Ensuring the availability of CAM medicinal products

Position paper highlighting the need for additional measures

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This document reflects the position of EUROCAM, the alliance of European umbrella organisations of patients, physicians and practitioners in the field of Complementary and Alternative Medicine (CAM).

The following European umbrella organisations work together in EUROCAM:
European Ayurveda Association – EUAA
European Central Council of Homeopaths – ECCH
European Committee for Homeopathy – ECH
European Council of Doctors for Plurality in Medicine – ECPM
European Federation of Homeopathic Patients' Associations – EFHPA
European Federation and Forum for Osteopathy – EFFO
European Federation of Patients' Organisations for Anthroposophic Medicine – EFPAM
European Herbal & Traditional Medicine Practitioners Association – EHTPA
European Traditional Chinese Medicine Associations – ETCMA
International Association for Veterinary Homeopathy – IAVH
International Council of Medical Acupuncture and Related Techniques – ICMART
International Federation of Anthroposophic Arts and Eurythmy Therapies – IFAAET
International Federation of Anthroposophic Medical Associations – IVAA

The objective of EUROCAM is to promote and facilitate CAM's role in maintaining citizens' health, highlight the health promotion and illness prevention aspects of CAM for EU public health policy and programmes, to advance the accessibility, affordability and availability of CAM, and generally promote CAM at European level.

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1. Introduction

In several EU Member States the availability of CAM (Complementary and Alternative Medicine) medicinal products – i.e. herbal, homeopathic, and anthroposophic medicines – is unnecessarily restricted. The lack of availability of these products inhibits increasing demand by EU citizens for low risk, health enhancing CAM medicines, hampering the ability of doctors, veterinarians and practitioners to provide effective CAM treatments. It also undermines the potential benefit of these products in helping to tackle specific health issues prioritised by the Commission e.g. combating anti-microbial resistance, managing non-communicable diseases (NCDs) and sustaining healthy ageing.

Herbal, homeopathic and anthroposophic medicinal products currently meet particular difficulties in accessing the European pharmaceutical market. These products are restricted in various ways for both patients and the public. These problems are not new and have been identified repeatedly by the stakeholders concerned.

The availability problems of CAM medicinal products were also acknowledged by the Matrix Insight report[1], an external study commissioned by DG Health and Food Safety for the Pharmaceutical Committee and published on the Committee's website in November 2014. The report said that further work is 'expected to inform policy options for the Commission to consider in order to address the issue of unavailability', and that a need for further action in this area was needed. Such action, the report said, 'should focus on ensuring that the process of authorisation of herbal, homeopathic and anthroposophic medicinal products is more consistent, both with the text of the existing provisions and between Member States.' Since then little has changed.

The EUROCAM document describes the needs of patients and health professionals seeking to make use of CAM medicinal products specifically suggesting measures that can improve the availability and use of CAM medicines.

2. Herbal medicinal products

In 2004 the European parliament adopted Directive 2004/24/EC which introduced the new category of Traditional Herbal Medicinal Products (THMP). At the time this was hailed as a landmark decision for CAM products, ensuring their availability throughout Europe. *The Matrix Report highlights the fact that despite a common regulatory framework for THMPs, the approach of the Member States (MS) is both heterogeneous and scattered.*

This remains the case more than 15 years after the Directive 2004/24/EC came into force. Surprisingly few THMPs are registered in the EU with only a few hundred THMPs registered in all the MS. This is a totally inadequate outcome for more than 10 years work under Directive 2004/24/EC. The MS with the most THMP–registrations are Poland, United Kingdom[2], Germany and Austria. The majority of MS have only registered up to 10 THMPs; some have registered only one while some have not registered any THMP products at all (Fig.1).

[1] http://ec.europa.eu/health/files/committee/73meeting/73plus/study_report.pdf

[2] And if Brexit is coming into effect more than 20% of THMP-registrations are nationalised, which reduces the number of available THMPs even further.

In view of this it is fair to say that *Directive 2004/24/* has failed in its intention to make herbal medicinal products available to EU citizens across the European Union and to provide herbal products for the use of CAM health professionals for the benefit of their patients.

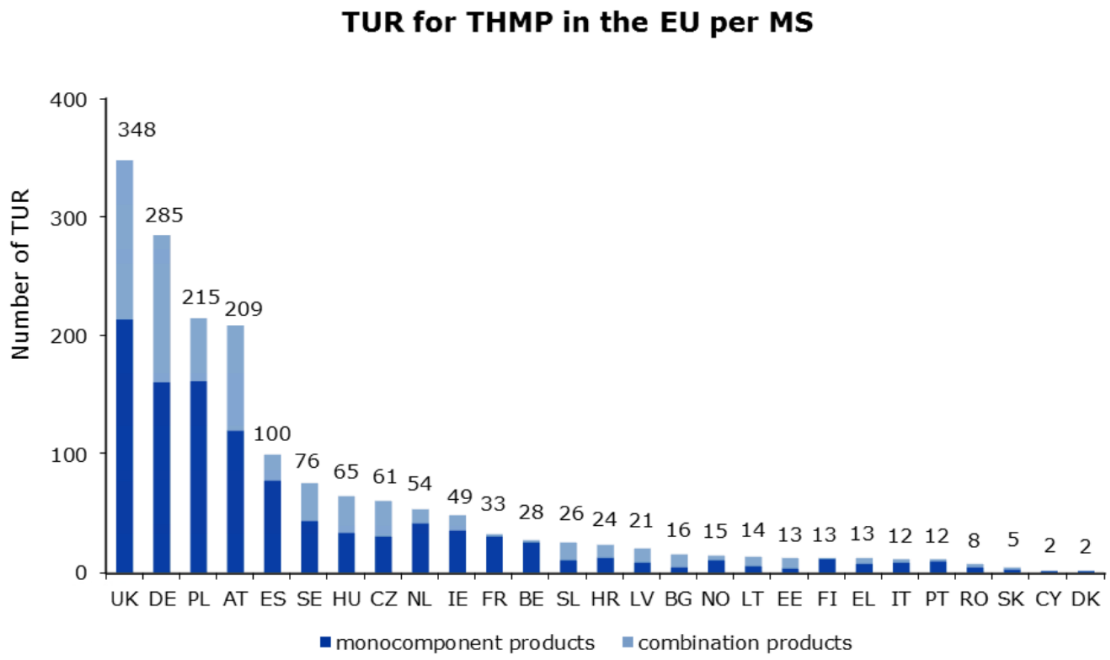

Fig.1: Number of granted THMP-registrations during the period 2004 – 2016. Total registrations numbered 1719 (1089 for mono-component products, 630 multi-component products).[3] This means that only 1719 registrations have been recorded after 12 years and only about 4 MS have actually made any serious use of the THMP-registration scheme (UK being the country with the most THMP-registrations). In the majority of the MS only an insignificant number of herbal medicines are available as THMPs.

Suggested options for the European policy makers, to address these shortcomings:

Strengthening the role of HMPC

The Herbal Medicinal Product Committee (HMPC) at the European Medicines Agency (EMA) was established with the inception of Directive 2004/24/EC. It seeks to unify the different MS standpoints. The HMPC prepares monographs and guidelines for registration. Despite the best efforts of the HMPC, the MS have so far failed to apply these guidelines in a coherent manner. As a result, THMPs registered in one MS face difficulties when an application is filed in another MS using the same data. Despite the fact that the same HMPC guidelines apply, the national competent authorities too often interpret them in completely different ways.

Such heterogeneous approaches undermine the intention of Directive 2004/14/EC, which states that MS should take 'due account' of positive decisions taken by another MS. Currently positive decisions on registering a herbal product taken by one MS are more

[3] Uptake of the traditional use registration scheme and implementation of the provisions of Directive 2004/24/EC in EU Member States. Status: 31 December 2016. EMA/HMPC/322570/2011 Rev.7 (18 April 2017)

often than not ignored by other MS for no apparent reason. In order to achieve a harmonised market, the recognition by all MS of positive decisions taken with regard to a THMP by a single MS should be the rule rather than the exception.

- *Support is needed from DG SANTE and the European Parliament to enable the HMPC to:*
    a) strengthen its status and coordinating power with respect to the MS. As the HMPC has to work on the basis of majority voting, MS with a poor record of THMP-registrations often inhibit the implementation of Directive 2004/24/EC across the EU;
    b) encourage MS to adopt a consistent application of the THMP scheme;
    c) clarify the 'due account' rule as given in Directive 2004/14/EC meaning that only serious objection based on solid data can justify an objection to the decision of a MS;
    d) extend and interpret the scope of traditional herbal registrations to enable a much more flexible TUR registration scheme.

Mutual recognition Procedure

For more than a year there has been an agreement that THMPs can enter a Mutual Recognition Procedure (MRP) on a voluntary basis. Here again the HMPC guidelines should facilitate mutual recognition. In fact, the MRP procedure results in controversy and thus this route of THMPs registration is difficult. This demonstrates the lack of European integration in this matter, as the MRP is one of the cornerstones of the European cooperation in the pharmaceutical field.

- *Support is needed from DG SANTE and the European Parliament* to monitor MRP progress, identify obstacles and encourage the MRP procedure.

Broadening interpretation of indications

The current interpretation of possible therapeutic indications permitted by the HMPC is limited. Directive 2004/24/EC states that THMPs 'have indications exclusively appropriate to traditional herbal medicinal products which, by virtue of their composition and purpose, are intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment.'

- *Support is needed from DG SANTE and the European Parliament to encourage the HMPC to broaden the indications for THMPs:* the scope of indications for THMP should be extended to say, 'after being diagnosed by a physician or health practitioner.' Such wording is already in use in some MS.

- *Support needed from DG SANTE and the European Parliament to clarify the borderline between food and medicine.*

To further strengthen the position and availability of CAM medicines in Europe an initiative is necessary to broaden the scope of Directive 2004/14/EC. The Commission clearly recognised the shortcomings already in 2008.[4] It reported:

> 'Medical traditions such as those mentioned above (i.e. traditional Chinese medicine, Ayurveda etc.) are based on a holistic approach, and the set of requirements for the simplified registration procedure under Directive 2004/24/EC is not appropriate for a global regulation of such medical practices. The regulation of such traditions would demand a different approach from that introduced by Directive 2004/24/EC. Therefore, the Commission does not envisage extending the scope of the simplified registration procedure to cover traditional medical systems as such. Nevertheless, independently of this report, the suitability of a separate legal framework for products of certain traditions should be assessed.'

Health professionals and patients require medicines to treat illnesses and health problems. The lack of availability of THMPs hinders European citizens who wish to make choices about their treatment options.

Food supplements as alternative route to market access

Some MS have chosen a different route to the market: they classify herbal products as Food Supplements (FS), which are regulated by the European Food Safety Authority (EFSA). By definition FS are intended to improve health and contribute to the normal function of the body. In the light of this definition FS cannot replace medicines.

France, Belgium and Italy currently favour the classification of herbal products as FS. Consequently, MS following this approach register very few if any THMPs. The European Commission has failed to clarify this situation. As a consequence, EFSA and the HPMC lack a coherent strategy to give clear and definite guidance to MS.

It is the clear opinion of EUROCAM that only an extension of the scope of Directive 2004/14/EC and consequently an increase of registrations of THMPs can ameliorate this situation.

Finally, policy makers should be aware that restricting the market access is not an option: as consumers and health professionals demand, legally available herbal products of good quality. If neither the option of Traditional Herbal Medicinal Products or Food Supplements are available the market will shift toward unregulated products from non-European sources via the internet or other channels, posing a risk to public health.

3. Homeopathic medicinal products

The two principal bodies of prescribers of homeopathic medicinal products (HMPs) in Europe, the European Central Council of Homeopaths (ECCH) representing practitioners and the European Committee for Homeopathy (ECH) representing homeopathic doctors and the European Federation of Homeopathic Patients' Associations (EFHPA) representing patients and users of HMPs welcome the commissioning of the Matrix Report by the European Commission. Furthermore, we endorse the findings of the report

[4] Communication from the Commission to the Council and the European Parliament concerning the Report on the experience acquired as a result of the application of the provisions of Chapter 2a of Directive 2001/83/EC, as amended by Directive 2004/24/EC, on specific provisions applicable to traditional herbal medicinal products. 2008. (Document on the basis of Article 16i of Directive 2001/83/EC).

with regard to HMPs. Their conclusions confirm our own understanding of the current situation with regard to the threats to continuing full availability of HMPs in Europe.

Use and availability

HMPs are widely used across Europe by citizens and homeopathy is widely practised across Europe by thousands of medical doctors and practitioners. Past surveys have indicated that some 25% of the European population use homeopathy and HMPs as an important and integral part of their health maintenance and treatment. It is therefore of considerable concern that the threats to availability of HMPs outlined in the Matrix report should exist.

In 2010 ECCH and ECH jointly published their own report on the availability of HMPs based on surveys carried out across Europe with our own national member associations. That report concluded: **'Revision of laws, new regulations and the increasing registration requirements on a European and national level have already resulted in a drastic reduction in the availability of the variety of homeopathic medicinal products in some countries.'**

In 2013 ECCH carried out an online survey with its membership on the availability of HMPs to which associations in 17 countries responded. The survey revealed a wide variability between countries as to the availability of HMPs to members of the public and wide variability in the availability of HMPS for practitioners who require these HMPS to prescribe for their patients, particularly with regard to the range of single medicines as well as for the range of potencies available. Many users and prescribers already have to source the HMPs they require across EU borders or outside the EU.

These findings also confirm the results of a Price Waterhouse Cooper study commissioned by the HAMP manufacturers group European Coalition on Homeopathic and Anthroposophic Medicinal Products (ECHAMP) in 2012 which similarly found wide variability in availability of HAMPs between MS.

The Matrix Report Case Study 6: homeopathic medicinal products

The Matrix report features a specific study into herbal, homeopathic and anthroposophic MPs. Although the € 1.05 billion market for HMPs constitutes less than one per cent of the EU pharmaceutical market, the report states 'sales of such products remain significant and warrant an exploration of the availability issues associated with these product groups.' It points out that despite the common EU regulatory basis for HMPs through Articles 14 and 16.2 of Directive 2001/83/EC, the different national medical traditions and difference in national approaches have led to their 'ineffective or inconsistent application.'

Homeopathic prescribers and users are particularly concerned about the diminishing availability of all single HMPs that are regulated under Article 14. Given the criteria for simplified registration which includes a baseline dilution of 1:10,000 set down by Article 14 as a guarantee of safety as well as the fact that therapeutic indications are not required, it is difficult to understand why availability of such products in all EU MS is not a straight forward affair that involves only minimal costs.

World Integrated Medicine Forums on Regulation of HMP organised by AYUSH ministry

Two forums have been held in India to date, in 2017 and 2019, gathering representatives of the homeopathy industry, regulators and prescribers from Europe and beyond. The needs for an adapted harmonisation of the pharmacopoeias, and also a willingness to support the continuity of the Directive 2001/83/EC which provides a safe environment for HMPs within Europe were the majors focal points emerging from the discussions. A fostered development of the European Pharmacopoeia should be also considered a priority.

Specific points of concern

A. The **centralised registration scheme** does not work for HMPs. It is difficult to get agreement on homeopathic products across the EU with regard to each country agreeing on a registration status. **Mutual recognition works** between some national agencies but not between others. These positive examples can be studied, with successful models being applied across the sector. Similarly, with **national rules schemes,** we recommend that agencies cooperate across MS borders to avoid duplication of paperwork. For example, it does not make sense that the UK's MHRA and Ireland's HPRA require completely separate new applications for national rules products. Divergent implementation, interpretation and enforcement policy in MS make it difficult for companies to operate across Europe. **A homeopathic product beyond the 1:10,000 dilution that meets EU criteria for good GMP and is registered in one MS should be easy to register in other Member States.**

B. The Regulatory environment is not appropriate or proportionate to the large range of stocks and multiple finished medicinal products required for use in homeopathy. Not only are there some established 3000+ source materials for HMPs but each source material can be developed into a number of potentised products and complex products. While many of the single HMPs are used frequently many others are used infrequently but because of the personalised nature of homeopathic treatment, when a lesser-used HMP is required by a patient its availability is crucial. This means manufacturers need to keep a full range of HMPs in stock. Unfortunately, due to the constraints of inappropriate and disproportionate regulatory requirements and the costs imposed by some medicine's agencies in a number of countries the required range is no longer available throughout Europe. This has resulted in patients and prescribers increasingly having to source HMPs across EU borders or from outside the EU.

We consider that

- **For Article 14 products, it should be possible to limit the administrative burden and costs required to a level that is proportionate to their simple status and safety profile so that manufacturers can maintain the full range of HMP source materials in stock.**
- **Article 16.2, regarding homeopathic products not covered by Article 14, should be implemented in all MS, also taking into account the traditional use of these products analogous to recognition of traditional use as with Traditional Herbal Medicinal Products. A more harmonised regulatory**

approach to Article 16.2 products should be made and an assessment policy be established to facilitate their supply across the EU.

C. Strengthening and supporting the role of the Heads of Medicines Agencies Homeopathic Medicinal Products Working Group (HMPWG) Despite HMPs being included in the Directive 2001/83/EC, EU legislators at the time chose not to establish a separate committee for HMPs under the aegis of the EMA as they did for herbal medicinal products. For this reason, were the Commission to support the work of the HMPWG, although being under-resourced, is carrying out the work an EMA committee would have done had it been established.

One of the major causes of varied availability of homeopathic products between MS identified by the Matrix Report is a lack of understanding of homeopathic pharmacy by national medicines agency officials, many of whom approach HMPs with only a conventional pharmaceutical background. The HMPWG is in the process of producing a set of commonly agreed guidance documents on all aspects of HMPs such as 'first safe dilution', in order to provide guidance on the assessment of HMPs and to facilitate the resolution of procedural, regulatory, and scientific issues arising from variation procedures pertaining to homeopathic medicinal products. **We urge DG SANTE to support and strengthen the work of the HMPWG in order to ease the way and allow for the full availability of HMPs across Europe.**

4. Anthroposophic medicinal products

Anthroposophic medicine and its products

As other non-conventional medicines, anthroposophic medicine is based on a holistic approach; it integrates conventional and complementary medicine and it includes all dimensions of the patient — physical, emotional, mental and spiritual, as well as the impact of a person's environment and social context. Anthroposophic medical doctors are qualified physicians who have received additional training to integrate anthroposophic medicine into their conventional practices.

Like other non-conventional medicinal products, anthroposophic medicinal products (AMPs) have a long tradition of medical use, have few adverse effects and are low cost. However, AMPs contain substances, dilution levels, manufacturing methods and descriptions of indications that are specific to anthroposophic medicine.

There is growing evidence that the anthroposophic medical approach, including AMPs, increase both patient satisfaction and overall health outcomes. There is also growing interest in this medical approach: an ECHAMP study on Homeopathic and Anthroposophic Medicinal Products in the EU found a steadily increasing demand, with an annual market growth rate of 6.5% between 2010 and 2013, even though there are countries "where there is a clear consumer demand [and where] availability is limited."

Authorisation and registration of AMPs

In 2008 and 2014, the European Commission released two studies on the availability of medicinal products in the European Union. Both highlighted, e.g., the pressing need to tackle the unsatisfactory legal situation of AMPs. Furthermore, the 2014 Matrix Insight

Report underlines that AMPs, together with homeopathic medicinal products (HMPs), as an indispensable part of the European pharmaceutical market and clearly states that the availability of AMPs is generally worse than in the case of HMPs.

Following the Directive 2001/83/EC on medicinal products for human use, the marketing of medicinal products is, as a general rule, subject to a marketing authorisation (MA) by the competent national authority. The Directive also contains specific chapters on homeopathic and herbal medicinal products that, given their long use and low risk of side effects, allow a registration rather than authorization, via a simplified procedure.

Anthroposophic products are only recognised but not specifically regulated by this EU pharmaceutical law. In general, the Directive 2001/83/EC does not consider the specific features of the traditional herbal medicinal products, HMPS, and AMPs. In consequence, requirements for marketing authorisation (MA), set out by the EU pharmaceutical law, do not work with AMPs, which, on the other hand, prevents these medicines from fulfilling the formal requirements for marketing authorisation. Unlike other non-conventional products, the EU pharmaceutical law does not envisage their registration under adapted safety and efficacy requirements. For most AMPs, applying the same standards as conventional medicinal products, is not only inappropriate but also disproportionate given their low risk profile and long tradition of medicinal use.

Only in the case AMPs meet the criteria to qualify as homeopathic or traditional herbal medicinal products, they benefit from the simplified legal regime. If not, standard MA procedures apply. In practice, many AMPs do not qualify as homeopathic or traditional herbal medicinal products due to their composition (substances, dilution levels), manufacturing processes, or traditional use. These AMPs are faced with a legal "grey area" that results in many AMPs not being authorised or registered. As a result, many AMPs have problems being placed on the national markets in the EU. This situation makes it difficult for anthroposophic physicians to prescribe them or for patients to access them.

In Germany, which has the most EU complete legal regime of anthroposophic medicine, despite the express recognition of anthroposophic medicine and products, no specific rule on authorization and registration have been adopted: it facilitates the authorization and AMP but only as homeopathic products.

Moreover, some member states have additional and divergent national requirements, that make the registration procedure even more burdensome and so demanding that fewer AMPs are registered than would be possible if the national rules were less stringent. The majority of the EU member states in their pharmaceutical legislation neither mention AMPs directly nor in connection with the registration procedures for homeopathic medicinal products.

Hence, producers, distributers, practitioners and patients have to cope with various and partly prohibitive provisions for the availability of AMPs in European countries. Their availability is fragmented to a surprisingly high degree in the markets of these countries, which has, again, negative repercussions for the application of anthoposophic medicine, as an accepted and patient-demanded part of CAM and Integrative Medicine.

Many arguments are in favour of an EU legal framework for anthroposophic products. Firstly, anthroposophic medicine is an established practice that has become part of the European health environment; the safety and efficacy of anthroposophic products is demonstrated by scientific studies and their regular use by qualified doctors since the 1920s. More importantly, no objective arguments explain why AMPs should be subject to

a much heavier regulatory regime than homeopathic or traditional herbal products. On the contrary, the characteristics shared with those products justify subjecting them to the same or a very similar simplified and more appropriate regulatory procedure. The example of Switzerland demonstrates that another, adequate authorisation regime for AMPs is possible, a regime which is compliant with the demands of patients and doctors, as well as with the necessary standards of good manufacturing procedure and safety requirements.

Switzerland is the only European country that recognises and regulates AMP as such. The Swiss marketing authorization system is very similar to the EU one, but the authorization of CAM products, including AMPs, has been significantly simplified by the Ordinance on Complementary and Herbal medicines; the Ordinance defines AMP and sets out a legal regime that recognizes their specific nature and low level of risks. As a result, many AMPs are available in the Swiss market. Also, a listing of recognized AMPs and directions for their preparation and use is available in the Swiss Pharmacopeia (an official publication of medicines and their indications). This document facilitates access to all AMPs in Switzerland, but no such parallel document exists within an EU member state or in the EU as a whole.

<u>IVAA Position on AMP Regulation</u>

1. The almost 100-year European tradition and the outstanding safety record of anthroposophic products justifies granting AMPs easier access to the markets in the EU, especially as they improve the quality of life for patients.
2. There is a need for a legal framework to facilitate access to AMPs in Europe. This could be done either as a new section in the existing EU directive on medicinal products, or via new and more comprehensive legislation on the regulation of complementary and alternative medicinal products.
3. In the meantime, flexible interpretations of existing EU rules should be adopted, in particular by accepting scientific publications as an indication of safety and efficacy.
4. Member states should apply the existing rules of the Directive better and should include AMPs in their pharmacopoeias or decide to recognize AMPs in other national pharmacopoeias, such as Switzerland's.
5. IVAA would like to see more EU consistent regulation in member states and that the EU ensures the availability of AMP's that have been prepared in accordance with good anthroposophic pharmaceutical practice.
6. Heads of Medicines Agencies and the European Medicine Agency should include anthroposophic sections in homeopathic and herbal monographs or adopt anthroposophic monographs.

5. Conclusion

Non-authorisation of CAM medicinal products is a major driver in non-availability of these products for European citizens in many countries and work is needed to improve the national implementation procedures for these CAM medicinal products.

Authorisation procedures for medicinal products is a principal area of EU competence and we call upon the Commission and the European Parliament to improve the situation with regards to future access to CAM medicinal products across the EU. This would be an appropriate part of the European Commission's Regulatory Fitness and Performance programme REFIT, the aim of which is to make EU law simpler and to reduce regulatory costs, thus contributing to a clear, stable and predictable regulatory framework supporting growth and jobs. **Measures by the Commission and the European Parliament are now urgently needed to increase the availability of herbal, homeopathic and anthroposophic medicinal products across the EU.**