Access to Highly-Innovative Therapies in CEE Countries: The Example of Croatia

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Background on health care in CEE countries

- Worse health status
- More limited healthcare resources
- Pay more penalties for inappropriate health policy and reimbursement decision compared to WE countries
- The need for evidence based health policy decisions is greater
- HTA implementation even more crucial due to budget limitations
- HTA implementation not at the same level in different CEE countries
- Countries in Eastern and Southern Europe, with low GDP per capita, have sales of cancer drugs at around 1/3 of sales in WE countries, both in 2005 and in 2014
- Low national income and health care spending per capita - major obstacles for access to new cancer drugs; new cancer drugs are traded at an international market, and while the absolute price per unit is similar, the relative price is higher for countries with lower income
- Parallel trade and international reference pricing limits the opportunities for price differentiation
- The correlation between health expenditure and mortality-to-incidence ratio throughout Europe

Health care spending in the EU


Sources: OECD Health Statistics, Eurostat Database, WHO Global Health Expenditure Database (data refer to 2015).
Crude rates for cancer mortality for all cancers combined and for both sexes

5-year relative survival rates for all cancers in European patients aged ≥15 years, 1990-2007

Costs of cancer drugs per capita in European countries (in 2014 prices), 2005-2014

Use of lung cancer drugs in 2014

Croatian status in 2017: all four pharmaceuticals listed below
Use of melanoma drugs in 2014

Croatian status in 2017: pembrolizumab, vemurafenib, dabrafenib and trametinib - listed and reimbursed (with specific CHIF note) for patient with metastatic or inoperable melanoma IIc, except uveal melanoma
Croatian decision-making process, reimbursement and HTA


Republic of Croatia

- Population ~4.2 million
- GDP per capita in 2015: 16 700 € PPP

Croatian Health Care System

Universal health care coverage

Principles of social health insurance, financed from several sources

- The agreement and payment of the national mandatory health insurance is conducted through the Croatian Health Insurance Fund (CHIF)
- Total spending on healthcare in 2015: 7.4% GDP
- Per capita spending on healthcare in 2015: €1 241
- The share of private expenditures for healthcare: ~1.18% GDP

In 2014:

- total expenditures from compulsory health insurance ~€2.8 billion
- for total health care ~€2.5 billion
- specifically, ~€522 million (15.4% ) for primary health care
- ~€1.05 billion (33.2%) for hospital health care and consultative specialist health care
- ~€435 million (16.9%) for prescription drugs
- ~€86 million (3.5%) for orthopaedic devices and prosthesis

Fund for very expensive drugs: ~€122 million (in 2017)
Legal framework in Croatia

- September 2012, Croatian National Health Care Strategy 2012-2020
- 2007, Act on Quality of Health Care
  The Agency should provide the procedure for HTA and database on HTA
- November 2011, Act on Quality of Health Care and Social Welfare (Ordinance on HTA should be delivered)

The Agency provides the procedure for HTA and database on HTA at national level; proposes Ordinance on HTA to the Minister of Health; provides continuous education in the field of HTA; national and international collaboration

- Ordinance on HTA - public consultation process finished in October 2016

- Ordinance on wholesale pricing of drugs

- Ordinance on wholesale pricing of medical devices

Ordinance regarding reimbursement on drugs

Determines the criteria for inclusion of medicinal products in basic and supplementary reimbursement lists of the Croatian Health Insurance Fund (CHIF):

- Drugs Committee is responsible for Appraisal process of Industry submission file (with Marketing authorization approval, calculation of drug price, scientific opinion; scientific evidence proving the benefits of the drug; tabular view of drug health insurance status in EU; Mandatory Budget Impact Analysis, BIA (should be according ISPOR Guideline); Optional: the applicant may submit the Cost-effectiveness analysis.

- HTA could be requested (if requested should be delivered in 1 month timeframe)

Ordinance regarding reimbursement on medical devices

Determines the criteria regarding reimbursement on medical devices

Conditional reimbursement

- No coverage with evidence development policy

- Manage-entry agreements in place (strictly confidential, i.e., CHIF: risk-sharing model on sofosbuvir for chronic hepatitis C - paying only for patients that experience treatment benefit, significant lowering of drug price; risk-sharing model on crizotinib in patients with non-small-cell lung cancer, NSCLC - company is paying the first cycle of therapy, with significant lowering of drug price
Croatian process of decision-making, reimbursement and HTA

Industry submission files

Croatian Health Insurance Fund (CHIF) Drugs Committee and Medical Devices Committee

APPRaisal

Recommendation

CHIF Board

DECISION

Request

HTA document with recommendation

Agency (AAZ) - HTA Department

ASSESSMENT

(Currently not mandatory)

HTA document with recommendation

Request

HTA document with recommendation

National adaptation

Active collaborative production

Request

HTA document with recommendation

EUnetHTA and HTA Network (Article 15, CBHC Directive)

Full Core HTA and Core HTA for Rapid REA of Pharmaceuticals and other health technologies

National/regional work produced in another country/region

Request

National adaptation

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Hospitals Management

DECISION

MoH

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Agency HTA Database, http://aaz.hr/hr/procjena-zdravstvenih-tehnologija/baza

HTA reports, 2011- May 2017 (>65% on Medical devices/procedures)

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<th>Rapid HTA - national level</th>
<th>HTA - national level</th>
<th>HTA - international level (author or co-author)</th>
<th>HTA - international level (adopted)</th>
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List of very expensive drugs in Croatia (examples, 2017)

• imiglucerase, agalsidase alfa, agalsidase beta, laronidase, alglucosidase alfa, galsulfase, idursulfase, velaglucerase alfa, eliglustat

• simeprevir, sofosbuvir, dasabuvir, ledipasvir + sofosbuvir, ombitasvir + paritaprevir + ritonavir, elbasvir + grazoprevir, sofosbuvir + velpatasvir, glecaprevir + pibrentasvir

• trabectedin, rituximab, trastuzumab, cetuximab, bevacizumab, brentuximab vedotin, pertuzumab, trastuzumab emtansine, obinutuzumab, pembrolizumab, gefitinib, erlotinib, sunitinib, sorafenib, dasatinib, lapatinib, nilotinib, temsirolimus, everolimus, pazopanib, afatinib, bosutinib, vemurafenib, crizotinib, axitinib, ruxolitinib, dabrafenib, trametinib, ibrutinib, nintedanib, cobimetinib, idelalisib, pirfenidone, olaparib, enzalutamide, abirateron...
Nusinersen (Spinraza) – Croatian case study

Recently approved orphan drug for 5q spinal muscular atrophy (SMA) under accelerated assessment due a significant unmet medical need

- Croatia was **not involved in clinical trials**
- **No Expanded Access Program (EAP)**
- **Manufacturer did not apply to CHIF for pricing and reimbursement process** on nusinersen, which is needed according to the Croatian legislation
- **Urgent HTA report** was requested by **Ministry of Health** in **July 2017**
- **AAZ prepared rapid HTA report** in **July 2017**
- **Final decision** was made by the **Ministry of Health** – decision document was published on MoH website, which facilitates access in restricted group of patients (with **SMA Type I**)
- **2 patients** with SMA Type I **started the treatment** in the **University Hospital Centre Zagreb**
Questions to Members of the HTA Network regarding HTA/Reimbursement/Decision on nusinersen (22-24/11/2017: replies from 22 MSs)

- Majority MSs: HTA/Reimbursement decision still in process

- Bulgaria, Romania, Cyprus, Estonia: Manufacturer did not ask for HTA/Reimbursement process
Conclusions

High cost of innovative drugs is a real problem – to deny access to effective drugs is not the solution.

Possible ways (legislative changes are needed):

- **Interactions** between the **manufacturers, regulators, HTA bodies, payers and patients**
- **Systematic and sustainable use of HTA to inform coverage decisions and disinvestment** and **sustainable international HTA collaboration** (in line with Article 15 of Directive 2011/24/EU; 2014, Strategy paper for EU cooperation on HTA; 2015, Reflection paper on Reuse of Joint Work in national HTA activities; 2014, 67th World Health Assembly Resolution: Health intervention and technology assessment in support of universal health coverage)
- **New payment mechanisms** for innovative medicines
- **Differential pricing** across countries
- **Greater transparency** around the costs of pharmaceutical products and the price of medicines
- **Joint procurement agreements**
- **Initial (conditional) reimbursement**
- **Post approval evidence generation** with **real-world data** (RWD) collection at EU level
- **Risk-sharing agreements**
- **Better information systems** and **data collection** at **regional, national and EU level**

“If you want to go fast, go alone. If you want to go far, go together.”