SURVEY

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Therapeutic advance: a comparison of assessments made by *Prescrire* and by the Swedish regulatory agency

● **A study has compared *Prescrire*'s and the Swedish regulatory agency's assessments of the degree of therapeutic advance provided by 54 drugs.**

● **Assessments were similar in 40 (74%) of the 54 cases. Most discrepancies were associated with differences in the comparators chosen by the two teams.**

All new pharmaceutical products are touted as "innovative" by the firms that market them, even when they offer no tangible therapeutic advance (1).

The global evaluation of the therapeutic advance provided by a given drug in a given indication is based on a series of factors relating mainly to the risk-benefit balance (intrinsic therapeutic value), and its "added value" relative to existing treatments in terms of efficacy, adverse effects and/or convenience.

54 drug evaluations

In late 2004 we reported the results of two studies comparing the assessments of the French Pharmacoeconomic Committee of the degree of medical benefit offered by more than 600 drugs and Prescrire's corresponding evaluations (2).

La revue Prescrire and *Information från Läkemedelsverket* (the bulletin of the Swedish regulatory agency) have now conducted a joint comparative study of their assessments of 54 new drugs (3). The conclusions of the 108 relevant review articles (54 published by *Prescrire* and 54 published by the Swedish agency, between 1997 and 1999) were compared for each product.

Prescrire summarises its assessments by using a 7-point scale that rates therapeutic advance (see this issue page 220), while the Swedish agency simply states its conclusions without using a rating system.

Similar assessments of 40 drugs. Several approaches were used to compare the assessments of the French and Swedish organisations (3). We report the results of the approach that consisted of wording all the information contained in the French and Swedish reviews into the Rosén scoring system (4). The latter rates therapeutic advantages by distinguishing eight basic categories: substantial (A1) or modest (A2) efficacy in a setting with no existing alternatives; a modest but concrete advantage over existing alternatives in terms of efficacy (B1) or adverse effects (B2); an advantageous route of administration (C1) or dose strength (C2); a new delivery system (D), or a "me too" (E) (4).

On the basis of this classification, 40 (74%) of the 54 drugs included in the study were assessed similarly by *Prescrire* and the Swedish agency.

Reasons for discrepancies

The conclusions reached by *Prescrire* and the Swedish agency differed somewhat in 13 cases (24%) (**a**). Analysis of these 13 cases highlights several factors that can influence the assessment of therapeutic benefit.

The authors identified seven sources of discrepancy.

Differences between national pharmaceutical markets. Four discrepancies were due to differences in the treatments available in the two countries. For example, the Swedish agency came to a more positive conclusion than *Prescrire* concerning penciclovir cream (for herpes), because aciclovir cream was already on the market in France but not in Sweden.

Cultural differences. One discrepancy was due to differences in the way alcoholism is managed in France and in Sweden, leading the Swedish agency to a more favourable assessment of naltrexone.

Convenience assessment. *Prescrire* and the Swedish agency both considered that imiquimod (a local treatment for anogenital warts) offered no advantage in terms of clinical efficacy; however, *Prescrire* viewed its simplicity of use as an advantage.

The choice of reference treatment. The choice of a different comparator explained two discrepancies. For example, *Prescrire* compared clopidogrel (an antiplatelet drug) with ticlopidine, while the Swedish agency compared it with aspirin. As a result, *Prescrire*'s opinion of clopidogrel was more positive.

Clinical endpoints. The choice of clinical endpoints explained two more discrepancies. For example, the Swedish agency reached a positive conclusion concerning desirudine (an anticoagulant) based solely on phlebographic criteria, while *Prescrire* examined the efficacy of this drug on the symptoms of venous thrombosis. As a result, the Swedish agency's opinion was more favourable.

Interpretation of trial findings. *Prescrire* came to a more positive assessment on the efficacy of naratriptan (an antimigraine drug), compared with sumatriptan, concluding (over-optimistically in the event) that the new drug reduced the frequency of relapses. The Swedish agency did not interpret the clinical data in this way.

Data access. In another two cases, only the Swedish agency had access to unpublished clinical trial reports that the manufacturers were obliged to submit in support of their marketing application. As a result, *Prescrire* concluded that gemcitabine (a cytotoxic agent) represented "nothing new", based on the interim results of a single trial (the only available information). The Swedish agency, having access to the full results of this trial, concluded that there was a survival advantage.

Conclusion

Overall, the Swedish and French teams agreed on the value of most of the new drugs included in the study. This comparative analysis highlights a number of factors, especially those of a conceptual and societal nature that can influence the assessment of a given drug by different teams.

Such collaborative studies are an excellent means of improving assessments of new drugs.

a- *One drug could not be classified using the Rosén system, for reasons that the authors did not provide.*

Selected references from Prescrire's literature search.

1- International Society of Drug Bulletins "ISDB Declaration on therapeutic advance in the use of medicines" available on www.isdbweb.org

2- Prescrire Editorial Staff "Comparaive advantages of new drugs: French authorities are not sufficiently demanding" *Prescrire Int* 2005; **14** (76): 75-76.

3- Ahlqvist-Rastad J et al. "Judging the therapeutic value of drugs: a comparison between La revue Prescrire and Information från Läkemedelsverket, the bulletin of the Swedish Medical Products Agency" *International Journal of Risk & Safety in Medicine* 2004; **16**: 83-90.

4- Rosén A and Beermann B "Rating innovative therapeutic benefits of medicines licensed in Sweden 1987-1997" *Int J Pharma Med* 1999; **13** (3): 123-126.