From strategy to higher sales

Workshop

CASE STUDY

PPIs

CONTENT

1. Introduction

This case study will examine the management of three pharmaceutical products (Emanera - esomeprazole, Nolpaza - pantoprazole, Lanzul - lansoprazole) in a fictional environment (Carinthia). The brand names of products are taken from the real situation; however there are slight changes in sales data and market situation.

Your objective is to prepare a Country Brand Strategy (CBS) for Krka's PPI (Emanera, Nolpaza, Lanzul). It should include the following:

- **Analysis of the situation on the market of PPI/H2Blockers** (you have whole year data for 2020)
- **Strategy for your PPIs**
- **Tactics**

Detailed instructions are provided at end of the case.

2. Disease overview

Acid-related disorder refers to a group of disorders affecting the gastrointestinal (GI) tract in which gastric acid plays a major role in the development of the disease and symptoms. Included among these disorders are gastroesophageal reflux disease (GERD) and peptic ulcer disease (PUD).

GERD

The term gastroesophageal refers to the stomach and esophagus. Reflux means to flow back or return. Therefore, **gastroesophageal reflux is the return of the stomach's contents back up into the esophagus.** When reflux stomach acid touches the lining of the esophagus, it causes burning sensation in the chest or throat called **heartburn**. **Regurgitation** is a return of the gastric content into the throat or mouth, which may cause an unpleasant sour taste. Reflux of stomach content is not necessarily pathological, as some reflux also occurs in normal individuals. This develops into the disease (GERD) when the **reflux causes troublesome symptoms or complications**.

Factors that may contribute to GERD include:

- illness (esophagitis, scleroderma),
- hiatal hernia,
- lifestyle (alcohol use, smoking, overweight…),
- medications (theophylline, tricyclic antidepressants, calcium-channel blockers…),
- mechanical damage of LES (myotomy, balloon dilatation, surgery),
- pregnancy (due to estrogen, progesterone).

Also certain food can provoke GERD, including: acid fruits and vegetables (oranges, tomatoes, apples, peppers), chocolate, drinks with caffeine, fatty foods, mint flavorings, spicy food, tomato-based food (like spaghetti sauce, chilli, pizza …), alcohol. General advise to patients is to leave certain foods out of their diet on individual basis if it causes problems.

The prevalence of GERD is approximately 20% of the adult population. Longer life expectancy in the developed world will lead to an increase in GERD prevalence in the years to come. Detection rate of GERD symptom, i.e., heartburn is averagely good, but in recent years the problem of frequent heartburn and GERD is becoming more actualized among doctors, pharmacists and patients, and the number of patients with confirmed diagnosis of GERD has been steadily increasing.

PUD

A peptic ulcer (PU) is a hole in the gut lining of the stomach, duodenum, or esophagus. Depending on their location, ulcers have different names:

- **gastric ulcer** (a peptic ulcer in the stomach)
- **duodenal ulcer** (a peptic ulcer in the first part of the small intestine – duodenum)
- **esophageal ulcer** (a peptic ulcer located in the lower section of the esophagus – often associated with chronic GERD).

PU is a result of a disbalance between **protective factors** (secretion of mucus and bicarbonate, good perfusion, regeneration of epithelium, prostaglandin synthesis) and **aggressive factors** (*H. pylori* infection, NSAIDs use, age above 70 years, concomitant use of clopidogrel, steroids, SSRIs, smoking, alcohol, hydrochloric acid, pepsin …). The lifetime risk for developing a peptic ulcer is approximately 10%. *H. pylori* infection and the use of ulcerogenic drugs (NSAIDs, ASA, clopidogrel and other anticoagulants) are the most common cause of peptic ulcer. In Carinthia the *H. pylori* infection rate is 80%.

3. Ways of treatment and treatment guidelines

There are several treatments options available and they are of a wide variety. The first step in treating GERD is lifestyle modification. Further treatment plans include variable medications, endoscopic treatment or surgery. Among medicines, there are generally three options: antacids, H2 blockers and proton pump inhibitors. Among those, the use of proton-pump inhibitors - **PPIs is the primary approach** for reducing reflux symptoms, healing esophagitis and maintaining remission. PPI are the most effective, do not develop tolerance after repeated usage as H2 blockers, and have once daily dosing (H2 blockers should be taken twice daily). Both groups are considered as generally safe.

Treatment of PUD consists of eradication therapy (if *H. pylori* is present) and suppression of stomach acid secretion to allow healing of the ulcer.

Local doctrine in the country Carinthia generally **follows European guidelines**:

- **GERD treatment** – To confirm the diagnosis of GERD patients are treated with PPIs. No differences among PPIs are mentioned in these guidelines, any PPI may be given for simple or complicated form of GERD. Recommended treatment duration is 8-12 weeks for GERD at diagnosis. Dependent on the frequency and severity of the complaints the patient continues with treatment as continuous maintenance therapy (months), intermittent therapy (weeks) and "on-demand" (days) therapy.
  In practice we see that patients are still treated much shorter to confirm the diagnosis, on average 4 weeks instead of the recommended 8-12 weeks in the guidelines
- **In at risk patients for gastrointestinal complications that are on NSAIDs, PPIs** are prescribed **as prophylaxis.** This is becoming a habit due to the strong evidence in favor of protection with PPIs, but studies show that many at risk patients still do not get a PPI as protection against gastrointestinal complications. There is also new strong evidence and a recommendation in the guidelines of the European Society of Cardiology that patients on anticoagulants (even the newer oral anticoagulants) also need gastroprotection with a PPI, especially those with risk factors for gastrointestinal bleedings. This has not been implemented yet on large scale.
- **Treatment of peptic ulcer disease** include *H. Pylori* eradication (two antibiotics + PPI), so called triple therapy or bismuth containing quadruple therapy (two antibiotics + PPI+bismuth) 10-14 days as first option. Resistance of antibiotics to *H. pylori* is low. The latest European guidelines recommend use of the newer PPI esomeprazole instead of first generation PPIs (omeprazole, lansoprazole and pantoprazole), because it increases the *H. pylori* eradication success rate.

Basic characteristics of each PPI:

- **Omeprazole** has been on the market for more than 30 years , it is the oldest PPI, however, still very popular among many doctors, especially GP. This is why we often refer to it as golden standard among PPIs. However, it has shorter duration of effect, so frequently twice daily dosing is needed, and is less effective.
- **Lansoprazole's** main advantage compared to other PPIs, is that it enables faster inhibition of gastric acid secretion after the first dose than omeprazole. It has comparable efficacy as omeprazole.
- **Pantoprazole** has good safety profile as it is the PPI with the least possibility for interactions with other drugs and has longer duration of action compared to omeprazole. It is even suitable for those who take many medicines concomitantly and for those with nighttime GERD symptoms. It is also the most appropriate PPI to be taken concomitantly with clopidogrel. It is considered as more effective than omeprazole.
- **Esomeprazole** has the strongest inhibition of gastric acid secretion as it is the PPI with the greatest antisecretory activity. It is considered a new generation PPI with strong effect. Recently, the latest European guidelines state that using the newer PPI esomeprazole instead of first generation PPIs (omeprazole, lansoprazole and pantoprazole) increases the *H. pylori* eradication success rate.

4. Country environment

Carinthia is a country located in Central part of Europe with approximately 25 million inhabitants. It has relatively stable economy, although it was not immune to the global economic crisis.
There are approximately **8,000 general practitioners (GPs)**, **1000 internists, 200 gastroenterologists, 80 rheumatologists, 500 cardiologists, 300 orthopedics, 500 surgeons, 450 neurologists and 450 pneumologists,** which can all prescribe PPI. There are around 1800 pharmacies, which are allowed to substitute generic medicines. They dispense H2B and also PPI without prescription.

5. Prescribing habits

In general, GPs generate majority of total PPI prescriptions (70%), followed by gastroenterologists (10%) and internists (10%). Rheumatologists prescribe approximately 5% of total PPI prescriptions, while cardiologists, pneumologists, neurologists and surgeons approximately 1% each. However, there are significant differences in terms of prescription of each separate INN. Gastroenterologists tend to adopt modern treatments more quickly than GPs and other specialists. Gastroenterologists are also more confident in using higher doses.
Omeprazoles are mainly prescribed by GP (75% of total omeprazoles), while esomeprazoles by gastroenterologists (40% of total esomeprazoles). GPs claim that patients are generally satisfied on omeprazoles. There are also differences among cities, in big cities there is an increasing trend among GP toward newer molecules (pantoprazole, esomeprazole), with esomeprazole however being reserved for more severe cases. In the periphery omeprazole is still the drug of choice, while pantoprazoles are being increasingly prescribed.

Rheumatologists prescribe PPI to patients on long term NSAID and/or ASA treatment and cardiologists to some patients on clopidogrel/ASA.
Intravenous (IV) forms are used in hospitals in case oral approach is not appropriate – for rapid reduction of gastric acid secretion (i.e. acute treatment of bleeding ulcers, stress ulcers prophylaxis). IV forms are sold by different channels than oral forms: commercially through tenders on each separate hospital basis with big discounts. Discounts are generally not accounted for in IMS data.

Table 1: Average prescription of each separate INN by target group

	total PPI	omeprazole	pantoprazole	esomeprazole	lansoprazole
GP	70%	75%	30%	25%	65%
gastroenterologists	10%	5%	27%	40%	15%
internists	10%	8%	25%	20%	15%
cardiologists	1%	1%	5%	5%	1%
rheumatologists	5,4%	5%	5%	3%	3%
pneumologists	0,3%	1%	1%	5%	
orthopedics	1%	3%	3%	1%	1%
neurologists	1%	1,5%	3,5%	1%	
surgeons	1%	0,5%	0,5%		

Gastroenterologists prescribe PPI to approximately half of all their patients, while other target groups much less. GPs often initiate treatment with PPIs themselves except in more complicated patients or patients with severe symptoms in which case they refer patients to specialists. Also GPs refer patients to specialists if treatment with PPI after 4 weeks doesn't reach the desired effect in patients with a suspected diagnosis of acid-related disorders.

PPI are often used as needed. Patients with symptomatic relapse or complicated disease are prescribed lowest effective dose of PPI for maintenance therapy.

Around 20% of **H2 blockers** are still prescribed by doctors, mainly in small villages, other sales of H2blockers is due to patient demand in pharmacies or recommendation of pharmacists.

There are some OTC pantoprazoles on the market.

There are approximately **1800 pharmacies**. They dispense drugs according to prescriptions, substitute among generics inside INN and also recommend the products without prescriptions. Without prescriptions, for majority of pharmacists the first recommendation for indication of heartburn are still H2 blockers. However, apart from H2 blockers pharmacists dispense omeprazoles without prescriptions as well, despite not having OTC status. Mainly pharmacists dispense omeprazoles without prescriptions to patients which already used omeprazoles for longer period of time (or frequently for short term), but also recommend them to new patients for heartburn. It is estimated that in big cities up to 30% of omeprazoles are dispensed in pharmacies without prescriptions. Recently pharmacists started to dispense pantoprazoles as well without prescriptions.

PPI are most often used for 1 month in the treatment of GERD.

6. Reimbursement

PPI are differently reimbursed: omeprazoles and lansoprazoles 90% while pantoprazoles and esomeprazoles 50% and there are **no prescription limitations**. H2Blockers are 90% reimbursed and very cheap.

The price of generics should be at most 65% of originator price. Generic substitution within the same substances is possible. The rate of generic substitution on pharmacies vary considerably, in average is approximately 30%.

On the prescriptions the INN name should be written and in some cases the brand name is written between brackets (not allowed in all regions). Alternatively, doctors might give patients a separate "note" with the brand of the product.

7. PPI /H2B market

PPI market in Carinthia is continuously growing in units in the last 3 years, however, stagnating in last year in EUR. The details on the market you can find in the excel document that will be available during the case study workshop..

8. Overview of competition

Dr. Reddy's is the leading company on PPI+H2B market and it is focused on promotion of Omez (omeprazole), mainly with continuous commercial actions in pharmacies with very strong KAM line of approximately 50 people. They promote Omez to GP with a team of 20 MR, with small reminder cards, however, in the last Q they promote celebration of 15 years of Omez on the markets with gadgets (cups). MR are not well experienced and not trained. Lanzap (lanzoprazole) is not actively supported by the company, while Seltraz (pantoprazole) is from time to time included in commercial actions in pharmacies together with Omez, very rarely Seltraz samples are given to GP.
Astra Zeneca is the second biggest company on PPI+H2B market. It is the originator of esomeprazole – Nexium. They have a very strong and constant, well experienced team of 100 MR with very good relationships with specialists especially in the south part of country and not so good relationship with GP. They are targeting GE, internists, rheumatologists and pneumologists, GP and pharmacies as well. They use typical originator tools: sponsorships for international events, projects for specialists, frequent events and round tables for specialists and some GP, occasionally also for pharmacies, donations for hospitals. Additionally, they are giving cards to doctors with 20% discount for patients (doctor give the card to patient, patients go with the card in pharmacies and get the products with discount) on continuous basis. Additionally, from time to time, they give 1+1 actions in pharmacies. They regulary organize events, workshops with specialists
Nycomed is the third biggest company on PPI/H2B market. It is the originator of pantoprazole – Controloc. In 2Q 2019 they launched second brand – Pantosal with lower price. Curently, both products are in promotion, in different lines. Controloc (pantoprazole 1) is promoted with well trained and experienced team of around 75 MR, which have good relationships with specialists. Pantosal (pantoprazole 2) is promoted by 50 less experienced MR. Only Controloc is promoted to specialists (GE, internists, rheumatologists) while both are promoted to GP and pharmacies. For Controloc, they use typical originator activities – sponsorships for international events, projects for specialists, round tables mainly for specialists, samples and donations for hospitals. For Pantosal, activities are limited to projects and some round tables. For both products, they give cards with 20 to 35% discount. Nycomed promote also Controloc Control (pantoprazole OTC) by 35 MR of OTC line, however, lately the promotion is limited to promotion to pharmacies and commercial activities without any TV activities and other investments, as the big investments in 2016 did not result in high growth of sales.
Krka is the fourth biggest company on PPI/H2B market. It has focus on two products; Emanera (esomeprazole) and Nolpaza (pantoprazole). Emanera and Nolpaza are well recognized brands on the market. Nolpaza differentiates itself from other generic PPIs by showing high efficacy and good tolerability in the treatment of GERD in the clinical study EXCELLENT. Emanera is different from other PPIs by its patented formulation of capsules containing pellets. The patient can also mix the pellets with water and drink the mixture. Krka's team of MedReps is well trained and motivated. However, there is a big fluctuation. MedReps who are in company for longer period of time have good relationship with gastroenterologists and GPs. MR from 4 lines promote Emanera and Nolpaza to GE, internists, GP, limited cardiologists, pharmacists (for details on line organization please see Chapter 9). Main activities for both products round tables for specialists and GP, events for specialists, continuous medical education for credit points for GP and specialists, SoV actions, limited sponsorships and continuous commercial activities in pharmacies by KAM line (25 people). There are limited activities to doctors for Lanzul (lanzoprazole) from Q2 2020 onwards (one line with 16 MR occasional promotion to GP and gastroenterologists), and it is supported by KAM line with occasional commercial actions.

GSK – Europharm is the fifth's biggest company on PPI/H2B market. It is domestic company with limited own distribution channels and about 25 MR. Omeran (omeprazole) is its main product with regular commercial actions by 50 KAM. In August, they started again low level of promotion at GP with reminders. There are no activities at all for Zantac (ranitidine).
Daiichi Sankio – Therapia; is a domestic company, bought by Ranbaxy and included in group Daiichi Sankio. The company has own distribution channels and is focusing on commercial actions with pharmacies with around 50 KAM. Its main product is Omeprazole, for which they have continuous commercial actions. In June 2018 they started commercial actions for its esomeprazole and have them on limited basis. They promoted esomeprazole to doctors only in the first three months of launch. Levant (lansoprazole) is not promoted at all for the last 2 years and is included from time to time in commercial actions. Pacid (pantoprazole) is very rarely included in commercial actions with pharmacies
Antibiotice – is a domestic company and not very active. Its main product is ranitidine, for which they have no activities, while Novogast (omeprazole) is supported with commercial activities in pharmacies by KAM. It is not known how many KAM they have.
Novartis – only Sandoz is present– Sandoz has a very strong KAM team, around 75 people, focusing on continuous commercial actions with pharmacies. With Ortanol (omeprazole) and Redacib (OTC pantoprazole, launched in 1Q 2020) they are doing just commercial actions, while for its main PPI esomeprazole additionally around 25MR promote it at doctors: GE, internists and GP with limited activities, such as projects and cards with 10% discount for patients.
Sanofi-Aventis – only Zentiva is present. Zentiva has very strong KAM team, around 75 people, focusing on commercial actions with pharmacies**.** Only Helides (esomeprazole) is promoted at doctors with around 50 MR and limited activities – samples. They have regular commercial activities for Helides and from October onwards started limited commercial activities also for Zencopan (pantoprazole). Helicid (omeprazole) is supported by limited and unregular commercial activities, while for their biggest product famitidine they have no activities at all.
Medochemie's only product is ranitidine, which is not supported by any activity.
Gedeon Richter's biggest product is Quamatel (famitidin), which is not supported by any activity. Omeprazol (omeprazole) is not promoted as well. They promote Pantexel (pantoprazole) at GP and some GE and internists with 25 MR and limited activities – projects and some round tables for specialists as well as GP. They have quite good relationship with GP, however, their promotion is focused on cardio portfolio. Additional, their 25 KAM are responsible for commercial activities in pharmacies and have regular commercial actions for Pantexel. Gedeon Richter has also some own pharmacy chains.

9. Position of Krka

Krka is a very well-known pharmaceutical company on Carinthia market. It has been present for many years and has established very solid position in the field of PPIs. Doctors see Krka as a good company with quality products for an affordable price. Nolpaza was launched in January 2019 and Emanera in June 2019.
Four out of five lines promote PPI (see details below). Currently Krka is on the fourth place among the producers of PPI with 10% MSh. There is a 90% cross – coverage among the lines. 25 KAM line (Key account Management) have Nolpaza and Emanera in their targets, this line is responsible for commercial actions with pharmacies. However, also MR promote products in pharmacies.

Table 2: Lines, target groups and priorities in promotion for Emanera (E), Nolpaza (N) and Lanzul (L)

	GREEN (24 MR)	**PINK** (16 MR)	**ORANGE** (20 MR)	**RED** (24 MR)
Target groups of line	GP, GE, internists, cardiologists, pharmacies	GP, GE, internists, psychiatrists, pharmacies	GP, internists, neurologists, psychiatrists, pharmacies	GP, internsits, cardiologists, neurologists, pharmacies
GP	E – 1st	N – 1st , (L-4th	E – 4th	N - 4th
GE	E- 1st; N – 2nd	N – 1st , E – 2nd (L-3rd)		
Internists		N – 1st	E – 4th	N – 4th
Cardiologists				N – 4th
Pharmacies	E – 1st	N – 1st, E – 4th		N – 4th

Case instructions

The objective of this case is to prepare a Country Brand Strategy (CBS) for Krka's PPIs (Emanera, Nolpaza, Lanzul) for the coming year, 2021. We have sales results until 2020 (= year 3). Your goal is to clearly present all key information on a limited number of slides. Which information and how you choose to present it, is up to you. In the template for reporting, you will find some pre-prepared tables and graphs that you can use.

1.1. Analyse the situation on the market of PPI/H2 blockers

1) **[TOGETHER] Select information from the provided excel sheet** (graphs or/and tables) **to present the situation on the market** of PPIs and H2 blockers. If you feel that a certain graph or table is not available, as exception you can design one using the provided pivot table (keep track of the time!).

2) **[TOGETHER]** Prepare **key conclusions** about the market and include key information about local doctrine.
   Key competitors and their main activities *have been defined from the text in the case and information from the excel file.*

3) **[EXERCISE 1]** Based on above data prepare **SWOT analysis** (max 3 main characteristics for each segment) for the Nolpaza and Emanera.

1.2. Prepare strategy for your PPIs

1) **[EXERCISE 2] Define strategic objectives/imperatives** for Nolpaza and Emanera on basis of your SWOT.
   Hint: A strategic imperative contains a verb (=action) and aims to change the current situation from one state to another.It is related to your SWOT and answers questions such as:
   - *for the identified Strengths, what are the conditions necessary for maintaining and amplifying them?*
   - *for the identified Weaknesses, what do you have to do in order to minimise their effects?*
   - *for the identified Opportunities, under what conditions will you be able to leverage them better than the others?*
   - *for the Threats, how will you succeed in preventing their effects?*

2) **[TOGETHER] Evaluate sales plans** for 2021 and comment on predicted growth (see excel sheet). Current prices of PPI in 2020 are not expected to change significantly from government side. Without our interference, Krka's PPI products prices in 2021 will be the same as in 2020. If you feel that the prices of Krka's PPI are not appropriate to reach the best sales results, you can propose changes. Be ambitious in setting your targets, but be also realistic. **Tip:** use the proposed average price to change price and recalculate the plan (see Excel, sheet named "PLANS").
   Define priorities of Emanera, Nolpaza and Lanzul on the market, with regards to the potential of the market and your sales plans.

3) **[TOGETHER]** Based on the situation on the market **define sales objectives** for all three PPI for 2021**.** Look at our current position on the market (e.g. Emanera among esomeprazoles and PPI, Krka among PPI producers) and set short term goal for all 3 products of PPI. Be concrete:
   - which position do we want to have on the market
   - how far or close do we want to be to our main competitor
   - what kind of growth do we expect (fast growth, growing with the market, maintaining sales).

4) **[TOGETHER] Describe pricing situation** (see also excel sheet "real prices") and prepare price positioning for all three PPI for 2021.

5) **[TOGETHER] Define your key target groups by priorities** for all three PPIs

6) **[TOGETHER] Potential users** for our priority products should be defined on basis of the definition in Krka:
   - *Existing on Krka's PPI - already treated with our brand (%)*
   - *New on Krka's PPI (%)*
     - *Not treated – naïve/newly diagnosed or currently not treated (relapsed) (%)*
     - *With changed therapy (%) **AND** define previous therapy (main competitors)*

7) **[TOGETHER]** Define the **positioning** for your priority products (keep in mind the whole portfolio), 1-3 key words connected to each brand and the key message you can use for each product.

1.3. Tactics

1) **[EXERCISE 3] Address strategic imperatives per target group** for Krka's two priority products, Nolpaza and Emanera.

   The activities should be in accordance with the strategy

At the end of today's exercise a possible solution of the CBS will be presented to you and you will see an example of how to summarise the strategy above (sales objective, strategy and tactics) in a strategic statement for each priority product.