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NOTE TO THE ATTENTION OF
THE HEADS OF MEDICINES AGENCIES AND
THE PHARMACEUTICAL COMMITTEE

Subject: Status of medicinal products as subject to prescription or not

In the context of the Commission decision authorising the first OTC product in the centralised procedure and, at the same time, the first "switch" of a medicinal product from prescription to non-prescription (for a new strength), we would like to summarise and put into context Community legislation and interpretation of this legislation with regard to a number of issues which have been raised by national competent authorities and by industry linked to prescription and non-prescription medicinal products. Notably, the questions have been raised whether the same medicinal product can have a dual status of both prescription and non-prescription (under 1. below), under which circumstances central and national marketing authorisations can/cannot co-exist, possibly with different prescription status (under 2.) and how we would address a potential conflict between central and national marketing authorisations (under 3.).

(1) Is it possible for the same medicinal product to have both a prescription marketing authorisation and a non-prescription marketing authorisation in the same Member State?

Irrespective of whether a medicinal product is authorised via the centralised procedure or nationally, the question arises whether it is possible for the same medicinal product to have both a prescription and a non-prescription status.

Article 71 of Directive 2001/83/EC sets out the criteria according to which medicinal products shall be subject to medical prescription. This shall be the case where the products in question:

"— are likely to present a danger either directly or indirectly, even when used correctly, if utilized without medical supervision, or

— are frequently and to a very wide extent used incorrectly, and as a result are likely to present a direct or indirect danger to human health, or

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— contain substances or preparations thereof, the activity and/or adverse reactions of which require further investigation, or

— are normally prescribed by a doctor to be administered parenterally."

The competent authority should make an evaluation whether or not the above criteria are fulfilled for the medicinal product in question. The purpose of these criteria is to make subject to medical supervision products which could otherwise entail inappropriate risks and, on the other hand, to facilitate access to those products which do not present such risks.

As these criteria are related to the intrinsic characteristics of each product, as a general rule the same medicinal product should not be both subject to prescription and not in the same Member State.

As "same medicinal product" we would understand in this context the definition referred to in the 1998 Commission Communication as "relevant medicinal product", i.e. any medicinal product which has the same qualitative and quantitative composition in active substances (i.e. the same strength) and the same pharmaceutical form as the product for which a marketing authorisation is sought.[1]

It is in our understanding possible that *different* medicinal products (e.g. different strength) with the same active substance, following an assessment of risks, may have a different prescription status.

However, we would acknowledge one situation where the above principle (the same medicinal product should not be both subject to prescription and not in the same Member State) may not apply: In the scenario of a different therapeutic indication, a different classification regarding the legal supply status could be acceptable, provided that applying the criteria in Article 71(1) leads to different results for different indications. If the authorisation of a given medicinal product entails certain risks justifying a prescription-status for one indication, but these risks are not present for the authorisation of that same product (same qualitative and quantitative composition and same pharmaceutical form) for another indication, a different classification is possible.

In that respect, it will be for the relevant competent authority to assess whether, for instance, different therapeutic indications proposed by the applicant justify a different prescription status. The risk of misuse, listed as one of the criteria of Article 71(1), in cases where the same product would be available both as prescription and non- prescription, should be considered in this regard.

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[1] Commission Communication on the Community marketing authorisation procedures for medicinal products (98/C 229/03), OJ C229, of 22.7.98, p. 4, under E.3.

(2) If a medicinal product has been authorised centrally, with status of non-prescription,

(a) what happens to pre-existing national MAs, possibly with conflicting prescription status?

(b) is there room for subsequent, additional national MAs, possibly with conflicting prescription status?

(c) what happens to national administrative decrees or decisions, determining a conflicting prescription status?

If a product falls under the optional scope of the centralised procedure (Article 3(2) of Regulation (EC) No. 726/2004), the applicant has the choice of using *either* the central marketing authorisation procedure *or* the national (decentralised/mutual recognition) route.

General principle: no co-existence of central and national authorisation

The 1998 Commission Communication clarifies as a general principle that this choice does not allow *both* a central and a national marketing authorisation to co-exist simultaneously for the same product: *"it has to be stressed that, once granted with a Community marketing authorisation based on Part B of the Annex[2], a medicinal product can no longer be the subject of a subsequent (or previous) national marketing authorisation".*[3]

A Community marketing authorisation is adopted on the basis of a scientific evaluation by the CHMP and of an opinion by the Standing Committee for Medicinal Products for Human Use – thereby involving the scientific expertise available throughout the Community. As the 1998 Commission Communication points out, the Community system for marketing authorisation guarantees that *"new medicinal products marketed in the Community have been evaluated to a high scientific standard of quality, safety and efficacy and it aims at assuring that the same medicinal products will be used under the same conditions throughout the European Union. ...*

It makes for more rational use of the resources needed for authorisation and monitoring of medicinal products by eliminating the duplication of evaluation..."[4]

This means that once a central marketing authorisation has been issued, as a general principle there is no room for an additional scientific evaluation and regulatory decision of the same medicinal product.

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2 Optional scope of the central procedure; the corresponding provision in the currently applicable Regulation (EC) No 726/2004 is Article 3(2).

3 Commission Communication 98/C 229/03 under A.2.

4 Commission Communication 98/C 229/03 under Conclusion.

Also applicable to: generics of centralised product

In this context, we would like to highlight the explicit provision of Article 3(3) of Regulation (EC) No 726/2004, which offers the opportunity to generics of a centralised medicinal product to choose either the centralised *or* the national route. Also in this case the choice offered to the applicant to use either the central or the national route does *not* allow him to use *both* procedures.

Exception: different therapeutic indications

However, in addition to the general principle from the 1998 Commission Communication cited above, a possible co-existence of central and national marketing authorisations for different therapeutic indications was also addressed in the Communication: "*In order to maintain coherence and transparency, and to preserve the unity of the Community Single Market, where the same marketing authorisation holder wishes to place on the market another medicinal product with the active substance which is already the subject of a Community authorisation, the Commission considers that the centralised procedure should be used, in particular when the therapeutic indication is within the third level of the ATC code.*

In cases where the applicant does not apply for a Community authorisation as described above, the therapeutic indication(s) authorised by the Community should not be part of the national authorisation. In such a context, the Commission will consider the benefit of referring the case to the EMEA through an arbitration procedure in accordance with Articles 11 or 12 of Directive 75/319/EEC[5] *in order to preserve the abovementioned coherence and transparency*".[6] (emphasis added)

It follows from the above that once a central marketing authorisation has been issued, the maintenance of existing national marketing authorisations or the issuing of new marketing authorisations for the same medicinal product could be envisaged only as long as the therapeutic indications are different in national and the central marketing authorisations.

In this case, the prescription status of such a national marketing authorisation could differ from the prescription status of the centrally authorised medicinal product for a different indication, provided that the conditions set out under 1. are met (i.e. product-inherent risks present for one indication but not for the other).

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5 The "*arbitration procedure in accordance with Articles 11 and 12 of Directive* 75/319/EEC" corresponds for the current legislation to the arbitration procedures in Article 30 (divergent decision referral) and Article 31 (Community interest referral) of Directive 2001/83/EC.

6 Commission Communication 98/C 229/03 under A.2.b)

(3) **How would the Commission deal with a situation of national marketing authorisations or other decisions conflicting with a Community marketing authorisation as regards prescription status?**

As a matter of principle, we understand that once a Commission decision has been adopted, on the basis of a CHMP opinion and an opinion of the Standing Committee for Medicinal Products for Human Use, subsequent conflicting national decisions on the same product have to be avoided (unless scientifically justified, as described earlier in the case of different indications).

If national decisions already exist at the moment of a Commission decision, the co-existence of central marketing authorisations with national decisions – where the scientific assessment of the same facts has led to different conclusions and regulatory action – would be a matter of Community concern.

To deal with these situations, in case the Commission services become aware of national decisions potentially conflicting with a Community marketing authorisation as regards prescription status, in accordance with the above-cited Commission Communication, we would assess the need to launch a Community interest referral, based on Article 31 of Directive 2001/83/EC.

We intend to present this note in the next Pharmaceutical Committee on 16 March 2009.

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