Making Medicines Affordable

EGA'S COMMENTS ON THE CONCEPT PAPER ON THE INTRODUCTION OF FEES TO BE CHARGED BY THE EMA FOR PHARMACOVIGILANCE.

EGA'S COMMENTS ON THE CONCEPT PAPER SUBMITTED FOR PUBLIC CONSULTATION ON THE INTRODUCTION OF FEES TO BE CHARGED BY THE EMA FOR PHARMACOVIGILANCE

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1. Introduction

The EGA[1] welcomed the new pharmacovigilance legislation as a mechanism to support improved patient safety and at the same time reduce the requirements on industry through a more centralised and coordinated way of working. However the European Commission's (EC) Concept Paper on fees to be charged by the European Medicines Agency (EMA) for pharmacovigilance activities raises major concerns for the generic medicines industry. The EGA agrees that proportionality and transparency are key principles to be observed when determining the fees, but we do not believe these principles have been taken into account sufficiently in the Concept Paper.

Firstly, Marketing Authorisation Holders (MAHs) belonging to the same group of companies[2] and acting under one Pharmacovigilance System Master File (PSMF), should only be required to pay one annual fee per active substance. The EGA has estimated that if MAHs belonging to the same entity are considered separate, an average-sized generic medicines company could have to pay a "maximum" fee of € 20 million on annual pharmacovigilance fees only because of the large portfolio of active substances and MAHs.

Taking the other fees into account (PSUR, PASS and referral fees), the EMA/EU pharmacovigilance system would be supported in a disproportionate manner by the generic medicines industry, while the pharmacovigilance workload for generic substances, which are well known substances with a well-established safety profile, is the lowest. Therefore the EGA stresses that it is important for the fees to be set proportionally for generic medicines.

Apart from the EMA pharmacovigilance fees, the new EU pharmacovigilance legislation also provides the legal basis for National Competent Authorities (NCA) to charge fees for activities that they undertake in relation to pharmacovigilance. The overall fee burden on industry will be the sum of EMA and member state fees and the overall impact assessment must be measured in this combined way. Multiple charging should be prevented in relation to these activities by all means.

The EGA would like to stress that prices of medicines have been steadily decreasing while regulations and fees are constantly increasing adding a large financial burden to the generic medicines industry and jeopardising its sustainability. The proposed fees may also lead to significant drug shortages in the European Union (EU) as companies will be obliged to reduce their portfolios.

[1] The EGA is the official representative body of the European generic and biosimilar pharmaceutical industry, which is at the forefront of providing high-quality affordable medicines to millions of Europeans and stimulating competitiveness and innovation in the pharmaceutical sector. Companies represented within the EGA provide over 150,000 jobs in Europe. Cost-effective generic medicines save EU patients and healthcare systems over €30 billion each year, thus helping to ensure patient access to essential medicines and providing urgently needed budget headroom for the purchase of new and innovative treatments.

[2] Commission communication on the Community marketing authorisation procedures for medicinal products - Application of Article 4(3)(11) of Directive 65/65/EEC in the context of the mutual recognition procedure

In order to properly assess the proposed fee structure, we suggest that a clear overview of the costs associated with all new pharmacovigilance activities is provided. Originally, it was anticipated in the impact assessment of 2008 that the total annual increase in fees payable to the EMA would be about € 10.5 million[3]. Now, according to EGA calculations, contributions to the EMA could be more than 10 times the originally estimated annual fee level for the entire industry.

[3] Pharmacovigilance Impact Assessment 2008 - page 55

2. EGA's Views on the Consultation Items

1. Consultation item N°1

Consultation item n°1: Do you agree with the proposed fee for single assessment of PSURs? If not, please explain and/or suggest alternative.

The EGA recognises that the fees proposed by the European Commission are maximum fees, however no fee range is presented; consequently, there is no comparison of values to allow for a proper assessment. The EGA feels that the proposed fees for the single assessment for a generic PSUR is not proportional at the moment. It should be further clarified what is meant by the wording "a basic fee" of a maximum of € 80,300 and that only one fee is charged for the assessment of a PSUR. Furthermore, no explanation has been given as to why the suggested fee has increased from € 6,100 as described in the 2008 Financial Statement[4]. Fees for PSURs that were submitted for DCP, MRP or National Procedures to the National Competent Authorities (NCA) are very disharmonised. Therefore the EGA would be interested in having more transparency concerning the fees and its ranges since at the moment it is unclear.

It is proposed by the Concept Paper that a lower fee of € 40,150 would apply for products that have been authorised for less than 2 years, and the maximum fee of € 80,300 would apply for products that have been approved for a longer period of time. While we do appreciate the concept of different fee levels reflecting different data volumes and therefore differences in workload, this concept does not take into account that as a result of the normal product lifecycle, the volume of additional pharmacovigilance data usually decreases significantly several years after product launch. Based on the principle of proportionality, the EGA believes that the fee for PSUR assessment should be reduced again 7-10 years after product launch, or at the latest when the product becomes generic, to reflect the lower workload for PSUR assessment.

It is also unclear how the experience from the PSUR work-sharing project will be taken into account for the determination of the fees. The PSUR assessment reports received so far follow the pattern that most of the scientific discussion (and the amount of work needed) was related to the originator's PSUR, with little or no additional impact from the generic PSURs. A single assessment can for example be performed on the originator company's PSUR and on the safety data from the EudraVigilance (EV) database.

It must also be taken into account that in many member states there are national fees so the newly proposed fees multiply the current fees. Extrapolating current NCA fees for PSURs in a scenario with 2 RMS and 25 CMS could add up to approximately € 40,000. Considering this scenario as equivalent to the workload under the new procedure this equates to a 91% increase compared to the proposed fee for PSUR assessments of € 80.300. This effect becomes even stronger if the PSUR or PASS Assessment Report leads to variations. Under this proposal a separate variation fee should no longer be charged by the

[4] Pharmacovigilance Impact Assessment 2008 - page 47

EMA for the implementation of changes to the MA of CAPs following the assessment of a PSUR.

MAHs with non-CAPs will still be required to submit requests for variations to the competent NCAs for which a fee is charged. As under the new pharmacovigilance legislation, EMA will be empowered to charge pharmacovigilance fees also for non-CAPs, it is important to avoid discriminatory treatment. In our view this arrangement will particularly put generic manufacturers and SMEs at a significant disadvantage in comparison to companies with predominantly CAPs in their portfolio and this can have a detrimental impact on the business.

The EGA is also concerned that it is still unclear for which products the generic medicines companies will be required to do PSUR submissions since the EURD list is not finalised yet, neither is the list of products that will require additional monitoring and where a PASS is required. Although PSURs for generic medicines are generally exempt, for about 40% of the required data lock point ((DLP) for generic PSURs is still required. As explained grouping for PSUR writing is not foreseen so the total amount of money generated by PSUR assessments will be very high.

2. Consultation item N°2

Consultation item n°2: Do you consider relevant the concept of grouping as proposed? If not, please explain and/or suggest alternative.

The EGA welcomes that grouping between companies of a different entity is encouraged, although it is unclear how this grouping will be seen.

- Grouping between MAHs of the same group of companies is inevitable and the concept paper should not be indicating this as grouping. There should not be a grouping fee of 500 € for all MAHs within the same group of companies (i.e. "same entity")[5]. This would not be appropriate, as this PSUR contains information from one pharmacovigilance system, collected and evaluated at one single point under global SOPs and under the supervision of one EU QPPV.
- Grouping between companies from a different entity is too idealistic. In reality it is not feasible to apply this to MAHs from different groups of companies, since individual PSURs should be submitted for other regions at the same time and companies will also need their own PSUR to submit in other regions. In addition commercially sensitive information, such as sales data, approval and marketing status at country level will not be easily exchanged.

If the different MAHs (not belonging to the same entity) do not group: Would this mean that all these generic PSUR's will be assessed in the same way and thus that a maximum fee of € 83,300 can be demanded for each PSUR submission from each MAH?

[5] Commission communication on the Community marketing authorisation procedures for medicinal products - Application of Article 4(3)(11) of Directive 65/65/EEC in the context of the mutual recognition procedure

The EGA understands that in case of the single assessment of a PSUR of the same active substance, the PRAC would not wish to receive all the safety information multiple times. Since only one single assessment will be performed per active substance, the EGA stresses that the fee for the single assessment should be divided between all MAHs with this active substance in their portfolio, regardless of the fact that they might need to submit a PSUR for the active substance too. The definition of the "same entity"[6] should also be taken into account. When all PSURs are taken into consideration this means that the data will be consolidated; subsequent work regarding analysis and conclusions will be done on the consolidated data set. This implies that the analysis and conclusion work is done only once. The total work is not the cumulative sum of individual PSUR reviews but significantly less. The fee structure should reflect this.

As an alternative to the EMA's grouping proposal we suggest that the size of fees for generic medicines is reduced to 10% of the standard fees. This takes into account that a single EMA assessment for a given active substance can be harmonised and applied across many generic marketing authorisations.

3. Consultation item N°3

Consultation item n°3: Do you agree with the proposed fee for the assessment of PASSes? If not, please explain and/or suggest alternative.

Concerning the assessment of PASSes, the EGA has the same concerns as discussed in consultation item N°1. At the moment, it is also difficult to assess the impact for the generic medicines industry as it is not known which products will require PASSes. The proposal only presents a maximum fee of € 80,300, but does not give any information what lower fees may be applicable, and on what basis such lower fee levels would be determined. Again, the used benchmark of a Type II variation is a very general one and does not provide any transparency on the specific amount of the work that would be involved in the assessment of the final PASS study reports, and how differences in workload for different studies would be taken into account. The fee should reflect the amount of data to be assessed and should reflect different data volumes due to differences in study size. It should also be clear that a proposed fee is for the assessment of the protocol, amendments and final reports as well as the assessment of the changed related documents like the RMP and SPC/PIL.

[6] Commission communication on the Community marketing authorisation procedures for medicinal products - Application of Article 4(3)(11) of Directive 65/65/EEC in the context of the mutual recognition procedure

4. Consultation item N°4

Consultation item n°4: Do you consider relevant the concept of grouping as proposed? If not, please explain and/or suggest alternative.

As mentioned earlier, MAHs of the "same entity"[7] should not fall under the definition of grouping.

5. Consultation item N°5

Consultation item n°5: Do you agree with the proposed fee for the assessment of pharmacovigilance referrals? If not, please explain and/or suggest alternative.

The maximum charge for pharmacovigilance referrals is € 267,400 with a minimum fee of 80,300 € for referrals under the structure proposed in the latest version of the concept paper. This is a significant increase on current fees of € 66,700 for safety referrals[8]. In fact the maximum amount is equivalent to the basic fee for the application for authorisation for medicinal products for human use under the centralised procedure for a full dossier.
We do not believe that pharmacovigilance referrals – even if they entail full benefit-risk assessment – are comparable to the assessment of an initial MA application. Further explanation on this particular subject is required. The current proposal does not include referrals initiated by EMA/PRAC (which might apply for medicinal products referring to the same ATC code). There should be a significant fee reduction for PRAC initiated referrals within the same class of medicinal products (e.g. referring to the same ATC code).

Given that providing an answer to questions raised within a referral remains a privilege, not an obligation, it is unclear how referral fees can be attributed to MAHs who are not able to contribute to the scientific discussion, e.g. generic medicine companies who did not conduct their own clinical trials, and/or do not market the product.

Additionally, after the assessment of a referral, a type II variation may be requested, presumably from all MAH marketing products containing the active substance investigated by the referral. If so, the fee for the requested type II variation must be included in the total amount of the proposed referral fee or even waived. If a MAH is paying € 267,400 plus type II variation in all Member States, the MAH will be paying almost a half million euro for the maintenance of a single medicinal product. Amounts like these will lead to drug shortage in Europe as such amounts are unsustainable for a generic medicines company. The fee range proposed should be clearly explained; i.e. what is the workload involved?

[7] Commission communication on the Community marketing authorisation procedures for medicinal products - Application of Article 4(3)(11) of Directive 65/65/EEC in the context of the mutual recognition procedure
[8] Explanatory note on fees payable to the European Medicines Agency

6. Consultation item N°6

Consultation item n°6: Do you agree with the concept of grouping as proposed? If not, please explain and/or suggest alternative.

As mentioned earlier, MAHs of the "same entity"[9] should not fall under the definition of grouping.
If the approach is to charge fees for each MAH who has at least one MA for the product under review, it should be clarified for the sake of transparency and proportionality on which basis the fees are divided.

7. Consultation item N°7

Consultation item n°7: Do you agree with the proposed pharmacovigilance service fee? If not, please explain and/or suggest alternative.

The EGA recognizes that the EMA has to deal with an increase of pharmacovigilance tasks such as literature searches, performing signal detection and the setup and maintenance of different ICT tools, but is should also be acknowledged that the database as such has also put a heavy workload on the MAHs and as such has and will cost a lot of money. It is not recognizable for what value the fees are to be paid. As referred to in the general introduction we think that the annual fee should not be initiated before more transparency on the EMA tasks and the benefits for industry are available.

Additionally, it was also made clear by EMA that literature monitoring will be only performed for selected substances and in selected journals, and that the legal obligation of the MAHs to monitor the scientific literature and to process literature reports on adverse drug reactions will remain unchanged. Besides this, global companies are unable to utilise the outputs of this literature monitoring service since such companies are not able to use this data in the required format or timelines to fulfill their global obligations. Therefore, literature monitoring by EMA does not shift any task or responsibility from the MAH to the EMA and can unfortunately as a consequence not be regarded as a service.

The same applies to the future work that EMA will undertake on signal detection. The final responsibility for signal detection and evaluation remains with the MAH; therefore the EMA's activities do not shift any task or responsibility from the MAH to the EMA and can as a consequence not be regarded as a service.

If there are fees with which the EGA strongly disagrees the EGA calls at least for high transparency and proportionality in the range and would also like to see what the industry will receive in return from the EMA. The concept paper also describes the purpose of this fee as "intended to cover general activities related to the new pharmacovigilance tasks of

[9] Commission communication on the Community marketing authorisation procedures for medicinal products - Application of Article 4(3)(11) of Directive 65/65/EEC in the context of the mutual recognition procedure

the Agency, including operation of specific ICT tools". The ICT tools required include "the EV database and the PSUR repository" and the activities covered include "literature monitoring and monitoring the effectiveness of public health measures". All these activities are not expected to be available to the industry before 2016.

The criteria laid down in the 1998 Communication on the Community marketing authorisation procedures for medicinal products regarding the definition of "same entity"[10] should be followed.
Specifically, this means that the pharmacovigilance service fees are charged per group of companies. Please consider the example, MAH A, B and C belong to the same company group called "GROUP X". All companies (A, B and C) have active substance S in their portfolio. The annual fee for pharmacovigilance should only be charged once for Group X instead of three times due to the 3 MAHs. The document should be more precise on the terminology and the list of products established under Article 57(2) should link different MAH to their group of companies. If not, considering a maximum annual fee of € 1000, a group of generic medicines companies can have for active substance S up to 20 different marketing authorization holders and thus could the maximum annual fee for pharmacovigilance for only substance S can be € 20.000. Taking into account that an average sized generic company has a portfolio of 1000 active substances, this could mean that one generic medicines company could have to pay up to € 20 million on annual pharmacovigilance fees only.

8. Consultation item N°8

Consultation idem n°8: Do you agree with the proposed approach for fee reductions for SMEs as regards the pharmacovigilance procedures at EU level (point 3.5.1)? If not, please explain why and provide suggestions how this could be improved.

We suggest that a methodology similar to the MedDRA subscription be applied, having in mind the company turnover and subsequently stratify the fees by cores.

9. Consultation item N°9

Do you agree with the proposed approach with regard to the pharmacovigilance service fee for SMEs (point 3.5.2)?

See comment to question 8. It should be further clarified for SME's that do not hold CAPs how they apply for SME status at the EMA in case a reduced annual fee for SMEs is adopted.

10. Consultation item N°10

What other aspects would you like to raise? Do you have additional comments?

[10] Commission communication on the Community marketing authorisation procedures for medicinal products - Application of Article 4(3)(11) of Directive 65/65/EEC in the context of the mutual recognition procedure

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3. Conclusion

The EGA stresses that at this stage financial justification for the pharmacovigilance fees is lacking since there is no information in the concept paper on the range of the fees and there appears to be no transparency at this moment how much funding the EMA requires for its services and how much they will receive at this stage with the fees proposed in the concept paper. The EGA requests for proportionate or even waived fees for generic medicines. If an average generic company is required to pay € 20 million on annual fees only generic medicines industry will not survive.

The EGA takes this opportunity to get further information from the Commission regarding what are the EMA's anticipated revenues based on the proposed fee structure and how does this line up with their actual and projected costs. The Commission/EMA should provide information on what its actual administration costs are for the pharmacovigilance program in order for the industry to properly assess the reasonableness of the fees being requested. This should be provided both in terms of an overall cost deficit under the existing program, as well as anticipated revenue projected based on anticipated services rendered.

In addition, we believe that it is important for the Commission to organize a workshop with the industry experts and EMA to discuss this fee regulation when all information is available in order to end up with a proportionate and transparent fee regulation.