

## WORKSHOP: EFFECTIVE RX-TO-OTC SWITCHING

# Switching around the world: Japan

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*The table below shows the chronological listing of the active ingredients switched from Rx to OTC in Japan for the period from 1983 through this year.*

| <b>Year</b> | <b>Ingredient</b>   |
|-------------|---|
| 1983        | Soysterol<br>Sodium Picosulfate   |
| 1984        | Semi-Alkaline Proteinase  |
| 1985        | Exalamide<br>Dimemorfan Phosphate<br>Indomethacin<br>Ibuprofen  |
| 1986        | Polyene phosphatidyle choline   |
| 1987        | Sodium polyethylene Sulfonate<br>Butylscopolamine Bromide<br>Bromhexine<br>Cetraxate hydrochloride<br>Timepidium Bromide<br>Cicopirox olamine *<br>Miconazole nitrate * |
| 1988        | Gefarnate<br>Econazole nitrate<br>Carbocisteine<br>Isothipendyl   |
| 1989        | Repronicate<br>Loperamide Hydrochloride   |
| 1990        | Ubidecarenone<br>Hydrocortison Butyrate<br>Bisoxatin Acetate<br>Ibuprofen piconol<br>Mequitazine  |
| 1991        | Tolcilate<br>Ufenamate<br>Eprazinone<br>Tioconazole   |

|      |  |
|------|--|
| 1992 | Mecobalamine<br>Prednisolone Valeroacetate<br>Calcium L-Aspartate                                    |
| 1993 | Sulconazole Nitrate *<br>Bifonazole *<br>Oxiconazole Nitrate *                                       |
| 1994 | Piroxicam<br>Ketoprofen  |
| 1995 | Oxethazaine<br>Trimebutine Maleate<br>Felbinac *<br>Pirenzepine Hydrochloride<br>Isopropamide Iodide |
| 1996 | None   |
| 1997 | Sodium Cromoglycate<br>Cimetidine<br>Famotidine<br>Ranitidine Hydrochloride                          |
| 1998 | None   |
| 1999 | (as of May) none   |

\* External application

Of these 47 active ingredients, much attention was drawn to the following five ingredients: Ibuprofen, Indomethacin, Cimetidine, Famotidine and Ranitidine Hydrochloride. Why was so much attention drawn to them? Because their efficacy as Rx had been very much talked about before the switch applications were filed. But the sales of these switched products were not necessarily satisfactory, failing to meet the high expectations.

There are a couple of reasons for the poor performance:

1. Firstly, the advertising climate: comparative advertising is banned, meaning that you cannot stress too much that "This medicine works better than an ordinary OTC drug because it combines an active ingredient used in Rx".

2. Secondly, the drug classification: medicines in Japan are classified into two classes: Rx and OTC. Only Rx products are subject to reimbursement. Therefore, switching of Rx to OTC means a decrease of business to physicians. They never welcome switching. Most notably, the Japanese OTC drug industry experienced a very chilly and hostile reception of the three H2 blockers by medical circles.

## Registration

In order to get your product registered as a drug, both Rx and OTC have to obtain Approval and Licence. Approval is an official confirmation that the product to be manufactured is both Safe and Effective. The Licence reflects the official findings that the applicant satisfies two major requirements:

### *Product Registration*

*Both Rx and OTC*

- (1) Approval (Shonin)*
- (2) Licence (Kyoka)*

*Approval & Licence in tandem*

1. Personal requirements that the applicant is not a legally incompetent person, has no record of sexual harassment, etc.
2. The applicant's manufacturing facilities and equipment conform to the standards (GMP for example).

## Switch applications

The same goes for a switch application.

### *Approval (Shonin)*

*Official confirmation of both Safety and Efficacy*

### *Licence (Kyoka)*

*Official findings of compliance with personal requirements conformity to manufacturing standards*

The data to be submitted with an application dossier range over seven groups such as "Data on stability", "Data on toxicity" and so on.

### *Range of data*

*Seven groups of data  
Clinical trials*

*Not less than 150 cases (patients)  
At not less than 5 medical institutions*

I will not dwell upon all of these data. Only I want to attract your keen attention that Clinical Trials are required to generate more than 150 cases (or patients) and to be conducted at more than five medical institutions.

When safety and efficacy profile has been well demonstrated by PMS or Post Marketing Surveillance, these

cases may be reduced to three medical institutions with 60 cases.

### *Timing of Switching Application*

*Prefectural Government*

*Ministry of Health and Welfare  
Central Pharmaceutical Affairs Council  
8 - 10 months*

An application is filed with Ministry of Health and Welfare through the Prefectural Government. The Ministry of Health and Welfare or MHW, which is relatively understaffed, entrusts the review of the application to the Central Pharmaceutical Affairs Council. Usually it takes 8 to 10 months before an approval is granted.

## Three unique aspects

It may be interesting to conclude my presentation by explaining three major aspects unique to Japan's pharmaceutical climate:

### *Unique pharmaceutical climate*

- (1) Safety first, Efficacy second  
Low dose in most cases  
Lower than Rx*

*Lower than doses in Western countries*

Aspect (1): Due to major tragic events caused by the medicines sold over the counter in 1965, a "Safety first, efficacy second" policy was established by the MHW. As for switching, a low dose in most cases except some epidermal drugs for athlete's foot is a prerequisite. The dose is usually lower than Rx and doses in Western countries.

### *Unique pharmaceutical climate*

- (2) Predominant physician-dispensing  
About 70% of prescriptions  
Extremely low profile of OTC  
Chilly reception of switching*

Aspect (2): About 70% of the total prescriptions written by physicians are dispensed by physicians. In such a predominant physician-dispensing climate, Rx products are a goldmine to physicians. On the other hand, OTCs in Japan have an extremely low profile in the eyes of physicians simply because OTCs are not subject to reimbursement under the Health Insurance Scheme which theoretically covers the entire nation.

### *Unique pharmaceutical climate*

- (3) Comparative Advertising banned  
"You are no better" Policy  
Approval Standards (Monographs)  
Subjective evaluation*

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Aspect (3): Comparative advertising is absolutely banned. A “You are no better” policy has been firmly established and is abided by all those engaged in the business. There are two major reasons for this ban:

1. As long as there were established Approval Standards which are very similar to the USA/FDA OTC Monographs, types and quantities of active ingredients, indications or effects, etc. should be same. Therefore, there is a “You are no better, no faster, no nothing...” policy.

2. “This medicine works wonderful” is after all a personal, individual experience, namely, the subjective evaluation of the user. A medicine may not work wonderful for you, or may not be so effective as it was for your friend.

So, the MHW has determined that there should be no comparison as far as OTC medicines are concerned.

