

Risk Sharing

US vs European Perspectives

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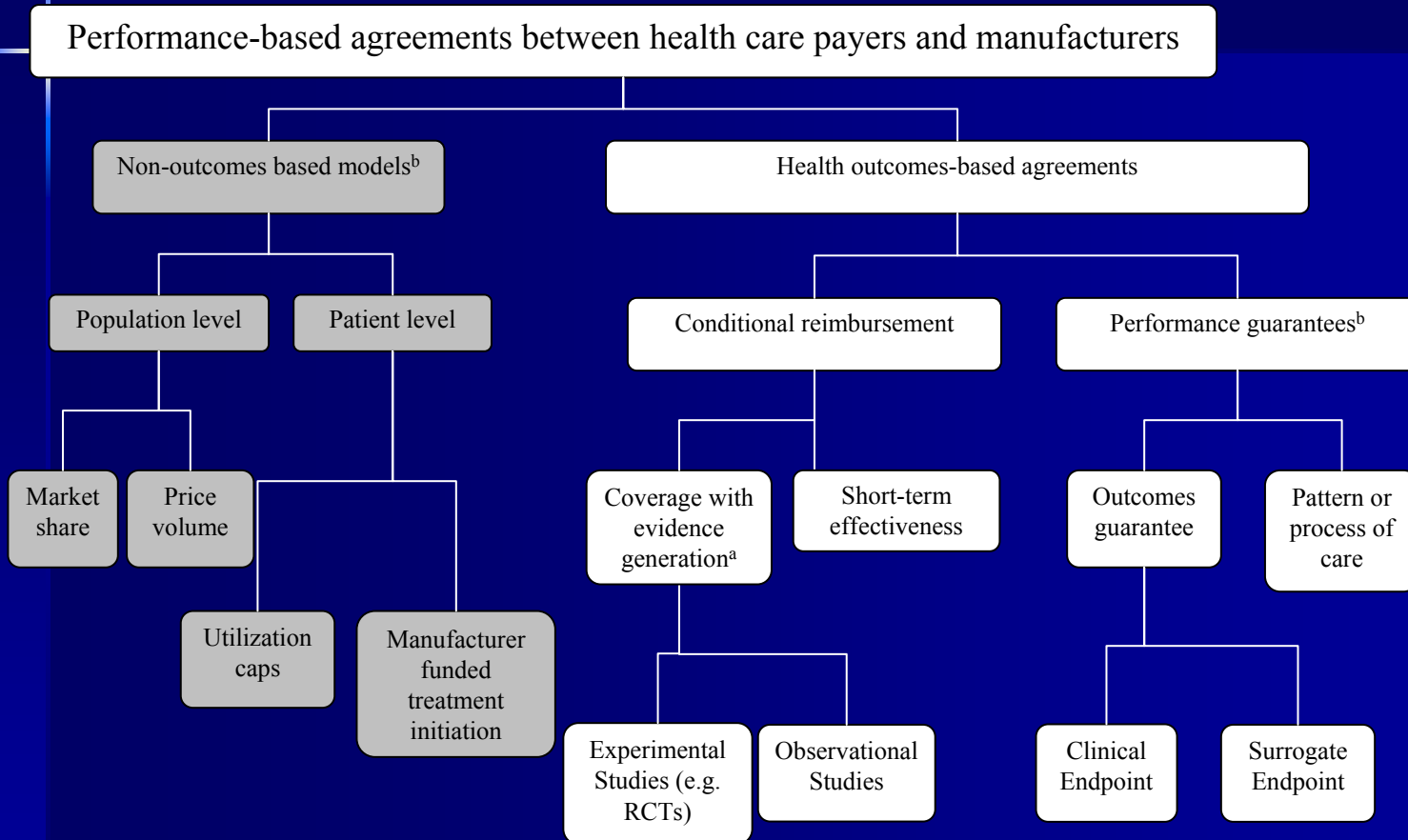
Sanofi aventis

Agenda

■ Taxonomy of Agreements

- Non-Outcomes Based vs Outcomes Based
 - Contracting, Market and Price Agreements
 - Performance Guarantees
 - Conditional reimbursement
 - Pay for performance/short term effectiveness
- Differences between EU and US in types of agreements
- Potential future scenarios

Taxonomy of Agreements



Source: Pharmaceutical Outcomes Research & Policy, University of Washington

^a Includes CMS coverage with evidence development initiative

^b Also termed “risk-sharing” in certain contexts

^c Includes UK’s Office of Fair Trading reform proposal for the PPRS toward value-based pricing

Non Outcomes Based Risk Sharing

- Financial Risk Sharing is popular in the USA
 - Discounting schemes (including rebates) Risk is also shared with the patient for high cost therapies
 - Co-payments
 - Co-insurance
- In Europe these are most often formed as utilization caps or price/volume agreements (e.g. France)

Performance Based Schemes

Performance-based health outcomes schemes:

Arrangements between a payer and a pharmaceutical, device, or diagnostic manufacturer where the price, level and/or nature of reimbursement are tied to future measures ultimately related to patient quality or quantity of life.

Conditional reimbursement: Binary coverage determination is conditioned upon patient participation in research or evaluation of short-term effectiveness

Performance guarantees^b: Level of reimbursement is tied to measure of clinical outcome in “real world” and includes pre determined consequences. Can be evaluated at the population or patient level

Coverage with evidence development^a:

Coverage conditioned upon the collection of additional evidence to support continued, expanded, or withdrawal of coverage.

Short-term effectiveness:

Coverage continuation tied to achieving short-term effectiveness goals

Experimental Studies

(e.g. RCTs):
Reimbursement tied to collection of additional evidence related to safety and efficacy

Observational Studies:

Reimbursement tied to collection of additional evidence related to effectiveness, cost-effectiveness, safety, utilization, and/or clinical impact

Outcomes guarantee: Refunds, rebates, or price adjustments if the product fails to meet agreed outcome targets

Pattern of care:
Reimbursement tied to the impact on clinical decision making or practice patterns

Clinical Endpoint:

A characteristic or variable that reflects how a patient feels or functions, or how long a patient survives

Surrogate endpoint:

A biomarker intended to substitute for a clinical endpoint, i.e., a biomarker that is expected to predict clinical benefit, harm, or lack of benefit or harm.

^a Includes CMS coverage with evidence development initiative

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Key Elements of Performance Based Schemes

- Agreements between a payer and a pharmaceutical, device, or diagnostic manufacturer where the price level and/or nature of reimbursement is related to the *actual* future performance of the product in either the research or “real world” environment rather than the expected future performance.
- Agreements are linking coverage and/or net price to health outcomes and/or value
- Issue is the level of uncertainty at launch regarding the benefits of allowing access versus the price/cost of new interventions
- Two main types of agreement
 - Performance Guarantees
 - Conditional Reimbursement

Published Performance Guarantees in the USA

Source, Year	Disease area	Manufacturer	Payer	Agreement
Moldrup, 1995	High cholesterol	Merck	Patients and Insurers	Merck promised to refund patients and insurers up to six months of their prescription costs if simvastatin plus diet did not help them lower LDL cholesterol to target concentrations identified by their doctors.
Pollack, 2007	Breast Cancer	Genomic Health	United Healthcare	United Healthcare agreed to reimburse the OncotypeDx test for 18 months while it and Genomic Health monitor the results. If the number of women receiving chemotherapy exceeds an agreed upon threshold, even if the test suggests they do not need it, the insurer will negotiate a lower price.

Published Performance Guarantees in Europe

Source, Year	Country	Disease area	Manufacturer	Payer	Agreement
Chapman ²⁰ , 2003	UK	High cholesterol	Park Davis (Pfizer)	North Staffordshire health authority	Park Davis (Pfizer) agreed to rebate the North Staffordshire health authority if a defined patient population did not achieve a low density lipoprotein cholesterol concentration target of < 3 mmol/l after using statins .
Sparrowhawk ²¹ , 2007	UK	Asthma	Novartis	National health service	Novartis offers UK hospitals replacement product for appropriately diagnosed, high-need Xolair (omalizumab) patients who fail to achieve target clinical response.
Thomson, 2008	UK	Colorectal cancer	Merck	Primary care trust	Rebate direct to primary care trust on the cost of any vials of Cetuximab used for patients who do not achieve a pre-agreed clinical outcome ('nonresponders') at up to 6 weeks (up to an agreed maximum of 3200 milligrams).
Anonymous ²² , 2008	Germany	Kidney transplantation	Novartis	Deutsche Angestellten-Krankenkasse (DAK)	Novartis and DAK (a German insurance company) have agreement to refund money for Sandimmun Optoral (Cyclosporin) , Myfortic (mycophenol acid) or Certican (Everolimus) if a patient loses his/her donor kidney.
Anonymous ²² , 2008	Germany	Osteoporosis	Novartis	DAK and Barmer	DAK and Barmer (a German insurance company) have a money back guarantee for Aclasta (Zoledronat) if an osteoporosis related fracture occurs
Green ²⁴ , 2006	UK	Multiple myeloma	Johnson and Johnson	National health service	J & J agreed to reimburse the NHS in either cash or product for patients who do not respond (Response measure: 50% decrease in serum M protein) after 4 cycles of treatment with Velcade . Responding patients receive additional 4 cycles.
Chadwick ⁷ , 2003	UK	Multiple Sclerosis	Biogen, Schering, Teva/Aventis, Sero	National health service	Patients using Interferon beta's or glatiramer acetate are followed for 10 years with treatment effects determined every two years. Drug price reduced to maintain cost effectiveness at £36,000/QALY

MS Risk-sharing : Key Elements

- Detailed monitoring over 10 years of a cohort of patients to confirm the cost-effectiveness of the MS treatments, various beta interferons and glatiramer.
- Treatments initiated by specialist MS centres based on ABN guidelines; no bar to clinicians prescribing for patients falling outside these guidelines.
- Central features are target outcome measures; agreed NHS price; threshold cost per QALY of £36,000.
- Outcome measure is Expanded Disability Status Score. Actual outcomes reviewed every 2 years against standard MS disease (non-treated) progression model through the EDSS scale.

Issues in the MS scheme

- Long negotiation process
- Danger of gold plating data requirements
- Difficulty in recruitment
- Difficulty in monitoring
- Awaiting interim results
- Untried reconciliation process and adjudication group /process
- Is this unique or endemic to risk sharing?

Conditional Reimbursement

- Main example of conditional reimbursement in US and EU is **Coverage with Evidence Development (CED)**
- Allows a technology to be made available under specific conditions, usually a defined period, after which the benefits of the technology are reviewed.
- Objective of the additional data generation is to reduce uncertainty around a specific aspect of the evidence base

CMS and Coverage with Evidence Development

- « The purpose of CED is to generate data on the utilization and impact of the item or service evaluated in the National Coverage Determination, so that Medicare can
- a) document the appropriateness of use of that item or service in Medicare beneficiaries under current coverage
 - b) consider future changes in coverage for the item or service
 - c) generate clinical information that will improve the evidence base on which providers base their recommendations to Medicare beneficiaries regarding the item or service ».

CMS Coverage with Evidence Development

- Actually covers two concepts:
 - Coverage with Appropriate Determination (CAD)
 - Coverage conditioned on specific additional data collection
 - Coverage with Study Participation (CSP)
 - Coverage conditioned on care being delivered in a setting with a pre-specified data collection process and additional protections in place such as are present in some research studies
 - Laid out in on-line document from CMS (see http://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=8)

CMS Coverage with Evidence Development Programmes

Source, Year	Disease area	Manufacturer	Payer	Agreement
CMS, 2004	Cognitive impairment	Multiple	CMS	An FDG-PET scan is covered in patients with mild cognitive impairment or early dementia in the context of an approved clinical trial.
CMS, 2005	Hearing loss	Multiple	CMS	CMS may cover cochlear implantation for treatment of hearing loss when the provider is participating in, and patients are enrolled in, an approved clinical trial
CMS, 2005	Oncology	Multiple	CMS	An FDG-PET scan is covered in patients with brain, ovarian, pancreatic, small cell lung, testicular cancers, and certain indications for cervical cancer in the context of an approved clinical trial.
CMS, 2005	Tachyarrhythmia's	Multiple	CMS	Implantable Cardioverter Defibrillators are covered in the context of an approved clinical trial or registry.
CMS, 2006	Chronic hypoxemia	Multiple	CMS	The home use of oxygen is covered for those beneficiaries with arterial oxygen partial pressure measurements from 56 to 65 mmHg or oxygen saturation at or above 89% who are enrolled subjects in clinical trials approved by CMS and sponsored by the National Heart, Lung & Blood Institute (NHLBI).
CMS, 2006	Atherosclerotic disease	Multiple	CMS	CMS covers Percutaneous Transluminal Angioplasty and Stenting of intracranial arteries for the treatment of cerebral artery stenosis $\geq 50\%$ in patients with intracranial atherosclerotic disease when furnished in an approved clinical trial.
CMS, 2008	Colorectal cancer	Sanofi-Aventis, BMS, Pfizer, Genentech	CMS	Oxaliplatin, irinotecan, cetuximab, or bevacizumab for the treatment of colorectal cancer are covered in the context of an approved clinical trial.

Coverage with Evidence Development in Europe

Source, Year	Country	Disease area	Manufacturer	Payer	Agreement
Whalen ¹⁰ , 2007	Fr.	Schizophrenia	Johnson and Johnson	French health authority	France's health care authority agreed to cover Risperdal Consta at J&J's asking price if J&J performed studies to evaluate whether Risperdal Consta helps patients stay on their medications. If the studies show otherwise, J&J will reimburse France a portion of the money it spent on the drug.
Chadwick ⁷ , 2003	UK	Multiple Sclerosis	Biogen, Schering, Teva/ Aventis, Serono	NHS	Patients using Interferon beta's or glatiramer acetate are followed for 10 years with treatment effects determined every two years. Drug price reduced to maintain cost effectiveness at £36,000/QALY

Source: Pharmaceutical Outcomes Research & Policy, University of Washington

Should also note that there is increasing use of CED in hospital settings for pharmaceuticals by the DHCIB in the Netherlands (see for example Retèl et al, IJTAHC 2009;25(1): 73-83)

Catalan Agency for HTA in Spain has also made CED recommendations

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Pay for Performance

- NHCQ pushed quality measures including HEDIS
- Center for Payment Reform
- CMS Value Based Purchasing
- No payment for « never events »
 - Avoidable rehospitalisations
 - Nosocomial infections
 - VTE

Short-term effectiveness

Source, Year	Country	Disease area	Product	Manufacturer	Payer	Agreement
IMS Health ²⁵ , 2007	Italy	Renal cell carcinoma	Sunitinib, Sorafenib	Pfizer, Bayer	Italian health authority	A hospital discount of 50% applies to the first two/three months of treatment with Nexavar (sorafenib) and Sutent (sunitinib) . For responding patients, the treatment is then reimbursed and the discount dropped.
Sparrowhawk ²¹ , 2007	Italy	Alzheimer's disease	Alzheimer's disease drugs	Multiple	Italian health authority	During first 3 months, patients starting Alzheimer's disease drugs are assessed for short-term effectiveness. Drug provided free by manufacturer. If treatment goals are met after 3 months, treatment is continued for a max of 2 years – drug costs reimbursed by national health service. Evaluation by UVA every 6 months
Green ²⁴ , 2006	UK	Multiple myeloma	Velcade	Johnson and Johnson	National health service	J & J agreed to reimburse the NHS in either cash or product for patients who do not respond (Response measure: 50% decrease in serum M protein) after 4 cycles of treatment with Velcade . Responding patients receive additional 4 cycles.

Source: Pharmaceutical Outcomes Research & Policy, University of Washington

Velcade (bortezomib)

- 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 bortezomib.
- 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 a win-win situation for patients and the NHS."

Lucentis (ranibizumab)

- NICE recommends that the NHS should pay for a maximum of 14 injections of Lucentis per eye, which should result in stable vision for most patients and improved vision for around a quarter of patients.
- It recommends that the manufacturer should pay if any further doses are needed.
- A dose-capping scheme will need to be agreed by both the manufacturer and the Department of Health.
- Responses to earlier consultation made clear that many people felt it was unacceptable for NICE to recommend treating only the second affected eye.
- NICE has taken these concerns on board, and now recommends treating the first eye to come to clinical attention.

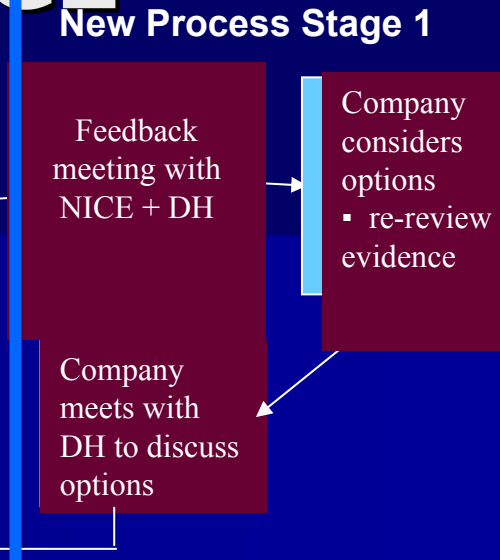
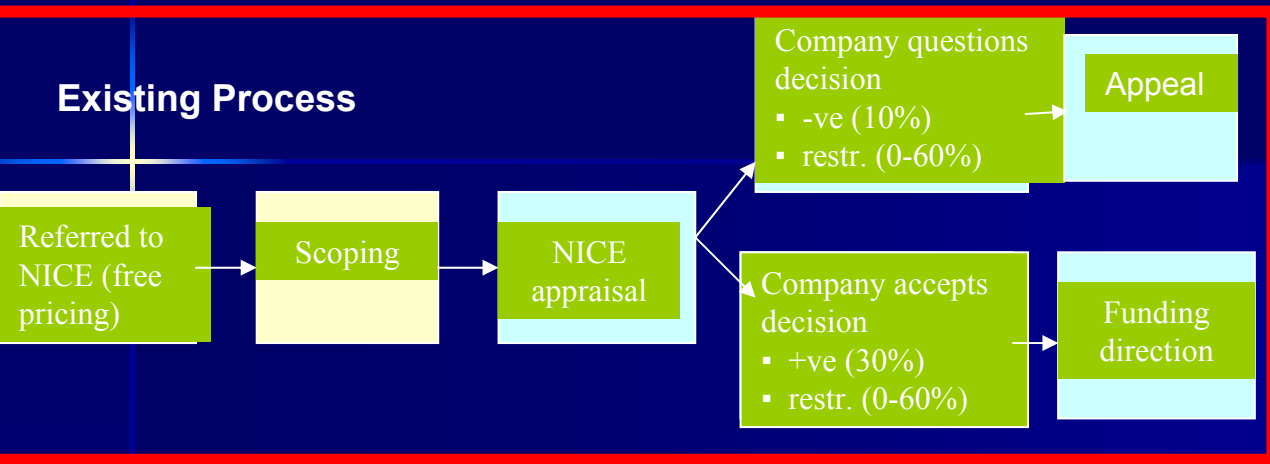
OFT on risk sharing

- Where data at the time of launch is insufficient to take an informed view on cost effectiveness, then, in a limited number of cases, a risk sharing approach could be adopted.
- This would require the company and payer to agree a contract in which the drug is reimbursed, contingent on claims of clinical effectiveness being realised in practice. This would be assessed through information on the use of the drug in clinical practice.
- If expected outcomes are not realised, prices would be changed and / or repayments made.
- Risk sharing arrangements could in principle be particularly relevant for the treatment of chronic (as opposed to acute) conditions, where final clinical outcomes may only become clear after several years of use.
- However, challenges for implementation remain and risk sharing would be the exception rather than the norm under an ex ante approach to pricing

OFT on non-linear pricing

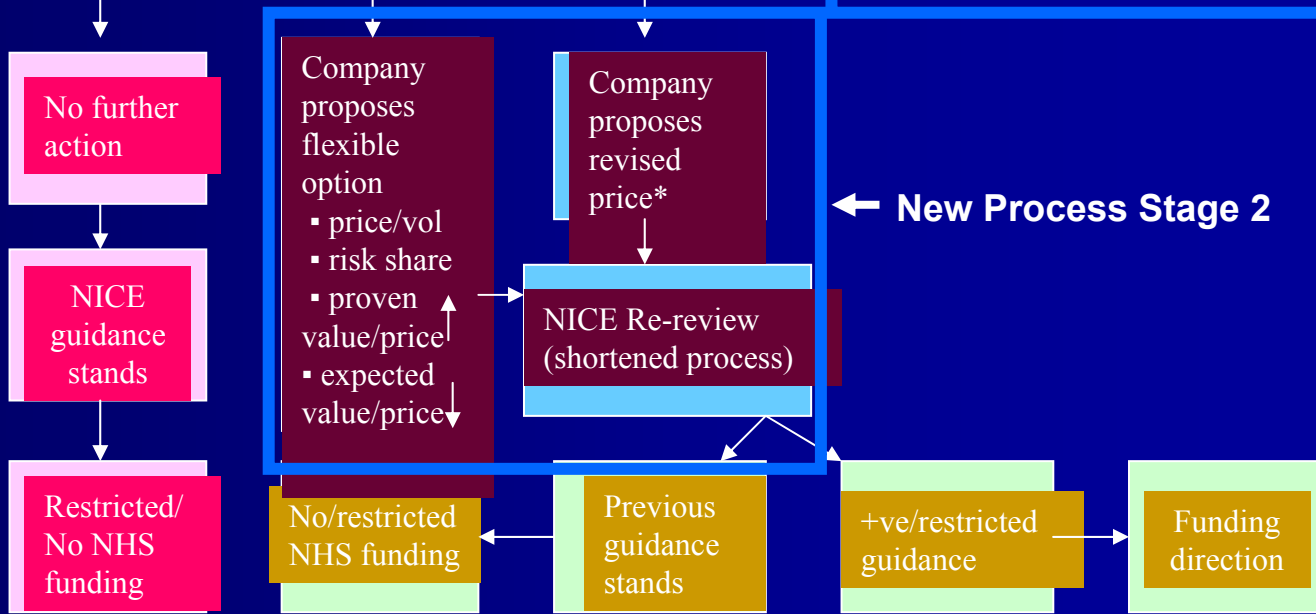
- We feel much could be achieved by allowing for more flexible price structures such as price volume agreements and rebate systems.
- This would be particularly useful for drugs for which cost effectiveness differs markedly by indication and patient subgroup. A higher price could apply for a particular prescription volume, reflecting the subgroup for which the drug will be particularly effective, and a lower price for excess volumes.
- The same outcome could be achieved through rebates between companies and payers and in practice, this may be a more practical solution.
- A more flexible pricing structure would help address the concerns that companies have incentives to incur marketing expenditure in an attempt to increase volumes beyond those for which the drug is cost effective.
- Changes to the price structure would therefore help ensure the incentives of firms are much more closely aligned with those of the NHS.

"Fast Track" Back to NICE



Process to be confidential
 Consultation only if guidance change proposed

* Proposed price to be implemented post +ve NICE review. Company reserves right to retain original price with -ve/restricted guidance if re-review negative



Financially-Based Patient Access Schemes

These are where:

- The company does not alter the list price of the drug, but offers effective discounts or rebates which may be linked to (for example) the:
 - Numbers or type of patients treated
 - Response of patients treated
 - Numbers of doses required
- Within these schemes the simplest type is one involving an adjustment to the price the NHS pays without a need for additional reporting of patient data as this places the least burden on the NHS

Outcome-Based Patient Access Schemes

- **Outcome-based Schemes can be split into three sub-groups:**
 - Proven value: price increase: The company seeks agreement to a later increase in price subject to a re-review of the drug in the light of additional evidence collection as agreed with NICE.
 - Expected value: rebate. The company seeks agreement to a price subject to the collection of additional evidence as agreed with NICE. Such an arrangement would be subject to a rebate and subsequent reduction in list price in the event of the additional evidence not supporting the current price
 - Risk Sharing: Outcomes are measured and price adjustments and/or cash transfers are made in one or both directions (between the company and the NHS) in the light of the outcomes identified relative to those anticipated in line with the terms of the scheme

Summary on Patient Access Schemes

- Introduces a “fast track” confidential post-Guidance route into the NHS
- Financially-based Schemes offer a tool for companies to offer flexibility to get value whilst maintaining international pricing policies
- Outcomes-based Schemes also offer a pre-agreed tool to adjust price to reflect better evidence
- Ends current ad hoc arrangements within the NICE process
- Maintains company control of price setting. NICE will not set or indicate price.
- Two year review point to assess operations in practice

Potential Future Scenarios

- Option One:
 - Increased use of the all types of the risk sharing framework but in the same ad hoc manner as currently observed
- Option Two
 - Decreased use of the performance guarantee/outcomes types of risk sharing frameworks but increased financial risk sharing
- Option Three
 - Move towards a “NICE-like” use of the risk sharing framework so that it is an integrated part of the pricing and/or reimbursement process

**Thank you for your
attention**

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