THE FUTURE OF ONCOLOGY: THE EUROPEAN MODEL?

Alex Bastian, Vice President, GfK Bridgehead

Seattle, Washington

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Oncology drugs in Europe: A thick accent
Faced with media and political support, not to mention dying patients, drug manufacturers have rapidly invested in oncology

“We came up with a pill that cures everything… but I’m warning you, it’s going to be expensive.”
Costs of cancer therapies have increased and raise serious questions of value, return on investment, & sustainability.
With costs increasing and incremental benefit slowing, Payers are raising the bar for acceptable trade-offs between cost and access.

**Increasing Colorectal cancer costs vs. Improvements in colorectal cancer survival are slowing**

**Incremental improvements push the paradigm, but at what cost?**


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Prices for oncology medications in the US and EU tend to be quite different, reflecting varying purchasing power and willingness to pay.

**Price per pack of selected oncology drugs**

Note: Prices are WAC in the USA and so do not take into account any non-transparent discounting (rare in oncology)

Sources: US price: AnalySource; French price: Base des Medicaments; German price: Lauer Taxe; UK price: Zenrx.org

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European oncology drugs are, on average, sold at a 29% discount compared to the prices in the USA

**Average EU prices as a discount of US prices (per pack)**

*Higher price only at launch*

Sources: US price: AnalySource; French price: Base des Medicaments; German price: Lauer Taxe; UK price: Zenrx.org

Note: Prices are WAC in the USA and so do not take into account any non-transparent discounting (rare in oncology)
How European Systems Work
Two philosophically different models

Value of health
- Health is a service
- Health is a right

Who pays for it?
- Employers and individuals
- The government

Source: GfK Bridgehead internal analysis
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Stereotypes abound but there is some truth in the myth of social healthcare in Europe
Incremental clinical benefit countries focus on the clinical aspects first, and then apply the conclusions to the pricing negotiation.

**French Pricing & Reimbursement Negotiations**

How severe is the condition and does the therapy prevent, cure or relieve symptoms in the interests of public health?

<table>
<thead>
<tr>
<th>SMR level (indicative)</th>
<th>Social Security Reimbursement</th>
<th>Patient Co-pay</th>
<th>Private Insurance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important</td>
<td>100%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>65%</td>
<td>Up to 35%</td>
<td>Up to 35%</td>
</tr>
<tr>
<td>Moderate/Low</td>
<td>30%</td>
<td>Up to 70%</td>
<td>Up to 70%</td>
</tr>
<tr>
<td></td>
<td>15%</td>
<td>Up to 85%</td>
<td>Up to 85%</td>
</tr>
<tr>
<td>Insufficient</td>
<td>0%</td>
<td>Up to 100%</td>
<td>Up to 100%</td>
</tr>
</tbody>
</table>

- At launch (negotiated pricing)
- Non-transparent
- Severity of disease rated
- Price-volume discounts
- Clinical, then economic considerations
Incremental clinical benefit countries focus on the clinical aspects first, and then apply the conclusions to the pricing negotiation.

The distribution of SMR scores remains stable over years and is strongly in favor of reimbursement.
Incremental clinical benefit countries focus on the clinical aspects first, and then apply the conclusions to the pricing negotiation.

French Pricing & Reimbursement Negotiations

Incremental clinical benefit

G-BA
HAS

Budget Impact

Regions
Regions

Cost-effectiveness

SMC
NICE

Does the drug improve patients’ clinical outcomes compared to the standard of care in this indication?

- ASMR I: Major therapeutic progress
- ASMR II: Significant improvement in terms of therapeutic efficacy and/or reducing side effects
- ASMR III: Moderate improvement in terms of therapeutic efficacy and/or reducing side effects
- ASMR IV: Minor improvement in terms of therapeutic efficacy and/or reducing side effects
- ASMR V: No improvement, reimbursed at cheaper price than comparator

HAS (French Health Authorities) annual report published mid-2012 mentioned the creation of a new score, the ITR, to replace the SMR and ASMR.

- ITR will represent the clinical value of a drug compared to the current standard of care regardless of its approval status.
Notably, in 2011, only 2 drugs were granted an ASMR above IV
Incremental clinical benefit countries focus on the clinical aspects first, and then apply the conclusions to the pricing negotiation.

Notably, in 2011, only 2 drugs were granted an ASMR above IV.

**French Pricing & Reimbursement Negotiations**

ASMR scores are indication specific, vary significantly across indications and over time.

**Example 1: bevacizumab**
- Bevacizumab has been granted:
  - ASMR V in breast cancer (initial assessment was ASMR III) and non-small cell lung cancer
  - ASMR IV in colorectal cancer (initial assessment was ASMR II) and renal cell carcinoma

**Example 2: sunitinib**
- Sunitinib has been granted:
  - ASMR V in pancreatic cancer
  - ASMR II in renal cell carcinoma and gastric cancer

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Incremental clinical benefit countries focus on the clinical aspects first, and then apply the conclusions to the pricing negotiation.

### German Pricing Negotiations

An additional benefit is an improvement in patient-related endpoints in comparison to the appropriate comparative therapy (by patient sub-population):

1. **Substantial** additional benefit ("erheblich")
2. **Significant** additional benefit ("beträchtlich")
3. **Marginal** additional benefit ("gering")
4. The additional benefit is **unquantifiable** ("nicht quantifizierbar")
5. **No additional benefits** documented ("nicht belegt")
6. The benefit is **lower** than the appropriate comparative therapy

- 1 year after launch (free pricing)
- Rigid hierarchy of evidence
- “Patient relevant” endpoints
- “Appropriate comparator”
- Sub-populations = slicing
Incremental clinical benefit countries focus on the clinical aspects first, and then apply the conclusions to the pricing negotiation.

**German Price Negotiation Results**

<table>
<thead>
<tr>
<th>Therapeutic benefit scores</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brilique</td>
<td>Gilenya</td>
<td>Victrelis</td>
<td>Trajenta</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zytiga</td>
<td>Eliquis</td>
<td>Incivo</td>
<td>Halaven</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jevtana</td>
<td>Nulojix</td>
<td></td>
<td>RasilAmlo</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Edurant</td>
<td></td>
<td></td>
<td>Trobalt</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yervoy</td>
<td></td>
<td></td>
<td>Benlysta</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zelboraf</td>
<td></td>
<td></td>
<td>Fampyra</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eviplera</td>
<td></td>
<td></td>
<td>Caprelsa</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- The score is the basis for price negotiation between sickness funds & manufacturer
- There appears to be little, to no, premium for products correlating with the “additional benefit” rating from the German Federal Committee
- Some manufacturers have decided not to launch their product in Germany
Budget impact creates a “cap” of sorts on the total budgetary impact a medication will have on the system.

### Italian Pricing & Reimbursement Negotiations

<table>
<thead>
<tr>
<th>Class</th>
<th>Assignment</th>
<th>(%) Reimbursement</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Chronic and critical Diseases</td>
<td>100</td>
</tr>
<tr>
<td>C</td>
<td>Not Reimbursed</td>
<td>0</td>
</tr>
<tr>
<td>H</td>
<td>Hospital</td>
<td>100</td>
</tr>
</tbody>
</table>

- An HTA is performed informally at the national level and increasingly at the regional level, which influences regional access.
- Cost effectiveness analyses (CEAs) are performed on an ad-hoc basis at regional and LHU/hospital level.
Budget impact creates a “cap” of sorts on the total budgetary impact a medication will have on the system.

**Italian Pricing & Reimbursement Negotiations**

- **Annual growth** in hospital drug expenditure will remain capped at 2.4% of the healthcare budget and drug companies will be required to pay back 35% of excess spending. In addition, the annual growth ceiling on reimbursed drugs dispensed through retail pharmacies will be lowered from 13.3% to 12.2% of the healthcare budget, and also a cap of 5.2% on medical devices put in place in 2013.

- Regional Healthcare budgets have been in deficit for many years and therefore they will be asked to provide additional funding:
  - Price-volume negotiations at initial pricing negotiations
  - LHUs monitor prescribing activities and provide guidance
  - Generic substitution by pharmacists
  - Off patent drugs are reference priced
  - Nationally coordinated risk sharing schemes for expensive drugs (oncology)
Budget impact creates a “cap” of sorts on the total budgetary impact a medication will have on the system.

**Italian Pricing & Reimbursement Negotiations**

- Risk sharing and rebate schemes are price reductions by another name
  - Risk sharing – e.g. company pays for first month+, 50% discount for first month+, etc. and then the SSN takes over if patient responds
  - Rebates – for sales exceeding agreed budgets
  - New law restricting off label use: intended to control inappropriate use of oncology drugs

<table>
<thead>
<tr>
<th>Italian Oncology drug registry (RFOM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(all oncology drugs monitored and list below had or has a risk sharing deal)</td>
</tr>
<tr>
<td>Avastin</td>
</tr>
<tr>
<td>Sutent</td>
</tr>
<tr>
<td>Sprycel</td>
</tr>
<tr>
<td>Tarceva</td>
</tr>
<tr>
<td>Tassigna</td>
</tr>
<tr>
<td>Revlimid</td>
</tr>
<tr>
<td>Vectibix</td>
</tr>
<tr>
<td>Tyverb</td>
</tr>
<tr>
<td>Nexavar</td>
</tr>
<tr>
<td>Torisel</td>
</tr>
<tr>
<td>Yondelis</td>
</tr>
<tr>
<td>Velcade</td>
</tr>
<tr>
<td>Erbitux</td>
</tr>
<tr>
<td>Alimta</td>
</tr>
<tr>
<td>Arranon</td>
</tr>
</tbody>
</table>

And many more
Budget impact creates a “cap” of sorts on the total budgetary impact a medication will have on the system.

Spanish Pricing & Reimbursement Negotiations

**Reimbursement criteria**
- The severity, duration and level of co-morbidities of the different pathologies for which they are indicated
- The specific necessities of certain groups of people
- The therapeutic and social usefulness of the pharmaceutical
- The public expenditure associated with the use of the pharmaceutical
- Existence of pharmaceuticals or other alternatives for the same diseases
- The degree of innovation of the pharmaceutical

**Decision criteria of CIPM to agree price include:**
- Cost per day compared with equivalent products in Spain
- ATC code, particularly if similar drugs already have a price
- Average price of product in other European countries
- Sales forecast
- Cost of R&D and manufacturing (historical)

- Decentralized decision making (to “regional autonomies”)
- While price is determined nationally, the autonomous regions can vary the conditions of reimbursement and negotiate local agreements
Cost-effectiveness markets arbiter the trade-offs that are considered worthwhile investments based on incremental cost and outcomes.

**Cost utility analysis and QALYs**

**What is a QALY?**
- QALY is a measurement of the time spent in a given health state.
- One QALY is defined as one year in full health.
- The health state (i.e., whether in full health or not) is measured in terms of the patient’s health related quality of life (HRQOL), also referred to as ‘utility’.
- Utility is measured on a scale of +1 to -1.

**Incremental clinical benefit**
- G-BA
- HAS

**Budget Impact**
- Regions
- Regions

**Cost-effectiveness**
- SMC
- NICE
Cost-effectiveness markets arbiter the trade-offs that are considered worthwhile investments based on incremental cost and outcomes.
Cost-effectiveness markets arbitrate the trade-offs that are considered worthwhile investments based on incremental cost and outcomes.

Share of SMC submission approved, rejected and restricted between 2001 and 2011

- Not recommended for use*, 80, 54%
- Recommended for use, 19, 13%
- Restricted for use, 49, 33%

*Cost in relation to health benefits are usually the reasons given by the SMC for a rejection.
Cost-effectiveness markets arbitrate the trade-offs that are considered worthwhile investments based on incremental cost and outcomes.

### NICE (England) Evaluations for Oncology Agents

#### Cost/QALY Results

<table>
<thead>
<tr>
<th>Product</th>
<th>Indication</th>
<th>Cost/QALY (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sutent</td>
<td>Advanced/metastatic renal cell carcinoma</td>
<td>29,340 – 105,000</td>
</tr>
<tr>
<td>Revlimid</td>
<td>Multiple Myeloma</td>
<td>22,589 – 69,500</td>
</tr>
<tr>
<td>Sutent</td>
<td>Gastrointestinal stromal tumours</td>
<td>20,618 – 90,500</td>
</tr>
<tr>
<td>Yondelis</td>
<td>Soft tissue sarcoma</td>
<td>28,712 – 70,000</td>
</tr>
<tr>
<td>Votrient</td>
<td>Advanced renal cell carcinoma</td>
<td>1,790 – 72,274</td>
</tr>
<tr>
<td>Vidaza</td>
<td>Myelodysplastic syndromes</td>
<td>32,823 – 85,790</td>
</tr>
<tr>
<td>Hycamtin</td>
<td>Small cell lung cancer</td>
<td>26,833 – 783,734</td>
</tr>
<tr>
<td>Alimta</td>
<td>Non-small cell lung cancer</td>
<td>33,732 – 105,826</td>
</tr>
<tr>
<td>Herceptin</td>
<td>Advanced/metastatic renal cell carcinoma</td>
<td>39,978 – 368,830</td>
</tr>
</tbody>
</table>

- The “End of Life” guidance has enabled at least 9 drugs to be recommended for NHS use.
Cost-effectiveness markets arbiter the trade-offs that are considered worthwhile investments based on incremental cost and outcomes.

NICE (England) Common Agreements for Risk-sharing of Oncology Agents

- **Performance based schemes**
  - Rebate for non-responders
  - Comparative effectiveness

- **Financially based schemes**
  - Discount/rebate
  - Initial treatment cycle free
  - Payment cap
  - Price cap/fixed price

- **Total of 22 patient access schemes, covering 20 products**
- **Almost all are a result of poor cost-effectiveness conclusions**
- **14 of the 20 products are for oncology indications**
- **8 schemes have confidential discounts**
- **7 of the 8 schemes agreed since March 2011 have confidential discounts**
Payers focus on different criteria and becomes crucial to understand how drugs will be assessed and how this can impact reimbursement.

### Drug assessment/Health Technology Assessment methodology in selected countries

<table>
<thead>
<tr>
<th>Incremental clinical benefit</th>
<th>Budget Impact</th>
<th>Cost-effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>G-BA</td>
<td>Regions</td>
<td>SMC</td>
</tr>
<tr>
<td>HAS</td>
<td>Regions</td>
<td>NICE</td>
</tr>
</tbody>
</table>

#### Priorities for reimbursement submissions in selected markets

<table>
<thead>
<tr>
<th></th>
<th>DE</th>
<th>ES</th>
<th>FR</th>
<th>IT</th>
<th>UK</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Therapeutic value</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Pharma-economic evaluation</strong>*</td>
<td>![Symbol]</td>
<td>✓</td>
<td>![Symbol]</td>
<td>![Symbol]</td>
<td>✓</td>
<td>![Symbol]</td>
</tr>
<tr>
<td><strong>Quality of life</strong></td>
<td>![Symbol]</td>
<td>![Symbol]</td>
<td>![Symbol]</td>
<td>![Symbol]</td>
<td>✓</td>
<td>![Symbol]</td>
</tr>
<tr>
<td><strong>Choice of comparator</strong></td>
<td>✓</td>
<td>![Symbol]</td>
<td>![Symbol]</td>
<td>![Symbol]</td>
<td>![Symbol]</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Budget impact</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>![Symbol]</td>
</tr>
</tbody>
</table>

- ✓ Must have
- ![Symbol] Nice to have
- ![Symbol] Increased importance
- ![Symbol] Less important

*Pharmaceoeconomic evaluation - measures such as cost-benefit, cost-effectiveness and others considered part of key priorities*

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Philosophical and regulatory differences are seen between the American and European healthcare systems.

**Value of health**
- Health is a *service* (American)
- Health is a *right* (European)

**Who pays for it?**
- Employers and individuals (American)
- The government (European)

**Pricing**
- Free pricing (American)
- Regulated/negotiated by governmental agencies (European)

**Utilization**
- More controlled (American)
- Less controlled (European)
“Europeanization” of US Oncology Pricing
Healthcare spending considerably higher in the US, than in selected European countries

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Oncology drug spending in the US is one of the highest in the world, and expected to increase.

**US & EU oncology spending, in USD (2009-2011)**

- **US$ 23.3 billion**
- **EU $ 5.2 billion**

Source: IMS Health Data, 2012. 
OECD Health Data 2011; IS-GBE, 2011. 
© GfK 2013
Annual US oncology spending is approximately $23.3 billion – 18.6% of total oncology expenditures.


Source: IMS Health Data, 2012.
Annual EU oncology spending is lower than in the USA – 11.8% of total oncology expenditures
European spending patterns for oncology drugs in the US would save $8.6 billion – <0.33% of the total US health spending.
What could we do instead?
How many nurses could you hire?

A) Actual US Spending on Oncology Drugs = $23,300,000,000
B) Hypothetical US Spending at EU ratios = $14,696,067,416
C) Average nurse salary = $50,000

\[
\frac{(A - B)}{C} = 172,078
\]

172,000 nurses

Source: Nurse salary estimate (Glassdoor.com estimated Sept 2013)
How many additional oncologists could you hire?

30,000 oncologists

A) Actual US Spending on Oncology Drugs= $23,300,000,000
B) Hypothetical US Spending at EU ratios = $14,696,067,416
C) Average oncologist salary = $285,000

\[
\frac{(A - B)}{C} = 30,189
\]

How much bonus could you give to each oncologist in the US?

A) Actual US Spending on Oncology Drugs = $23,300,000,000
B) Hypothetical US Spending at EU ratios = $14,696,067,416
C) Estimate number of oncologists in the US = 12,500

\[
\text{Bonus} = \frac{(A - B)}{C} = \frac{688,134}{12,500} = US$700,000
\]

What would we lose?
What is the US **getting** for these higher prices?

### Faster access to drugs

**Time from FDA to EMA approval and to reimbursement**

<table>
<thead>
<tr>
<th>Drug</th>
<th>FDA</th>
<th>EMA</th>
<th>France</th>
<th>Italy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vectibix</td>
<td>288</td>
<td>442</td>
<td>588</td>
<td></td>
</tr>
<tr>
<td>Herceptin</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Zelboraf</td>
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<td>Tyverb</td>
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<tr>
<td>Tarceva</td>
<td></td>
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<tr>
<td>Erbitux</td>
<td></td>
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<tr>
<td>Xalkori</td>
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<td>Sprycel</td>
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<td>Perjeta</td>
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<td>Nexavar</td>
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<tr>
<td>Tasigna</td>
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</tr>
</tbody>
</table>

- **Time lapse for EMA approval**
- **Time lapse in France**
- **Time lapse in Italy**


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What is the US **getting** for these higher prices?

Broader access to utilization of new medicines

**Outcomes from reimbursement assessments in Europe of recently launched oncology drugs**

<table>
<thead>
<tr>
<th></th>
<th>France</th>
<th>Germany</th>
<th>Spain</th>
<th>England</th>
<th>Scotland</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xtandi</td>
<td>Green</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Red</td>
</tr>
<tr>
<td>PERJETA</td>
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<td>Yellow</td>
<td>Yellow</td>
<td>Red</td>
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<tr>
<td>ZALTRAP</td>
<td>Green</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Red</td>
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<td>ADCETRIS</td>
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<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
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<td>XALKORI</td>
<td>Green</td>
<td>Yellow</td>
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<td>Red</td>
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<tr>
<td>DACOGEN</td>
<td>Green</td>
<td>Yellow</td>
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<td>Yellow</td>
<td>Red</td>
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<td>Inlyta</td>
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<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Red</td>
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<td>Green</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Red</td>
</tr>
<tr>
<td>Caprelsa</td>
<td>Green</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Red</td>
</tr>
</tbody>
</table>

**Legend:**
- Positive outcome from assessment
- Access leading to heavy price restrictions
- Negative outcome from assessment

Source: GfK Analysis of individual country HTA websites
© GfK Bridgehead 2013
What is the US **getting** for these higher prices?

**Broader access to utilization of new medicines**

Number of medicines “available” (% of EMA approved medications)

<table>
<thead>
<tr>
<th>Country</th>
<th>% of Drugs Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Switzerland</td>
<td>86%</td>
</tr>
<tr>
<td>Greece</td>
<td>86%</td>
</tr>
<tr>
<td>Denmark</td>
<td>79%</td>
</tr>
<tr>
<td>Sweden</td>
<td>77%</td>
</tr>
<tr>
<td>Austria</td>
<td>75%</td>
</tr>
<tr>
<td>France</td>
<td>67%</td>
</tr>
<tr>
<td>Ireland</td>
<td>64%</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>64%</td>
</tr>
<tr>
<td>Spain</td>
<td>64%</td>
</tr>
<tr>
<td>Slovenia</td>
<td>62%</td>
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<tr>
<td>Finland</td>
<td>57%</td>
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<tr>
<td>Portugal</td>
<td>55%</td>
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<tr>
<td>Norway</td>
<td>54%</td>
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<tr>
<td>Italy</td>
<td>43%</td>
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<tr>
<td>Belgium</td>
<td>43%</td>
</tr>
</tbody>
</table>

Source: EFPIA W.A.I.T. Indicator
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What is the US getting for these higher prices?

More effort required to justify treatment

Delay of treatment because of coverage restrictions (% of patients)

What is the US getting for these higher prices?

Better clinical outcomes? Access to cutting-edge technologies?

Mortality per type of cancer

Source: IMS Health Data, 2012.
OECD Health Data 2011; IS-GBE, 2011.
What is the US *getting* for these higher prices?

**Hesitancy from patients to seek care**

*Reasons for not going/go ing to the physician (US, 2008)*

- I go to the Dr only when I am sick: 49%
- Financial reasons: 43%
- I am healthy: 25%
- Time constraints: 12%
- Time to get to an appointment: 12%
- Inconvenient hours: 9%
- Hassle of getting to the Dr: 6%
- Distance to the Dr: 4%
- Difficulty in finding a Dr: 3%


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Thank you

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Case study: Avastin in second line metastatic colorectal cancer

**Reason for request:** Inclusion on the list of medicines approved for use by hospitals in the extension of indication (second-line treatment of metastatic cancer of the colon or rectum).

**Comparator:** An open-label randomised pivotal phase III study (E3200) comparing AVASTIN in combination with the FOLFOX 4 regimen (5-FU, folinic acid and oxaliplatin) with FOLFOX 4 alone with AVASTIN as monotherapy.

**Assessment:** Considering the data available (2 months improvement in overall survival during an open-label trial), a low impact on patients morbidity and mortality can be expected for AVASTIN.

However, there is no guarantee that the results of the trial can be transposed into actual practice. Patients taking part in the trial could have been eligible for first-line treatment with AVASTIN, which could not be the case under real conditions of use (patients who did not receive AVASTIN as first-line treatment because of a contraindication). Therefore, it is impossible to know whether AVASTIN, in this indication, will meet the identified public health need.

Consequently, in the current state of knowledge, the proprietary drug AVASTIN is not expected to benefit public health in this extension of indication.

Advice: following a full submission, pemetrexed (Alimta) is not recommended for use within NHS Scotland.

Indication under review: monotherapy for the maintenance treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) other than predominantly squamous cell histology in patients whose disease has not progressed immediately following platinum-based chemotherapy. First-line treatment should be a platinum doublet with gemcitabine, paclitaxel or docetaxel.

In a sub-group analysis of patients with non-squamous NSCLC, progression free survival and overall survival (secondary endpoint) were significantly longer for pemetrexed plus best supportive care (BSC) compared to placebo plus BSC.

However, the manufacturer did not present a sufficiently robust economic case and their justification of the treatment's cost in relation to its health benefits was not sufficient to gain acceptance by SMC.

The analysis shows that in addition to a comparatively high base case ICER, there are uncertainties in terms of the overall survival with treatment and the results were sensitive to this parameter. As such the economic case was not demonstrated.

There was concern from Scottish clinical experts that using this medicine in a maintenance setting may mean it would no longer be an effective second-line option.
The rejection of Jevtana by NICE suggests that payers will require significant clinical benefit and additional evidence to justify high prices for late-stage therapies.

Key Conclusion
Cabazitaxel in combination with prednisone or prednisolone is not recommended for the treatment of hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen.

The Committee considered the incremental cost-effectiveness ratio (ICER) of £89,000 per quality-adjusted life year (QALY) gained the starting point for its decision.

4.21 The Committee discussed whether cabazitaxel fulfilled the criteria for consideration as a life-extending end of life treatment. [...] The Committee considered the degree to which cabazitaxel extended life. It noted that the median overall survival gain was 2.4 months in the TROPIC population, that the mean overall survival gain estimated using the model was 4.2 months … The Committee agreed that further exploration and validation of the modelled mean survival benefit using updated trial-based or observational data would be necessary …

NICE may decide to approve non-cost effective therapies if significant clinical improvements are noted at the end of life, but the “end of life” threshold is generally accepted to be about £55,000 per QALY.

Demonstrated overall survival benefit (from pivotal trials) of 2.4 months was not adequate to grant an exception for Jevtana as a high-cost, end of life treatment.

A model estimating 4.2 months of overall survival gain was rejected and further observational data were requested.

NICE has issued a similar recommendation for Halaven, but also noted that there the side-effects that may prohibit it from replacing current standard of care.

Commenting on the draft guidance NICE Chief Executive, Sir Andrew Dillon said: "Although the evidence presented to the independent advisory committee indicated that eribulin may help some patients live for a little longer, it also caused more undesirable side effects than other treatments already available, and the effects on health-related quality of life had not been adequately assessed.

"The advisory committee heard from clinical experts that in current practice, patients at this stage usually receive sequential treatment of vinorelbine, capecitabine and, more rarely, gemcitabine. The experts also stressed that even if eribulin were approved by NICE, it would be unlikely to replace capecitabine and vinorelbine in the established sequential pathway because of its related side effects."

Notes from the final guidance

- Eribulin did not fulfill all the end-of-life criteria
  - Eribulin did not offer an extension to life of at least 3 months (overall survival gain was 2.7 months in ITT population over treatment of physician choice)
- Most common adverse effects: fatigue, alopecia, peripheral neuropathy, nausea, neutropenia, leukopenia and anaemia
- Cost per QALY of eribulin compared with 'treatment of physician's choice' is estimated to be in excess of £68,600

Source: NICE. 2011.
Case study: Sutent benefited from both the patient access scheme and the end-of-life medicine provisions

- Sutent for first-line treatment of advanced and/or metastatic renal cell carcinoma was taken out of the MTA process and treated as an STA
- A risk sharing scheme was agreed with DH
  - “The manufacturer of Sutent (Pfizer) has agreed a patient access scheme with the Department of Health, in which the first treatment cycle of Sutent is free to the NHS. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS”
- Cost per QALY for the target patient population was calculated
  - “The agreed pricing strategy of the first cycle of Sutent being free to the NHS resulted in an ICER of £54,366 per QALY gained for Sutent compared with IFN-α”
- The technology was then assessed against the end-of-life treatment criteria
  - “The Committee was satisfied that Sutent currently meets the criteria for being a life-extending end-of-life treatment, and that the evidence presented for this consideration was sufficiently robust”
Velcade was accepted by NICE for the treatment of multiple myeloma with an "efficacy guarantee"

NICE recommended Velcade as a possible treatment for progressive multiple myeloma for people:

- Who have relapsed for the first time after one treatment, and
- Who have had a bone marrow transplant, if suitable for them

After not more than four cycles of treatment, a blood or urine test should be done to check how well the cancer has responded to Velcade

- Treatment should be continued only if there has been at least a partial response to the drug

A response-rebate scheme will allow patients at first relapse who show a full or partial response to Velcade to carry on with the treatment, fully funded by the NHS, and patients who show no or minimal response to be taken off the drug and the drug costs refunded by the drug's manufacturer

This is an “efficacy guarantee” scheme using a defined biological marker for response

“This is a win-win situation for patients and the NHS.”
Neither bevacizumab (Avastin) or cetuximab (Erbitux) in metastatic colorectal cancer were recommended for use by NICE - (published January 2007)

Clinical evidence
- No direct comparisons with UK standard of care
- Patient populations not necessarily representative
  - Performance standards higher than typical
- Erbitux clinical endpoints less helpful
  - Primary endpoint was tumour response
    - Clinically relevant but hard to model implications
  - For Avastin primary endpoints were Overall Survival (OS) and Progression Free Survival (PFS)

Economic models of cost-effectiveness
- Were not based on direct comparison to UK standard of care
- Focus was on PFS (NICE would clearly have preferred OS)

Roche offered a registry to track performance of Avastin
- Rejected by NICE – implications for an imminent indication extension
Revlimid is an example of cost capping in the UK

REVLIMID® Receives Positive Final Appraisal Determination from National Institute for Health and Clinical Excellence (NICE) for Use in the National Health Service (NHS) in England and Wales, 2009

The recommendation states that the drug cost of REVLIMID (excluding any related costs) for patients who remain on treatment for more than 26 cycles (each of 28 days; normally a period of two years) will be met by Celgene

Taking into account the limitation on patient numbers, and the price capping scheme, the assessed cost per QALY was in the range £41,300 to £43,800 (the company’s corresponding figures were £28,941 to £30,350)

The predicted average savings from the cost capping were in the range £3,500 to £8,000, applying to between 11% and 17% of patients

Average lifetime treatment costs (with the cost cap) were estimated at between £46,300 and £51,800
Votrient (pazopanib) is recommended as a first-line treatment option for people with advanced renal cell carcinoma who have not received prior cytokine therapy and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.

COMPARZ: head-to-head non-inferiority trial of pazopanib versus sunitinib in patients with advanced renal cell carcinoma. Only the indication for Votrient for the first-line treatment of advanced renal cell carcinoma is within the remit of the appraisal.

NICE: Restricted access with a PAS (discount plus conditional rebate dependent on trial outcomes)

Iressa fixed price deal

NICE final appraisal determination May 2010

The manufacturer and Department of Health have agreed a patient access scheme in which gefitinib (Iressa) for first-line treatment of NSCLC will be available at a single fixed cost of £12,200 per patient irrespective of the duration of treatment.

The manufacturer will not invoice the NHS until the third monthly pack of gefitinib is supplied. This means that patients who need less than 3 months treatment will not incur a charge.

The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

The company submission proposed ICERs in the range £19,400 to £36,000 per QALY gained, depending on comparator treatment regime.

NICE accepted ICERs in the range £23,600 to £64,500.

The accepted ICER, as published, does not appear to reflect the agreed “fixed price” deal.