Jouhou Koukai Services LLC
International Fax: +81-3XX-XXX-XXX
Email: j_koukai@zaa.att.ne.jp

JKS

Memo

To: Mr. Pharbaron

From: JKS

CC:

Date:

Re: Your email letter

Case Study – Triptans in Japan

Sir:

Thank you very much for your letter and the request for additional information regarding a projected Case Study on oral triptans recently introduced in Japan. After an internal analysis and check of all sources and resources, we would like to confirm that we do have the answers to all questions you have listed in your letter, and thus we can prepare a report (free style or under a format you might wish to provide) within the desired period.

First, as background, we have understood several issues regarding the introduction of triptans in Japan that are considered to be addressed in a tentative Case Study Report:

1. What process was used to obtain regulatory approval (regulatory agencies involved, public documents available, etc.)?
2. What were the major differences?
3. What clinical studies were undertaken?
4. Were Japanese CSOs used to conduct any bridging studies?
5. Were other Japanese agencies critical to their success?
6. Any other descriptions or comments on the specifics of the development and approval process in Japan.
7. Cost of the launch.

The objectives of our potential assignment at hand, therefore, would be to provide concise information and latest intelligence on those selected topics– with strong focus on the accelerated delivery.

Please, find the following preliminary answers:

1. **What process was used to obtain regulatory approval (regulatory agencies involved, public documents available, etc.)?**

Answer:

In the reviewed cases the process used for obtaining the regulatory approval was the standard (ordinary) process – i.e. neither product was approved by using Orphan Drug Designation, Priority Review and other processes stipulated for special cases by the *Pharmaceutical Affairs Law (PAL).* The formal name (translated in English) of the "ordinary process" is *Application for Manufacture and Import Approval of Medicinal Product*.

The regulatory agency involved was the Pharmaceutical and Medical Safety Bureau (PMSB) of the Japanese Ministry of Health, Labour and Welfare (MHLW). Although it is not an independent entity, the PMSB is the medicines agency of Japan, and it is functionally equivalent to the Medicines Control Agency and Medical Devices Agency in UK, or to US FDA.

Regarding the currently publicly available documents the Table below lists the documents we have confirmed to be retrievable:

Table 1. Publicly available documents (various sources, in Japanese only)

Document	Imigran ®		Zomig ®	
	No.	Pages	No.	Pages
Package Insert	1	4	1	4
Evaluation Reviews	2	30	2	32
Summary Basis for Approval	26	435	17	626
Deliberation Committee Report *	1	5	-	-
Definition of the regulatory category	1	1	1	1

* Note: Available only for the injectable Imigran, approved in 2000.

Aside from the listed documents additional documentation related to the development process and/or the review and approval process might be disclosable under the *Public Access to Information Law (PAIL)*. However, for each individual document a formal request should be placed with the Office for Disclosure of Information of the MHLW.

2. What were the major differences?

Answer:

Although a number of characteristics of the two oral triptans are – if not equal, at least paralleled, in our opinion the major differences could be seen at:

- The programs for clinical development
- The patient groups
- The marketing approach

Table 2. Oral triptans approved in Japan as of June 2002

Characteristics	Imigran	Zomig
Manufacturer	GlaxoSmithKline KK	AstraZeneca KK
Brand	Imigran ®	Zomig ®
Generic name	Sumatriptan succinate	Zolmitriptan
Formulation	Tablets 50 mg	Tablets 2.5 mg
Approval date	June 2001	June 2001
Marketed	August 2001	August 2001
Price	1,092.9 Yen/tablet	1,092.9 Yen/tablet

3. What clinical studies were undertaken?

Answer: The development of both products in Japan includes domestic bridging studies.

4. Were Japanese Contract Service Organisations (CSO) used to conduct any bridge studies?

Answer: Yes. (Details available)

5. **Were other Japanese agencies critical to there success?**

Answer: Two other agencies were involved in the development/approval process. (Details available)

6. **Any other descriptions or comments on the specifics of the development and approval process in Japan.**

Answer: Details to be provided

7. **Cost of the launch.**

Answer: Details to be provided.

TIMELINE AND COST

Providing we could get a Purchase (Requisition) Order from Pharbaron in writing (fax) by the beginning of the next week, we can deliver 45-50 pages Report within a month.

Given the scope of the report, we can quote the cost for the report with the following (tentative) breakdown: consulting fee of for work, plus data acquisition and preparatory fee.

I hope this is helpful for your internal discussion. Let me know if there are other points to be clarified further.

Best regards,

JK S

Tokyo, June 2002