad perspective on products or services designed to have access to public funding. The assessment takes into account efficacy, safety, efficiency, social, legal and ethical aspects, etc. A large range of medical interventions benefit from HTA, such as: the introduction of a new drug or a biological product, an intervention like organ transplant, a practice protocol, finally allowing a comparison of them. [1]

2. PREVIOUS EFFORTS AND RECOMMENDATIONS FOR HTA INTRODUCTION IN ROMANIA
Introduction of HTA in Romania is a goal and effort to start this process is dating back for more than a decade. The need of using HTA in health policy decisions in Romania was highlighted in 1992, following a study funded by the World Bank. [2] [3] Even at the time, the use of HTA was a well established process in many EU countries. For example, Spain has appealed to HTA specialists since 1988, and in 1991 was created the HTA Office in the Ministry of Health of Catalonia [4] National Institute for Health and Care Excellance (NICE), the best known institution of this type in the world, was founded in the UK in 1999 [5].

The following will highlight a proposal for a methodology which takes into account a modified version of several recommendations made for Romania by foreign consultants and supplemented with measures to minimize the bias and direct involvement of officials in the interim evaluation of health technology.

3. A CRITICAL ANALYSIS OF THE CURRENT LEGAL FRAMEWORK ON ACCESS TO THE REIMBURSEMENT DRUG LIST
After a period of six years, the authorities have not granted access to the list of subsidized drugs due to substantial arrears toward drug manufacturers. In June 2013 the Ministry of Health (MoH) issued Order 724 (referred to as "Order"). This methodology of "interim HTA" - was intended as a form of transition to a future evaluation allowing a revision of the reimbursement drug list starting immediately. Although it should have been a step forward in introducing HTA, the new procedure does not approach the minimum requirements of an economic evaluation; its effects represent just another version of the previous legal framework.

For more than a decade health technologies assessment (HTA) introduction in Romania was a recommendation made by various consultants engaged in reforming the Romanian health system. In the last 6 years no new products have been accepted on the reimbursement drug list. In the spring 2013 Ministry of Health issued a new methodology for assessing pharmaceutical products, considered to be a form of interim HTA, and to start the use of similar methodologies to the ones used in most European countries.

We deem that this process is a stagnation or even a step backward in introducing full health technology assessment and we listed some of the pressing issues.

Given these shortcomings we presented a proposal for a methodology inspired by some of the foreign consultants' reports, amended and completed with new recommendations, with the purpose of ensuring the transition from 2015 to full HTA, aiming ultimately for an increase in cost-effectiveness of the health system and, eventually an increase in equity.

Keywords: HTA - Health Technology Assessment, health policy, health reform, economic evaluation

Some of the drawbacks of the Order include:
- The absence of a time table for the transition from a interim to a full HTA;
- The scorecard used, decisive for accepting the compensation status, is not enough influenced by the reimbursement status in other jurisdictions,
• comparable to the economic status of Romania; the points awarded for efficacy and safety profile can be viewed as formal given that most products have already passed through the filter of the European Medicines Agency. It has qualified the the drugs in question as being equal or greater to the the comparison treatment in terms of aforementioned criteria! Most of candidate products generally receive at least 6 points and lead to automatic compensation!

• Budgetary Impact Analysis serves only an informative purpose; it is self-assessed and does not bind in any way the manufacturer for undervaluation. This analysis could have been one of the main grounds for negotiating the future sales of the reimbursed drug;

• The procedure does not indicate how the additional costs will be covered and what will be the impact on the pharmaceuticals budget; a welcomed measure would have been to allocate a designated budget for innovative medicines. In Romania over-spending of the reimbursed drug’s budget is supported entirely by the drug manufacturers. Today drug producers have to “payback” to National Health Insurance House (NHIH) around 10% of their income. An increase by 10-15% in the market will force the manufacturers to pay in addition to VAT, income tax, etc., almost 25% of their turnover, which is unlikely to be accepted. The reimbursement of new technologies will require a substantive change to the payback system which will rise the risk that this will leave behind a financial imbalance which will be difficult to manage for the NHIH;

• The Order fails to provide any negotiation mechanism of the price after the new drugs will be accepted on the reimbursement list. Once the assessment is concluded, the third party payer, NHIH, will be obligated to include the new products on the reimbursed list without having any legal means of negotiating the quantity and/or price of the products;

• There is no procedure in place that can reevaluate over the course of time the admission decision on the reimbursement list;

• The order does not provide evaluation of the products already reimbursed, some of which have questionable cost and effectiveness. At least theoretically, in the absence of any barrier, the Order allows drugs considered to be too expensive or even not cost-effective in some economically advanced countries to access the list of subsidized drugs in Romania! In 2011, 30 of the top 50 drugs ranked by spending were rated by NICE international consultants as being too expensive, considering the purchasing power of our country; [7]

• We believe that the current methodology marks a stagnation which will have negative consequences. It is not based on a budget impact analysis which can lead to malfunctions and arrears and thus waste the opportunity to make a full assessment of more than 150 molecules and new indications.

In a previous issue of the journal [8], Radu and Pana raised the idea that different evaluation agencies usually come to the same conclusions - giving the example of NICE (UK) and the SMC (Scotland) evaluations, the last one’s methodology being more pragmatic and using far less resources; this could back up the idea for the use of evaluation from other countries in the case of Romania or at least the most simplified methodology possible. The extrapolation of study results without regard to the specifics of Romania is completely erroneous and misleading for the uninformed reader. There are supporters of the idea that the HTA process may be carried out centrally, at an EU level, as the actual centralized licensing for a new drug. Article 15 of the Cross-border Patients’ Rights Directive (2011/24/EU) includes cooperation on Health Technology Assessment as relevant area for cooperation between Member States in the field of public health and sets up a voluntary network connecting national authorities and bodies responsible for HTA. In my opinion this is an important step to a harmonization of HTA around UE, but the process will be long and difficult.[9]

The actual procedure requires mentioning the cost-effectiveness indicator (incremental cost-effectiveness ratios – ICER) as it was calculated using data from advanced economic countries. Several studies have shown that the transfer of conclusions from studies conducted in jurisdictions of greater economic power than the target countries is unlikely to be suitable and a proper adaptation of these conclusions and results should be made. [10] Romania does not meet most of the criteria for the transferability of cost-effectiveness studies and budget impact analysis, and consequently, new studies should be performed, using our country specific data.

4. PROPOSALS FOR THE TRANSITION TO A FULL HTA IN ROMANIA

In order to properly defining the current assessment as ‘interim’ the first step is to determine when and how a full assessment of new technologies will be carried out. In our opinion an interval of 6 to 9 months is sufficient for Romania to have a stabilized method of assessment and a sufficient number of officials trained in HTA to verify the validity of the assessments provided by the manufacturers. Our proposal is that the new drugs, which meet the minimum criteria to be included in the evaluation process, should be accepted for financing under special conditions for a period of 12 months with the possibility to extend for another 6 months. In the first 12 months all the necessary data will be gathered regarding the clinical efficacy, epidemiology and healthcare structure specific for Romania. In the last 6 months of funding the producers will have to complete their studies and submit the results to the authorities for a final reimbursement decision, without patients already receiving treatment in question to be forced to stop their treatment.
The transition period will be split into a series of phases, some of them already suggested by independent experts who advised the Romanian Government. [7]

**Phase I – cessation of ineligible products that are ineligible**

Given that Romania is among the EU’s poorest countries [11] - borrowing experience from some of the richest countries, like the UK or France, is inadequate. We believe that, for the moment, at least until the development of its own expertise, Romania should rely on precedents set in five countries, with an close GDP / capita according to Eurostat - namely Slovakia, Hungary, Estonia, Lithuania, Bulgaria.

A. Seiter proposed in his Pharmaceutical Sector Analysis Report [12] a scorecard considering jurisdictions with close economic power superior to Romania. Each product would receive 2 points for their status recorded unrestricted 1 pt - pt product registered with restrictions (limited number of patients, stated, price-volume, etc) and 0 points for unregistered products.

For a product to qualify should accumulate at least 5 points obtained from the comparison with the reference countries. A product reimbursed with restrictions in all 5 countries will accumulate 5 points. The same number of points can be obtained if the two countries have unrestricted reimbursed the product and one reimbursed with restrictions.

In conclusion, if comparable countries with Romania were given 2-6 years and have not decided for listing, provided that all applicable comprehensive economic assessment procedures were used it is not appropriate for Romania to proceed otherwise.

Afterwards products will be evaluated using specific criteria as follows (see table 1):

- From the special criteria the eligible items should accumulate at least 7 points. In an extreme scenario, a product would be intended only for the individual treatments (1pt), have a higher price than current therapy (0 pts), have clear advantages over current treatment (2 points), could be applied in Romania (2 points) and should be possible to prevent off-label administration (2 points).

### Table 1 - Special evaluation criteria for candidate pharmaceutical products [after Seiter, modified] [12]

<table>
<thead>
<tr>
<th>Special criteria</th>
<th>Coding</th>
</tr>
</thead>
<tbody>
<tr>
<td>The disease has a high importance for public health in Romania</td>
<td>2= It affects Public health</td>
</tr>
<tr>
<td></td>
<td>1= It affects only certain individuals</td>
</tr>
<tr>
<td></td>
<td>0= other situation</td>
</tr>
<tr>
<td>(Note = the most of products them will get 1 pct)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2= Is not more expensive</td>
</tr>
<tr>
<td></td>
<td>1=Is in a coplarable range (0-10% more than current therapy)</td>
</tr>
<tr>
<td></td>
<td>0= Is more expensive than current therapy</td>
</tr>
<tr>
<td>(Note = the most of products will receive 0 pct)</td>
<td></td>
</tr>
<tr>
<td>• The new treatment is not more expensive than current standard treatments in Romania</td>
<td>2= Has proven and semnificative advantages in clinical trials.</td>
</tr>
<tr>
<td></td>
<td>1= Is a “mee too” drug.</td>
</tr>
<tr>
<td></td>
<td>0= Has no proven advantages.</td>
</tr>
<tr>
<td>(Note = most of products will receive 2 pcts)</td>
<td></td>
</tr>
<tr>
<td>• It is possible to deliver the new treatment according to good practice in the Romanian health system</td>
<td>2= Out-of- label use can be prevented</td>
</tr>
<tr>
<td>(diagnostic tools available, control instruments available etc.)</td>
<td>1= Out-of- label use can be prevented if additional preventive measures will be enforced</td>
</tr>
<tr>
<td></td>
<td>0= Out-of- label use can’t be prevented</td>
</tr>
<tr>
<td>(Note = the most of product will get 2 pcts)</td>
<td></td>
</tr>
<tr>
<td>Out-of-label use can be contained easily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2= Has proven and semnificative advances in clinical trials.</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
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</table>

Priority will be granted to studies using as a comparator products already reimbursed in Romania. From these data we can extract the number of QALY gain by introducing new technology compared to standard technology, information that will be used in the next step.

**Phase III Setting budget and number of patient to be treated in the transitional state till full HTA**

- **III.1 – Budget setting for each product**

For each tranche of innovative products that will enter into transitional reimbursement phase the Government / Parliament will allocate a budget to them according to economic opportunities.

Each product will be assigned a budget in accordance with the number of QALYs generated (eg. Let assume the approved budget of 200 million Euros - and a total generated of 50 QALY per patient gathered from all products
Phase V-a Reassessment of data – at every 5 years from acceptance on the reimbursement list

Given the changes in time of costs and prices of various procedures and drugs entering the market, and the occurrence of new technologies, etc, periodically a reassessment of the initial decisions is justified. Reassessment of the initial evaluation will be based on the economic models originally submitted or using new studies that could be carried out every 3-5 years.

**DISCUSSION AND CONCLUSIONS**

- This methodology would be a transition period, and since 2015 all products will aspire to public financing will opt for the use it or providing their own funded studies using Romania data.
- NHIH may demand of the manufacturers of the first 150-200 medicinal products (ranked according cost per year / course) already reimbursed to produce scientific evidence for a full HTA. During this evaluation a temporary price could be imposed, for example low enough to cover the treatment of the patients existing on the waiting list.
- The same principles, with minor modifications, could be applied to any other medical technologies that are currently publicly funded, such as devices, vaccines, dialysis, etc.
- NHIH and/or MH must publish guidelines for emergency budgetary impact assessment studies and for studies of cost-effectiveness and to fund a clinical trial for calibration of utility values specific to Romania.
- Agreeing on the World Health Organization recommendation for a threshold for ICER or Country specific thresholds.
- Integrated Information System (SIUI) should be adjusted to allow even before the introduction of electronic patient safety modules that act as patient registries or disease used to assess new technologies under evaluation.
- Products in transitional period of assessment should not be taken into account in computing the clawback tax.
- In 12 months the Ministry of Health should complete training of officers who will be responsible for HTA. a year ago MS started a training process, a total of 15 physicians completing courses through a project funded by the World Bank specialists only one of them beeing used in the current evaluation system.

**Prices in Romania = Price in country A \( \times \) PPP adjusted according GDP per capita in Romania

PPP-adjusted according GDP per capita in the country of reference
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- The prospect of implementing a full system of HTA in 2015 must be done simultaneously with the enactment of a series of legislative changes such as the introduction of new levels of compensation, the change of the claw-back tax and the introduction of cost-volume contracts, cost-volume-outcome and even switching to contracts where payment to be made only for patients who achieve the outcomes (pay for performance) [13].
- Such a system would also reduce the interim evaluation bias and suspected corruption, imposing maximum transparency, aiming for a higher standard as is the case in all advanced countries.

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