Conclusions and perspectives (EU)

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Vienna, BDA, Sept 2012
Bridging the gaps

US/EU
Rolling Assessment / Stepwise Process

The European HTA Authority Map is complex...

Different outcomes from different reimbursement agencies in Europe

Patient Access to Health Technologies

EU

<table>
<thead>
<tr>
<th>Benefit (Marketing Authorization)</th>
<th>EMA</th>
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<td>Drug (therapeutic, preventive)</td>
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<td>Devices (implantable, well)</td>
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<td>Diagnostic (lab tests, imaging, well)</td>
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<td>Procedures (surgery, physical)</td>
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<tr>
<td>Other (educational, campaign, well)</td>
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Horizontal and vertical inconsistency between member states
Trend in actual clinical development time for new development projects approved between 2000-2009

Median

Actual clinical development time is calculated for new development projects as the time between ‘First human dose’ (T-1-1) and ‘First approval’ (T-4-2). Data represent all new development projects that reached ‘First approval’ (T-4-2) between 2000-2009, where the start and end milestone dates for the interval are available. (n) = number of projects analysed in each year. This analysis is based on data from a consistent cohort of 17 companies participating each year between 2001 and 2010.
‘Eroom’s Law’: The number of new drugs approved by the FDA per billion dollars (inflation-adjusted) spent on R&D has halved roughly every 9 years.
The binary nature of drug regulation

Current model of licensing
“The Magic Moment”

Evidence vs. access tradeoff
The regulator’s dilemma

“…it has been said that the FDA has just two speeds of [drug] approval – too fast and too slow.”

Hamburg MA & Sharfstein JM. NEJM 360;24: 2493-5; 2009
Adaptive licensing *in a nut shell...*

Taking a less ambitious regulatory review route that would limit the drug to a far smaller and higher-risk group of patients, at least initially

San Diego Union-Tribune (10 Feb 2011)
“Precursors” to Adaptive Licensing

- Conditional Marketing Authorization
- New Pharmacovigilance legislation
- Risk Management Plans
- Periodic Safety Update Reports
- Five-year renewal of marketing authorization
- (Compassionate use programs)
A better model for evolution?

Current model of licensing
“The Magic Moment”

Adaptive Licensing
Possible AL model rare cancer

Knowledge, investment

Small RCT in enriched severe patient population

Multi-stakeholder SA; payers, HCP, and patients

Real-life treatment experience recorded in all patients + RCT in less-severe population; PFS/OS endpoint, safety assessments

Initial, narrow MA; reimbursement mirrors label; restrictions on prescribers

Revision of label (restrictions up or down)
Different names, same ideas

- EMA: staggered approval
- FDA: progressive reduction of uncertainty
- Health Canada: progressive authorization
- HSA Singapore: test bed for adaptive regulation
- Payers: managed entry (HTAi), CED
- MIT/NEWDIGS: adaptive licensing project
Current scenario:
Post-licensing, treatment population grows rapidly; treatment experience does not contribute to evidence generation.

Adaptive Licensing:
after initial license, number of treated patients grows more slowly, due to restrictions; patient experience is captured to contribute to real-world information.
Obstacles to Adaptive Licensing

• concerns over lowered standards
• how to communicate uncertainty?
• doable under current statute?
• getting commitment from industry to conduct “stage n+1 studies”?
• are follow-on studies doable after “loss of equipoise”?
• alignment between regulators and payers
• different reward structure required to incentivise drug development enterprise?
• ensuring appropriate prescriptions
Addressing the obstacles; next steps?

• Address economic consequences for drug development
• Design pilots cases using current sponsor assets
• Address legal underpinnings of AL
• Explore opportunities for collaboration with payers
• Obtain buy-in from all ranks of regulatory community
• Conduct pilots (EMA work program 2012)
EMA Road map to 2015

[...] a key issue for regulators will be whether a more ‘staggered’ approval (or progressive licensing) concept should be envisaged for situations not covered by conditional marketing authorisations [...] The Agency would like to launch a debate with all stakeholders on the appropriateness of introducing such a concept, including a consideration of appropriate incentives to support new medicines development.
Thank you!

Acknowledgments: Hans-Georg Eichler (EMA)