Role of Institutional Committees for admission of new medicines and innovative medical devices in French Hospitals

Pr Philippe Lechat

Pharmacology Unit, Hôpital St Louis, University Paris-Diderot
Head of Medicine and Device Committee of Assistance Publique des Hôpitaux de Paris
French Society of Pharmacology and Therapeutics (SFPT)
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Inspections by regional health agencies and health insurance authorities on the different points of such contract:

Hospital payment by public health care system under conditions of performance and results of « contrat de bon usage » (= Good Therapeutic management contract) between hospitals and regional health agencies (ARS).

Many quality and safety items are measured about therapeutic management issues such as preventive strategies of “never events”, non-inhalative dispensation of drugs, centralised chemotherapy preparations, implementation or computerised prescription, morbidity-mortality reviews, prevention of « never events », non-inhalative dispensation of drugs, centralised chemotherapy preparations...
Role of institutional medicine and device committees in French Hospitals (1): Three targets

**Cost “containment”:** Admission of medicines and devices at the best cost/efficacy ratio for the institution.

**Safety:** Prevention of drug-induced adverse reactions and device-related errors.

**Efficacy:** Implementation of good clinical use of medicines (according to SPC labeling) and official recommendations for prescription by physicians, validation by pharmacists, administration by nurses.

The institution (optimal benefit/risk ratio for the patient at the lowest costs for the institution).
Role of institutional medicine and device committees in French Hospitals (2): Main tasks

- Decisions on admission of innovative drugs and devices for the institution based on criteria of medical benefit for hospitalised patients ("hospital interest") with the objective to provide patients access to therapeutic innovations (medicines and devices) according to "medical need" or "yet unmet medical need".
- Cost analyses of therapeutic innovations with the overprescription of antibiotics with the risk of highly resistant bacteria development.
- Monitoring of prescriptions (detection of off-label prescriptions) and Publications of recommendations of good clinical practices, in order to restrict prescriptions to the appropriate patients and reduce drug induced adverse reactions and medical errors (example: overprescription of antibiotics with the risk of highly resistant bacteria development)
- Decisions on admission of innovative drugs and devices for the institution based on criteria of medical benefit for hospitalised patients ("hospital interest")
Different steps before hospital admission of a new medicine in France (1)

- Therapeutic value (amplitude of treatment effect versus placebo or versus absence of treatment)
- Relative benefit/risk evaluation compared to reference therapies in the applied indication

Health Technology Assessment (HTA)

Haute Autorité de Santé (HAS)
Different steps before hospital admission of a new medicine in France (2)

- Decision of Hospital admission
- Level of reimbursement for drug delivered outside hospitals by pharmacists
- Public commercialisation (outside hospitals by pharmacists)
- Inscription on the hospital « retrocession list » (direct drug sale by hospitals to non hospitalised patients)
- Inscription on the Hospital list of high cost drugs (« hors T2A ») which will be directly remunerated by the Health care system
- Level of drug prices
- Agreement to hospitals
- Decisions on possible restrictions of such remunerations among accepted indications by Marketing Authorisation for some very expensive drugs (ex: new anti viral drugs for hepatitis C)
- Health ministry and Health care system authorities
Steps before hospital admission of a new implantable medical device (Type III)

Much more simple with the EC certificate...
Financement des dispositifs médicaux

Marquage CE + commercialisation

Prise en charge financière

DM pris en charge intra GHS

DM pris en charge hors GHS :
Inscription sur la LPPR (durée d’inscription : 5 ans)

Amélioration du SA (ASA) par rapport au comparateur de référence:
- Efficacité, tolérance, qualité de vie
- ASA I à IV (majeure à mineure)

Attribution d’un Service Attendu (SA) par indication:
- bénéfice/risque, place dans la stratégie thérapeutique, intérêt de santé publique

Inscription sur une ligne générique :
- Tout DM qui répond à la définition et aux spécifications d’une des lignes génériques de la LPPR (1 ligne / service rendu)

Inscription sous nom de marque :
- Si revendication d’un caractère innovant et/ou d’un suivi particulier
- +/− création acte CCAM (1 ligne / DM)

Pas d’inscription sur LPPR, pas de remboursement hors GHS

Si DMI et à l’initiative de l’industriel auprès de la CNEDIMTS (HAS)

2 modalités possibles, selon le choix de l’industriel
- Généralisation de l’usage : radiation de la LPPR
- Perte du caractère innovant ou concurrent identifié :
  - avis favorable pour bénéficier d’un financement temporaire et dérogatoire (article L165-1 CSP)

Evaluation CNEDIMTS = délai de 90 jours

Prise de charge hors GHS

Avis CEPS

Détermination du tarif de remboursement :
- SA, ASA, du DM mais aussi des comparateurs, tarifs des actes suffisant
- Incription sur la ligne générique (sauf exceptions)
- Auto-inscription: Pas d’évaluation de la CNEDIMTS à l’inscription mais programme annuel de révision des lignes génériques + déclaration ANSM
- Autres modalités possibles : MIGAC, PRME, PHRC.

Dépôt dossier CNEDIMTS

Ministère de la santé :
- Arrêté d’inscription sur la LPPR : prix remboursement + code LPPR

4 caractéristiques obligatoires pour être éligible à une inscription sur la LPPR (DMI) :
- Implanté en totalité dans le corps humain
- Implantable uniquement par un médecin
- Dans l’organisme pour une durée > 30 jours
- Objet principal de l’intervention
Procedural steps leading to the decision by the ad-hoc committee of therapeutic innovation

External demands: Pharmaceutical companies willing hospital admission of a new medicine or a new device (procedure instruction on APHP-COMEDIMS website).

Internal requests: Possible demands by physicians or by hospital pharmacists (38 hospitals for APHP) in front of a medical need.
Different steps of evaluation by the « medicine and medical device » committee

- Internal Expertise (scientific team of the committee)
- External experts (physicians in the different fields)
- Discussion and decision taken during meetings of the committees (medicines, devices, anti-infectious drugs)
- Answers sent to applicant
- Publication of committee decisions
Hospital admission criteria and questions for new medicines:

- What is the therapeutic hospital need? Do we really need it? Can we afford it?
- Marketing authorization labeling of indications
- Cost / Status

HTA evaluation (Commission de Transparence de l’HAS)

- Marketing authorization labeling of indications
- Population target: in general population? Among hospitalized patients?
- How many patients are expected to be treated in APHP hospitals?
- How innovative is the new proposed treatment?
- How much innovative is the new proposed treatment?
- Alternative therapies:
- Cost / Status

- Did the Medico-scientific committee recommend the new medicine?
- Therapeutic value, Relative benefit/risk assessment
- HTA evaluation (Commission de Transparence de l’HAS)
Hospital admission of new medicines: Criteria and questions

Which impact of the new medicine on organization of hospital activities ("rupture treatment effect")?

- Major points of impact:
  - Duration of stability for chemotherapy preparations and reconstitutions
  - Syringes or auto-injector pens
  - Readiness to use formulations versus reconstitutions (powder to be diluted in saline versus pre-filled)
  - Security of packaging labeling and manipulations for nurses
  - Informations on administration through enteral nutrition devices or on the possibility of crushing pills or opening capsules (pediatric and geriatric uses)
  - Readability of formulation and presentation to hospital use (multiple use vials versus unitary dose)

- Minor points of impact:
  - Impact of expected or avoided adverse reactions or complications
  - Ambulatory surgery versus surgery requiring more than one day hospitalisation
  - Impact on hospitalisation requirements
  - Impact on type of hospitalisation
  - Duration of hospitalisation
Hospital admission of new medicines

Criteria and questions:

- Evaluation of costs
  - Hospital Cost for treatment of patients with the reference treatment
  - Expected impact of the new medicine on direct costs
    - price of the drug itself compared to available drugs
    - the expected number of patients to be treated by the new medicine
    - Status of the medicines (reference and new treatments) regarding reimbursement by the health care system
  - Assessment of potential reduction (or increase) of hospitalisation related costs by the new medicine
  - It is not a classic cost/effectiveness study but a specific hospital cost/benefit study

- Expected impact of the new medicine on direct costs
  - Hospital Cost for treatment of patients with the reference treatment
Hospital admission of new medicines

Other parameters and criteria to be taken into consideration

- Potential of off label prescription
- Management of patients hospitalized with their personal treatments that can be not available in hospital pharmacy
- Impact of hospital prescriptions on out of hospital prescriptions (possible differential costs)
- Interaction between GP Medical practice and Hospital care

- Early access programs (ATU/RTU/Early Access Programs by companies)
- Interaction between GP Medical practice and Hospital care
Application of the therapeutic "equivalence" principle

Hospital admission of new medicines: Criteria and questions

Basic principle: Hospitals have to provide personalized treatments to all admitted patients (at least those reimbursed by the health care system)

However, hospitals cannot manage to buy and stock all marketed medicines in their pharmacy... (too many, too expensive, not enough room, many losses if unused after conservation limit)

What happens if a treatment is prescribed by a physician to a patient which is later hospitalized in one hospital where such new treatment is not available?
Hospital admission of new medicines: Issue of therapeutic equivalence

- Institutional committees may indicate the list of drugs that can be considered as therapeutically equivalent (diabetic, hypertensive, epileptic, schizophrenic patients etc...)
- Patients are used to their treatments and it is not appropriate to change them when hospitalized
- Patients are used to their treatments and it is not appropriate to change them when hospitalized
- Possible tolerance differences within a same pharmacotherapeutic class
- Which pharmacological class?

Question:
Can a therapeutic equivalence be established between available medicines (hospital pharmacy) and those being previously prescribed to one patient?
Different decisions by the committee on APHP admission of a new drug or device

- Need for complementary information, data or additional expert opinions
  - "On hold « decision (Sursis à statuer) :

  » Rejection

  - Tender (mise en concurrence) for medicines considered as "therapeutically equivalent"

  - Potential significant impact of hospital prescription on out of hospital prescriptions (sourcing effect)

  - High numbers of patients in APHP hospitals

  APHP Arguments to obtain reduction of prices:
  - "Marché négocié « = negotiation of price with the pharmaceutical company or manufacturer

  Approval

APHP admission of a new drug or device

- Negotiation of price with the pharmaceutical company or manufacturer
Off label use of authorised medicines

Evidence based versus Marketing authorisation (MA) process

- Immuno globulines in prevention of Chronic Kidney graft rejection of treatment...

- Stem cell transplantation: which value in prevention? (Off label) = 100 K€uros per patient for 21 days

- Preventive versus curative established therapies: ex defibrotide in veno-occlusive hepatic disease post (which quality of life gain?)

- Especially Xth line of chemotherapy in cancer treatments (which quality of life gain?)

- Physicians have the right to prescribe any medicine in case of strong scientific justifications for a given patient

- Medicine hospital committees are requested to track and ban off label unjustified prescriptions

- Physicians in France have the right to prescribe any medicine in case of strong scientific justifications for a given patient

- For expensive medicines, hospital budget and the national health care system cannot afford such behavior

- Physicians are enclined to prescribe according to the latest published studies results and early access procedures such as ATU, PTT/RTU

- Scientific publications are well in advance compared to MA labeling for drugs justifying the
Implantable innovative medical devices

- Quality monitoring, unsatisfactory financed
  Registers are often useless (not exhaustive, uncompleted follow up, poor
  Very often absence of comparison with reference therapies
  Small numbers of included patients
  Small number of clinical studies, under-powered in most cases
  « Learning period »

- Strong interaction with surgeon implanting the device with a necessary
  Absence of marketing authorization process and labeling
  EC certificate, small companies in most cases
  Similar process of evaluation and decisions by hospital committees
Implantable innovative medical devices

How to promote innovation for these devices in such a situation?

- Case by case discussion according to the innovative aspects of the device, the available therapies, the amplitude and nature of clinical expected benefit, the differential costs, etc...

But hospital admission demand always occurs long time before HAS decision

Only in the cases when the new device is listed by HAS on the LPPR list, hospital admission is always accepted since its costs is directly taken in charge by the health care system (and not by the hospital budget). This is the problem!!
Early access program for innovative implantable medical devices

« Formal Innovation » established by HAS in 2015

Developing innovative devices (hospitals have to get their money back... in case of success (i) allows validation of such investigation is defined by each contract between hospitals and companies

- Provision of recruitment of patients
- Provision of scientific and methodological environment and support in order to set up clinical studies

Public academic hospitals have a role to play to support such innovation and may invest part of their budget to such co-development with companies:

- Provide scientific and methodological environment and support in order to set up clinical studies
- Provide recruitment of patients

Vortech steps beyond when health care system does not yet pay for them. Small companies cannot afford to set up expensive large scale clinical trials. What steps beyond when health care system does not yet pay for them? Small companies cannot afford to set up expensive large scale clinical trials.

But how to proceed to reach this level of evidence-based medicine for innovative devices? How to proceed to reach this level of evidence-based medicine for innovative devices?

...
Conclusions

Hospitals have the obligation to provide patients access to therapeutic innovation. Financial constraints obligate hospitals to a more strict regulation of care organisation. Regulatory obligations may induce contradictory debates and results: Off label use, therapeutic equivalence.

Look at the debate on MAB biosimilars...