REGenableMED

E·S·R·C ECONOMIC & SOCIAL RESEARCH COUNCIL

*Regenerative Medicine in the UK Health System, 23 May 2017, London*

# Negotiating regulation, evidence and reimbursement

*Alex Faulkner & Aurélie Mahalatchimy*

*Centre for Global Health Policy*

UNIVERSITY OF SUSSEX

# Outline

1. Negotiating regulation for Market access

2. Reimbursement landscape;
   Negotiating payment scenarios

UNIVERSITY OF SUSSEX

# 1. Different Pathways for market access

- Different regulations according to
  - Products' types
    - Medical Devices
    - Medicinal products
    - Tissues and cells
    - Blood and blood components
- Scales of development
  - Industrial or non industrial
- Degrees of manipulation of tissues and cells
  - Substantial manipulation or not
  - Homologous use or not

UNIVERSITY OF SUSSEX

# Medicines pathways - EU

- The most promoted regulatory pathway
  - Advanced Therapy Medicinal Products
    - Gene therapy, cell therapy, tissue engineering products
    - Specific regulation: Centralised marketing authorisation at the EU level, specific Advanced Therapies Committee at EMA,…
  - ‘Flexibilities’ for medicines with ‘unmet need’ and public health emergency
    - Conditional approval
    - Exceptional circumstances
    - Compassionate use

UNIVERSITY OF SUSSEX

| | Accelerated Assessment - AA | Conditional MA | Compassionate use |
|---|---|---|---|
| What | Assessment time for MA ≤ 150 days | Less complete data for earlier authorisation | For seriously ill patients without authorised treatments and outside Clinical Trials |
| Why | Early access | Early access | Early access |
| How | Major interest for public health (unmet medical need)<br><br>MA criteria | Seriously debilitating or life- threatening diseases, emergency situations, orphan drugs, unmet medical needs<br>MA Criteria | Unauthorised MP for chronically, seriously debilitating or life-threatening diseases, scope of centralised procedure, undergoing MAA or CTA; Targeted at a group of patients |
| Who | MA Applicant to EMA | MA Applicant to EMA | NCA to EMA |
| When | Before submission of MA<br>BUT can be discussed earlier via PRIME | Before submission of MA<br>BUT should be discussed earlier via scientific advice/protocol assistance | Parallel pathway to conventional MA |

Withdrawal

Withdrawal

| Chondrocelect | Glybera | MACI | Provenge | Holoclar | Imlygic | Strimvelis | Zalmoxis |
|---|---|---|---|---|---|---|---|
| TEP | GTMP | Comb. TIP | CTMP | TEP | GTMP | GTMP | CTMP |
| Orthop | Gastro. | Orthop. | Onco. | Ophtal. | Onco. | Immun. | Graft vs. host |
| 2009 | 2012 | 2013 | 2013 | 2015 | 2015 | 2016 | 2016 |
| Norm. MA | Norm. MA | Excep. MA | Norm. MA | Cond. MA | Norm. MA | Norm. MA | Cond. MA |
| - | Orphan | - | - | Orphan | - | Orphan | Orphan |
| Tigenix (BE) | UniQure (NL) | Vericel (USA) | Dendreon/ Valeant (USA) | Chiesi (IT) | Amgen Europe (NL) | GSK (UK) | MolMed (IT) |

MA Not to be renewed

SUSPENDED

TEP: Tissue Engineered Product; GTMP: Gene Therapy Medicinal Product; CTMP: Cell Therapy Medicinal Product; Comb.: Combined; MA: Marketing Authoristion

# The Council of the EU

"NOTES WITH CONCERN **an increasing number of examples of market failure** in a number of Member States, where **patients access to effective and affordable essential medicines is endangered by very high and unsustainable price levels**, **market withdrawal** of products that are out-of-patent, or when **new products are not introduced to national markets for business economic strategies** and that individual governments have sometimes limited influence in such circumstances"

*Council conclusions on strengthening the balance in the pharmaceutical systems in the EU and its Member States, 17 June 2016.*

UNIVERSITY OF SUSSEX

# Is market access real?

- Gap between medicines access to the market and medicines access to patients
- If no access to patients> no market
- Full patients access to medicines where full reimbursement

BUT

- Marketing authorisation at European level (ATMPs) and reimbursement decisions at national levels
- Different criteria for market access (efficacy, benefits/risks balance) and for reimbursement (cost effectiveness)

UNIVERSITY OF SUSSEX

# Flexible pathways for early access

- The current regulatory trend
  - At EU level: To support medicines development
    - Adaptive Pathways
    - Enhanced early dialogue to facilitate accelerated assessment for PRIority Medicines (PRIME)
  - At UK level
    - Promising Innovative Medicines designation (PIM)
    - Early Access Medicines Scheme (EAMS)
    - Accelerated Access Review (AAR)

Regulatory flexibilities for patients' access to medicines where there is an 'unmet medical need'/ a medical need

UNIVERSITY OF SUSSEX

## At EU level

| | Adaptive Pathways | PRIME |
|---|---|---|
| What | A prospectively planned, iterative approach to bringing medicines to market | An enhanced interaction and early dialogue with developers of promising medicines, to optimise development plans and speed- up evaluation |
| Why | To support medicine development | |
| How | Unmet medical need/ high medical need<br>Iterative development plan<br>Proposals for involved stakeholders<br>RCTs + plan for real world data as a complement | Major interest for public health (unmet medical need)<br>Same as AA |
| Who | Involvement of HTAs and other downstream stakeholders | Potential candidate for AA to dedicated person at EMA |
| When | Before parallel HTA/SA request<br>Use of existing routes of approval, esp. conditional MA | Clinical (or earlier for academics and SMEs) stages of development<br>Use of existing routes of approval, esp. AA |

## At UK level

| | PIM | EAMS | AAR |
|---|---|---|---|
| What | An early designation to facilitate eligibility to EAMS | An approval to give patients patients with life threatening or seriously debilitating conditions access to medicines when there is a clear unmet medical need | A proposed approach for patients quicker access to innovative medicines, medical devices, digital products and emerging forms of treatment |
| Why | Early Access | Early Access | Early access and to make the UK a world-leader in healthcare innovation |
| How | Early clinical data assessed during MHRA scientific meeting | An MHRA scientific opinion on the benefit/risk balance of the medicine, based on the data available | Enhanced horizon scanning process, new transformative designation, involvement of patients, new strategic commercial unit at NHS England… |
| Who | MHRA | MHRA | New partnership including NHS England, NHS Improvement, NICE and MHRA |
| When | Several years before Licensing | (After PIM and) before licensing/ Marketing authorisation | An entire new Accelerated Access pathway along the whole product life |

# 2. Reimbursement/Payment landscape and scenarios

- Publications analysis

- Interviews and online documents

UNIVERSITY OF SUSSEX

# Reimbursement – UK linked publications landscape

- Publication trends?
- In which types of publications?
- In which perspectives/fields of research (clinical, soc sci, economics, public health, business, other)?
- Which clinical areas?
- What payment scenarios? Risk-sharing?
- UK position and authorship

UNIVERSITY OF SUSSEX

# Publications profile

**Journals** publications dominate (74%; N= 37/50)

- public health/innovation (4/4), economics (3/4), clinical (22/23)

**Dominant perspectives:**

- clinical (23/50); social science (14/50); economics (4/50).

UNIVERSITY OF SUSSEX

# 22 articles in clinical journals 2015

| | |
|---|---|
| General | 10 |
| Haematological | 2 |
| Neurologic | 1 |
| Skin | 3 |
| Respiratory | 3 |
| Gastroenterological | 0 |
| Orthopaedic | 2 |
| Cancers (other than blood) | 0 |
| Ophthalmologic | 1 |
| Cardiovascular | 0 |
| **Total** | **22** |

# RM reimbursement focus

- Reimbursement of RM products growing topic 2015 - 2016 (independently from orphan drugs - high volume).
- Reimbursement methods, including risk- sharing, are discussed as distinct topics.
- No publication *title* included reimbursement + risk-sharing and UK involvement.
- USA (416 publications 2015), Japan (239), Germany (237), France (188), **UK (183),** S. Korea (56).

UNIVERSITY OF SUSSEX

# Stakeholders' payment considerations (interviews)

**6 dimensions in stakeholder discussions about payment principles, methodologies and proposals**:

- Product type issues;
- Organisation, infrastructure, roles;
- Evidence, uncertainty, cultures;
- Payment scenarios, market building;
- Data needs
- Explicit 'value' and values

UNIVERSITY OF SUSSEX

# Product type

**"… cell and gene therapy… will have an easier route** into adoption…They will face challenges on cost, I think but they will be straightforward challenges because they will be compared with current (drugs)

…as we move forward into the **more medical device type** areas like orthopaedics and like wound care, I think that's going to become much **more complex**".

(Innovation network 1, 2015)

UNIVERSITY OF SUSSEX

# Organisation

"**All of these medicines will come under specialised commissioning** and there is the mechanism there…for commissioning policies to be developed, for the evidence base to be reviewed and for recommendations to be made".

(Trade organisation 4, 2015)

UNIVERSITY OF SUSSEX

# ‘Evidence’

“costing the impact of something **where you don’t know the durability of the product is very difficult**… They’re not going to build your cartilage forever so we’re back at … the limits of the evidence base”.

(National body 2, 2015)

UNIVERSITY OF SUSSEX

# ‘Evidence’

“for regenerative medicines to be successful, I think we’ll need **a new mindset in HTA approvals which is more forgiving**, if you like, to benefit patients…perhaps within a structured framework of **additional data collection**”.

(Trade organisation 4, 2015)

UNIVERSITY OF SUSSEX

# ‘Evidence’

“… So we want to be able to **see how real-world evidence collection can be used more actively** in appraisals…
HTA bodies are not used to having to take that kind of evidence into account”.

(Trade organisation 4, 2015)

UNIVERSITY OF SUSSEX

# Data needs

"**There is a great reluctance on the part of both pharmaceutical companies and the NHS** on the ground to enter into these schemes that involve collecting data".

(Business Consultant 2, 2015)

UNIVERSITY OF SUSSEX

# NICE: exploration of applicability of methods to RM, 2015-16

"…**demonstrate the versatility and adaptability of NICE's approach** to appraising health technologies to enable appropriate consideration of these innovative treatments."

(NICE, 2016)

UNIVERSITY OF SUSSEX

# NICE's exploratory study

'Where there is a combination of **great uncertainty** with **potentially** very **substantial patient benefits**, **innovative payment methods** may have a key role to play in managing financial risk …

(*https://www.nice.org.uk/News/Press-and-Media/nice-publishes-report-on-approaches-to-assessing-innovative-regenerative-medicines*) 29 March 2016

UNIVERSITY OF SUSSEX

# Innovative payment scenarios

"part of our work that we're trying to with NICE to create the opportunity for **conditional approvals**, so that medicines may be approvable with a limited evidence base… **Coverage with evidence development**."

(Trade Organisation 4, 2015)

UNIVERSITY OF SUSSEX

# Range of conditional valuation and payment scenarios

- Risk-sharing
  + Real World Evidence
- ‘Lifetime leasing’ (NICE)
- Capped annuity with risk sharing

- Patent prizes; prolonged patent rights
- Out-licensing of technology rights;
- Dedicated ‘silo’ funding

UNIVERSITY OF SUSSEX

# NHS England flexible routes

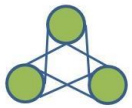
- **'Specialised Services' (NB** *'funding experimental and unproven treatments'* part of Specialised Commissioning public consultation Oct 2016**)**
- **'Commissioning through Evaluation'** scheme
- **Individual patient requests (-> policy need)**
- **NHS Tariff innovations?**
- **CCGs discretion**

UNIVERSITY OF SUSSEX

# Concluding: patient access

- Rare disease applications
- Exceptional ‘compassionate’ use etc regulatory routes; ‘unmet need’
- Provisional ‘managed’ reimbursement models
- ***‘Value’ and needs-driven?***

REGenableMED



UNIVERSITY OF SUSSEX

E·S·R·C ECONOMIC & SOCIAL RESEARCH COUNCIL

# THANK YOU


REGenableMED
E·S·R·C
ECONOMIC & SOCIAL RESEARCH COUNCIL
Regenerative Medicine in the UK Health System, 23 May 2017, London
Negotiating regulation, evidence and reimbursement
Alex Faulkner & Aurélie Mahalatchimy
Centre for Global Health Policy
US
UNIVERSITY OF SUSSEX