

Protocolisation, Use and Development of Anti-Cancer Drugs in the Context of T2A (Case-Mix Based Payment System) Set-Up

Anne Mathieu-Boué,¹ Pierre Demolis,² Jean-François Bergmann³
and the participants in Round Table N° 7, Giens XXI*

1 Novartis Pharma SAS, Rueil Malmaison, France

2 Afssaps, Saint Denis, France

3 Hôpital Lariboisière, Paris, France

Keywords:

good practice;
oncology;
therapeutic protocol;
reference guidelines;
case-mix based payment
system

Abstract – Drugs used in oncology represent more than half of the innovative and costly drugs which are not covered by a Group Homogène de Soins (DRG type classification) within the context of the case-mix based payment system (termed T2A). For these drugs, good practice reference guidelines have been drawn up by scientific societies and registration agencies. Recognised indications, relevant indications and situations where the treatment should not be prescribed are defined by the National Institute of Cancer. The reference guidelines should lead towards the good use of these drugs and allow the sick funds to control prescriptions. They should evolve with time, which means that bibliographic monitoring and independent expert opinion is necessary to update them as science provides new data. Manufacturers are involved in this process which in no case should undermine developmental efforts leading to registration. The objective of this protocolisation is to allow all patients early and legitimate access to drugs representing real therapeutic progress. These reference guidelines should be integrated into the life-cycle of a drug and should give rise to new developments allowing the good use of cancer products in situations which have been properly validated.

1. Definitions and situation overview

The implementation as of January 2006 of a case-mix based payment system (termed T2A) will introduce new rules for the hospital invoicing of certain drugs which are defined as particularly innovative or costly. The cost of these drugs will not be covered in the context of a GHS (“Groupe Homogène de Séjours” equivalent classification to Diagnostic Related Groups - UK) but will instead be the subject of agreements between hospitals and the ARH (Regional Hospitalisation Agencies) within whose jurisdiction they fall. These agreements will be good practice agreements detailing,^[1] on a drug-by-drug basis, which practices do not undermine the principle of reimbursement. Any discrepancy in relation to these agreements will need to be justified, failing which the hospital taking part in the agreement may see coverage of non-GHS drugs reduced to the detriment of its own budget. This sys-

tem is therefore intended to establish a framework for practices with any financial burden resulting from unacceptable practices being borne not by patients but rather the hospitals which have deviated from the framework.

The use of a drug according to the terms described in its Marketing Authorisation naturally corresponds to a validated practice recognised as such in good practice agreements. Prescription during a clinical trial and use in the context of an ATU (Autorisation Temporaire d’Utilisation = Temporary Authorisation for Use) are both governed by specific regulations to which good practice agreements do not apply. The central issue dealt with in these agreements is the acceptance or rejection of practices which are not covered by the Marketing Authorisation.

The list of so-called “non-GHS” drugs includes numerous anti-cancer agents. Yet, more than any other medical field, oncology makes considerable use of practices which, though not formally recognised by the medical authorities, are sometimes

* For a list of participants, please see the end of the article.

founded on cast-iron scientific evidence. However, the Marketing Authorisation Application is submitted at the manufacturer's initiative and some situations (*e.g.* rare indications) cannot justify the significant financial outlay required by a Marketing Authorisation Application. Moreover, it may be that the application has already been submitted and the decision of the regulatory authorities is pending in which case the practices in question have yet to be recognised by a Marketing Authorisation.

Before drafting the good practice agreements it is important to identify practices which are not covered by the Marketing Authorisation and subject them to critical review so that they can be deemed either admissible for coverage equivalent to that applied to practices compliant with the Marketing Authorisation or, conversely, unacceptable.

Reference guidelines drawing on published data and specialist opinion are therefore necessary before drafting these agreements. To prevent inter-regional discrepancies, it has been decided to implement these guidelines at a national level. Numerous structures already set up think tanks and established guidelines before the full implementation of T2A.

These structures include the Hospices Civils de Lyon, the Assistance Publique-Hôpitaux de Paris (AP-HP), the Fédération Nationale des Centres de Lutte contre le Cancer (FNCLCC), the OMIT (Drug and Therapeutic Innovations Monitoring Unit) Bretagne-Pays de Loire. The work of writing the national guidelines will therefore consist of harmonising, completing and updating these bodies of work. The National Cancer Institute of France (INCa), assisted by the Afssaps (French Medical Agency Safety of the Products of Health) and the HAS (National Authority for Health), is overseeing coordination of the work to produce reference guidelines in the field of oncology. The drafting procedure for these was defined in preparatory meetings.^[2-4]

The roundtable organised in Giens brought together practitioners and hospital, institutional and industrial pharmacists to focus on current and foreseeable practical issues relating to the preparation and application of oncology reference guidelines.

2. How should a reference guideline be drafted?

There are two possible outcomes for the good practice agreements: either the drug used will be accepted for reimbursement without application of a penalty or its use will be deemed unacceptable and the hospital will face financial sanctions. This dual outcome can be envisaged for any situation listed and it is important to sort the practices into three categories at an initial stage:

- certain practices are accepted automatically or without extensive scientific debate: they have received Marketing Authorisation or are likely to obtain a favourable Marketing Authorisation opinion;

others are clearly acknowledged as being unacceptable, resulting in a refusal: practices for which a Marketing Authorisation has already been refused or which have been deemed harmful in scientific literature;

- the final category requires a particular effort when drafting a reference guideline: it includes practices for which published data is incomplete or debatable and for which there is no clear favourable or unfavourable opinion. When such practices are declared to be accepted by the guidelines, they are described in a PTT (Temporary Treatment Protocol) which thus serves as a complement to the Marketing Authorisation. These protocols are termed 'temporary' because their validity must eventually be confirmed by a Marketing Authorisation or negated either by the refusal of a Marketing Authorisation or by the fact that a Marketing Authorisation Application cannot be compiled. All PTTs therefore carry an expiry date.

It should be stressed that no document in this field can claim to be truly exhaustive and there may be practices not listed for which coverage will be negotiated out of the scope defined by the reference guideline.

3. Analysis and further reflection

Any examination of the consequences of drafting oncology reference guidelines should focus on four key areas:

- non-GHS invoicing: expected benefits and potential negative consequences,
- guideline updates,
- interaction between an established guidelines and the drug life-cycle,
- consequences of the system on the prescribing physician's daily practices.

4. Non-GHS invoicing: expected benefits and potential negative consequences

The main advantage highlighted by the participants in the roundtable was that a quality-based approach based on expert literature review has been established whereas, in the past, practices which were non-compliant with Marketing Authorisations were isolated decisions possibly taken on the basis of thin evidence. This quality-based approach was, moreover, why reference guidelines had been prepared before the establishment of the T2A system.

It is important for reference guidelines to be clearly written, taking account of practical imperatives relating to oncology. In this respect, the drafting of PTTs has made it possible to establish a clear framework for practices declared acceptable following a consensual process supported by scientific evidence.

The publication of reference guidelines and the implementation of good practice agreements will guarantee equal access to therapeutic advances throughout the country.

Finally, monitoring these agreements will provide invaluable information as to how often PTTs are applied. This in turn will allow retrospective comparison of this frequency against expected frequency and validation against the accuracy of the situations described during the application for coverage.

As regards the drawbacks, apart from the risk of exposing prescribing physicians to a greater administrative burden, the participants mentioned the risk of seeing prescriptions transferred from a treatment covered in the context of GHS to a non-GHS solution, thus freeing the hospital from the cost, and imposing an additional, more significant strain on the public purse.

5. Reference Guideline Updates

The drafting of reference guidelines began in 2005 and will continue through 2006 under the aegis of the INCa in association with the Afssaps and the HAS. Expert boards will be set up by drawing on groups which are already operational within hospitals for instance, and making full use of documents currently available. Most of the work will consist in describing accepted elements and drafting the corresponding decisions in the form of a PTT while specifying unacceptable practices. The PTTs may vary in size, from the mere mention of an indication in a single sentence through to a comprehensive document describing not only the indication but also its justification, limits, precautions and conditions of use as well as measures established to facilitate prescription practices and monitor associated risks. The first PTT was published in October 2005 concerning the use of Herceptin® in adjuvant treatment of HER2-overexpressing breast cancer. The documents will be proposed for consultation by the manufacturers concerned and will be signed jointly at the end of the process by the three supervisory authorities. It is important to stress that the reference guidelines currently available only differ marginally from each other and that the work will primarily consist in ruling on the rare differences of opinion and updating to take account of more recent data. When similar documents are found to exist in other countries, they will also be used for drafting the French guidelines.

The necessary updating will be done at least once a year using the literature and conference papers as well as information from the pharmaceutical industry and regional monitoring units.

6. Interaction between an established reference guideline and the drug life-cycle

The influence of the publication of a national reference guideline on a drug's (international) development can be analysed differently according to two scenarios. If a new indication covered by a PTT is merely a stepping stone to the probable granting of a Marketing Authorisation and is part of a planned development, no specific interaction is expected. However, when the situation recognised by the guideline falls out of the scope of the development programme planned by the manufacturer, its role becomes more complex.

The expenditure required to convert a PTT into a Marketing Authorisation can be significant. It may be desirable, or even essential, to seek the assistance of institutional partners and to consider adapting the levels of stringency (for instance, in rare situations where a standard clinical trial is not feasible). Initially, it could be reasonable to strengthen the pool of evidence without necessarily aiming for Marketing Authorisation.

7. Consequences of the system on the daily practice of the prescribing physician

This final area for consideration involved all participants and, first and foremost, clinical oncologists. To be useful for prescribing physicians the guidelines must be clear and concise, with simple descriptions of the situations defined by criteria accessible in daily practice.

Last resort treatments administered for compassionate reasons should not be included in these guidelines: in such situations the general instruction should be to opt for less costly drugs which are covered by the GHS.

Prescription of a non-GHS treatment out of its Marketing Authorisation scope should be a collegial decision, thus stressing the changeover from individual practices based on isolated consideration to practices decided in common on the basis of summary documents.

Respect of the reference guidelines necessarily dovetails with considerations of self-assessment and accreditation but also of clinical trials.

8. Conclusion

The implementation of reference guidelines in oncology is an important step forward and not only in terms of keeping a tight rein on health expenditure. Patients too will benefit from earlier access to medical advances validated by collective input from experts and in keeping with optimised equality of opportunity.

Areas for further consideration and proposals.

The topic covered here does not lead to a range of proposals for further consideration or action. It has merely been a question of observing a process of development and describing the probable consequences for covering the cost of cancer treatment in France. The process touched more on describing the issues than investigating or resolving them. A further consideration of the assessment of T2A in oncology will no doubt be of value in a few years time and will enable comparison of 2005 perspectives with those of 2008 or 2010.

In the immediate future, the implementation of reference guidelines depends on an organisational agreement between Afs-saps, HAS and above all for oncology, on the INCa. Their validity must be ensured as well as their upgradeability so as to take new data into account (bibliographical monitoring), their acceptance by all prescribing physicians and their systematic use. Prescription audits may be developed, particularly via local COMEDIMS (Drug and Sterile Medical Device Committees). Analysis of how reference guidelines are used will be conducted by the paying authorities (ARH and DHOS – “Direction de l’Hospitalisation et de l’Organisation des Soins” – Directorate of Hospitals and Health-care Organisation) as per procedures to be defined in greater detail.

Participants

Aoustin M. (DGS), Atlani C. (Sanofi Aventis), Bassompierre F. (AP-HP), Benamouzig R. (Hôpital Avicenne, Bobigny),

Bonavita M.-J. (AP-HM), Borella L. (INCa), Calvo F. (Hôpital Saint Louis, Paris), Caulin C. (Hôpital Lariboisière, Paris), Cellier D. (Merck Santé), Dahan M. (INCa), Daura V. (AP-HP), De Beels F. (HAS), De Vernejoul N. (HAS), Diebolt V. (FHF), Dumarcet N. (Afssaps), Durand Zaleski I. (HAS), Fery Lemonnier E. (AP-HP), Genève J. (BECT-FNCLCC), Giri I. (Consultant, Verrières le Buisson), Golinelli D. (DGS), Labreuveux C. (Lilly France), Latour J.-F. (Centre Léon Berard, Lyon), Maraninchi D. (Institut Paoli Calmettes, Marseille), Meresse V. (Roche Produits), Mignot L. (Hôpital Foch, Suresnes), Morlet D. (GlaxoSmithKline), Pépin S. (CNAMTS), Ravaud P. (Hôpital Saint André, Bordeaux), Riché C. (CRPV, Brest), Rouleau A. (Afssaps), Tilleul P. (Hôpital Saint Antoine, Paris), Viens P. (Institut Paoli Calmettes, Marseille).

References

1. Décret n° 2005-1023 du 24 août 2005 relatif au contrat de bon usage des médicaments et des produits et prestations mentionné à l’article L. 162-22-7 du code de la sécurité sociale <http://www.legifrance.gouv>
2. <http://www.e-cancer.fr>
3. <http://www.afssaps.sante.fr/htm/3/t2a/indt2a.htm>
4. <http://www.anaes.fr>

Correspondence and offprints: *Jean-François Bergmann*, Médecine Interne A, Hôpital Lariboisière, 2 rue Ambroise Paré, 75475 Paris cedex 10, France. E-mail: jf.bergmann@lrb.aphp.fr