

# ESMATAC



# PROTON PUMP INHIBITORS

- The proton pump is the final stage of gastric acid secretion.
- PPIs work by irreversible inhibition of the hydrogen – potassium adenosine tri phosphatase enzyme system ( $H^+/K^+$  - ATPase) or more commonly called ( proton pump ) of gastric parietal cells via **disulfide bond** .

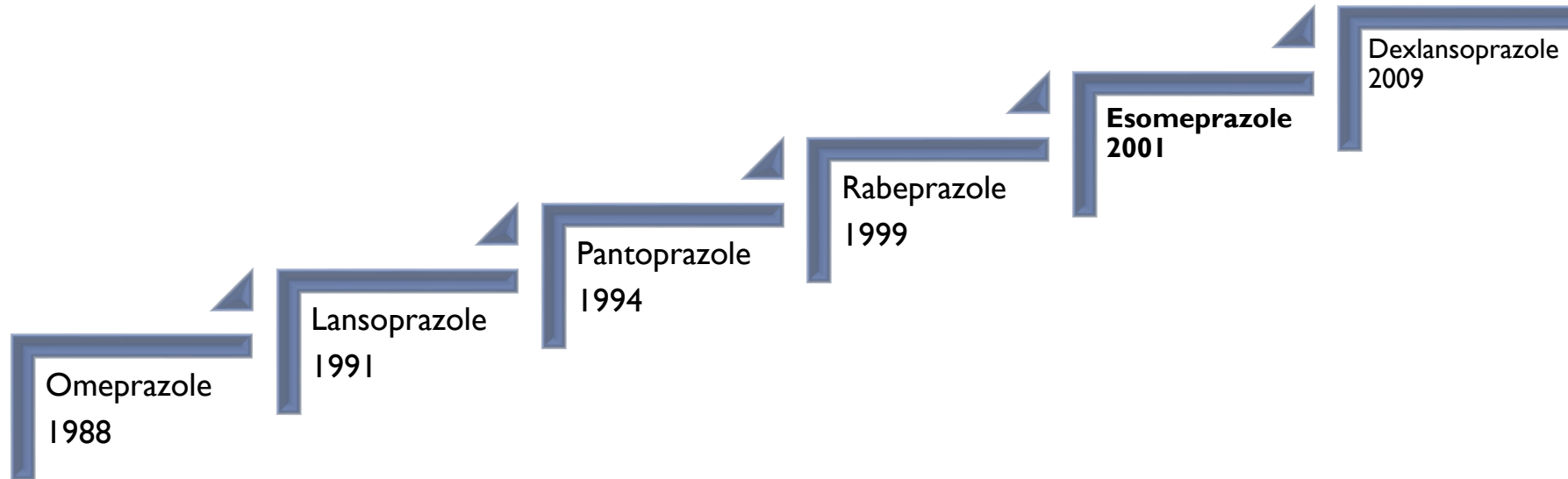
# PROTON PUMP INHIBITORS

- Taken before food, as food increases acid production by parietal cells.
- Given as enteric coated to prevent degradation by acid in stomach and esophagus.
- Max. Response can be accelerated by more frequent doses(bid).

# PROTON PUMP INHIBITORS

- Rapidly absorbed with high plasma protein binding.
- Extensively metabolized by CYP450 in liver, metabolites exc. In urine and feces.
- No dose adjustment in renal or hepatic impairment.
- Used to promote healing of gastric and duodenal ulcers, GERD, ZES.

# PROTON PUMP INHIBITORS



# PROTON PUMP INHIBITORS

Active Ingredient	Trade Name
Pantoprazole	Pantoloc, Controloc, Zurcal.
Omeprazole	Omez, Napizole, Pepzole.
Esomeprazole	Nexium, Esmatac, Nexicure, Esmorap.
Rabeprazole	Pariet, Beptra.
Lansoprazole	Loral, Zollipak.
Dexlansoprazole	Dexilant, Protolans.

The acidic environment activate the proton pump inhibitor, its active form binds irreversibly to the proton pump thus deactivate it.

# PROTON PUMP INHIBITORS

## Omeprazole

- Father molecule & Traditional group
- 2 isomers (S-isomer & R-isomer)
- Lower price range
- Brand: Losec (Astra Zeneca)
- Market Leader: Omez (pharopharma)

# PROTON PUMP INHIBITORS

## Pantoprazole

- 2 isomers (S-isomer & R-isomer)
- Price range is higher than omeprazole
- Brand: Controloc (Takeda)
- Market Leader: Zurcal (AUG)

# PROTON PUMP INHIBITORS

## **Esomeprazole**

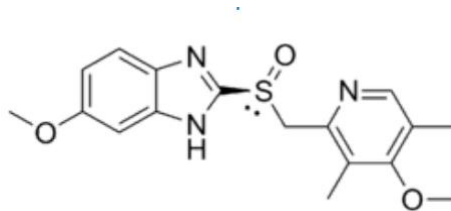
- Single active isomer
- Higher plasma conc.
- Efficacy cover longer time
- Brand: Nexium (Astra Zeneca)
- Market leader: Nexicure (Zeta)

# ESOMEPRAZOLE



# ESOMEPRAZOLE

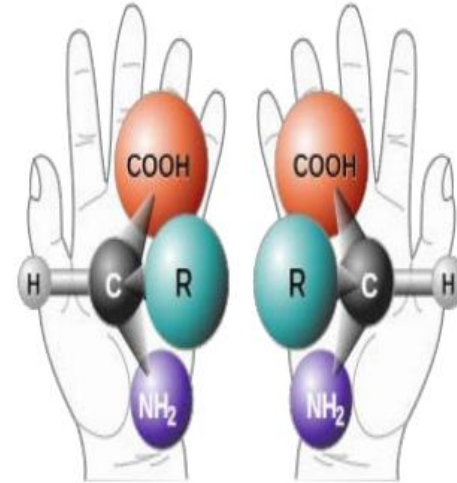
- Esomeprazole is the S-enantiomer of omeprazole “Racemic Mixture”



- Esomeprazole is the first single isomer PPI developed for the treatment of patients with acid-related diseases.

# ESOMEPRAZOLE

- **Stereoisomers** are molecules that :-
  - Have the same molecular formula and sequence of bonded atoms.
  - But differ only in the spatial arrangement of atoms in a molecule.



# ESOMEPRAZOLE

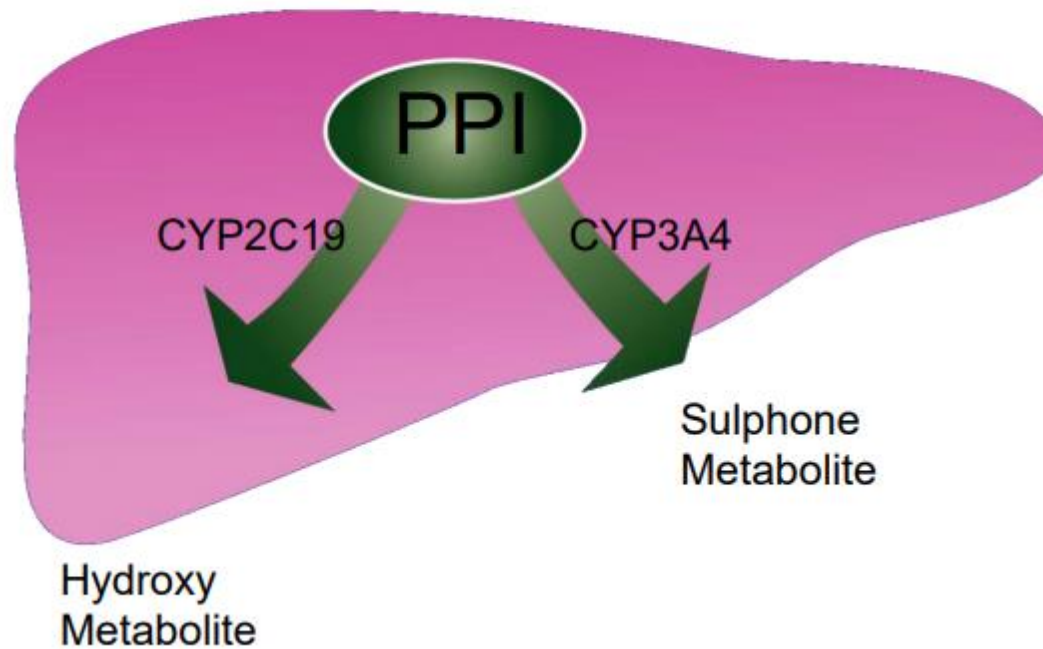
## Stereoisomers

- **A racemic mixture**, is one that has equal amounts of left and right-handed enantiomers of a chiral molecule.



# PPIS METABOLISM

## Hepatic Metabolism of PPIs



# OMEPRAZOLE METABOLISM

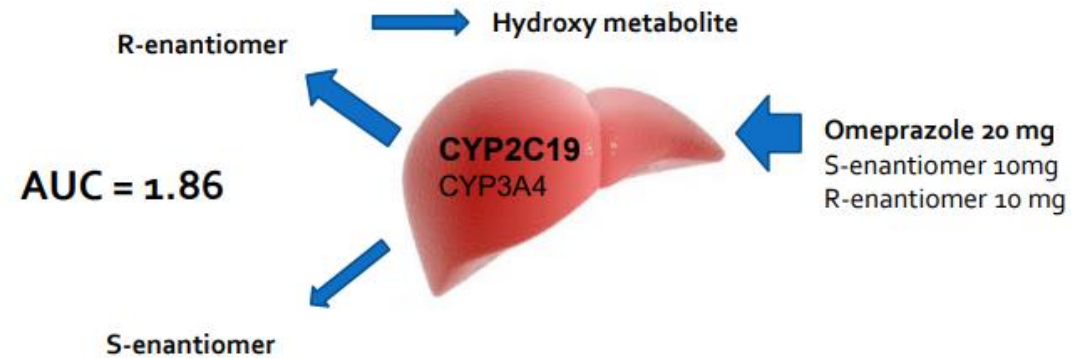
Aliment Pharmacol Ther 2001; 15: 1563–1569.

## *Pharmacokinetics and pharmacodynamics of esomeprazole, the S-isomer of omeprazole*

T. ANDERSSON\*, K. RÖHSS†, E. BREDBERG† & M. HASSAN-ALIN†

\*Clinical Pharmacology, AstraZeneca LP, Wayne, PA, USA; and †Clinical Research & Development, AstraZeneca AB, Mölndal, Sweden

Accepted for publication 6 June 2001



# ESOMEPRAZOLE METABOLISM

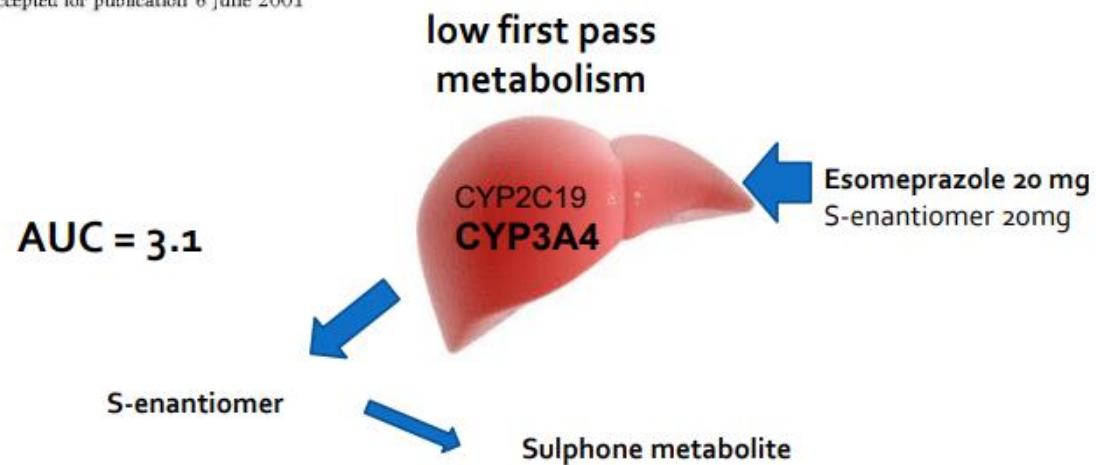
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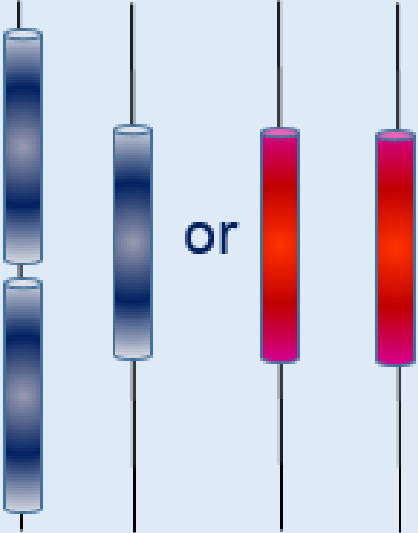
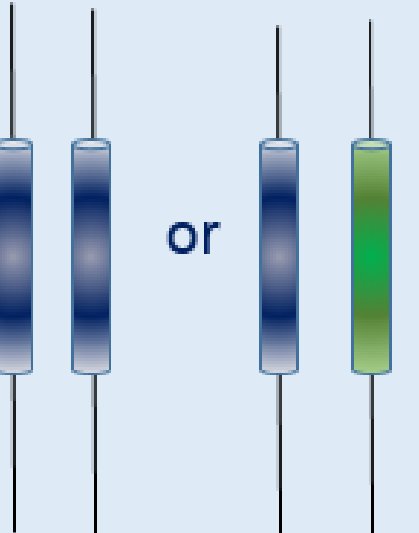
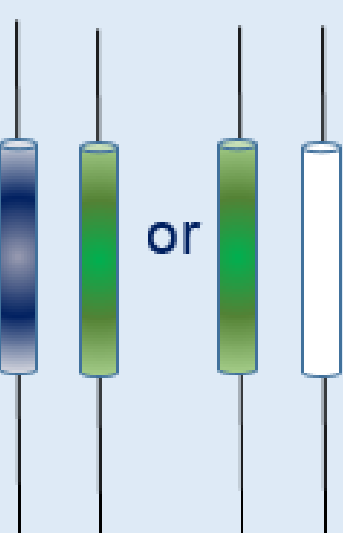
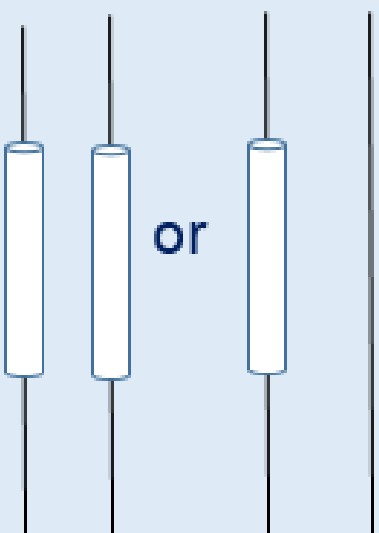




\*Clinical Pharmacology, AstraZeneca LP, Wayne, PA, USA; and †Clinical Research & Development, AstraZeneca AB, Mölndal, Sweden

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## ESOMEPRAZOLE METABOLISM

- Esomeprazole is metabolized more slowly than omeprazole, resulting in a higher (AUC) after administration of the same dose.
- Less first pass metabolism ..... Higher bioavailability .... More effective & long-lasting acid blockage ..... 24 hrs interval.

Genotype				
Phenotype	Ultrarapid Metabolizers	Normal Metabolizers	Intermediate Metabolizers	Poor Metabolizers
				

# CYTOCHROME P450 2C19 POLYMORPHISM

- 3 genotypes: extensive, intermediate and poor metabolizers.
- PPI response rate: 52% of extensive, 57% of intermediate, 61% of poor metabolizers (P=.04)
- 66% of extensive metabolizers more likely to experience refractory symptoms on standard-dose PPIs compared to poor metabolizers.
- Empiric PPI transition to CYP2C19-independent PPI therapy (rabeprazole or esomeprazole) is cost-effective than performing genetic testing.

-El Rouby et al. PPI: from CYP2C19 pharmacogenetics to precision medicine. Expert Opin Drug Metab Toxicol 2018.

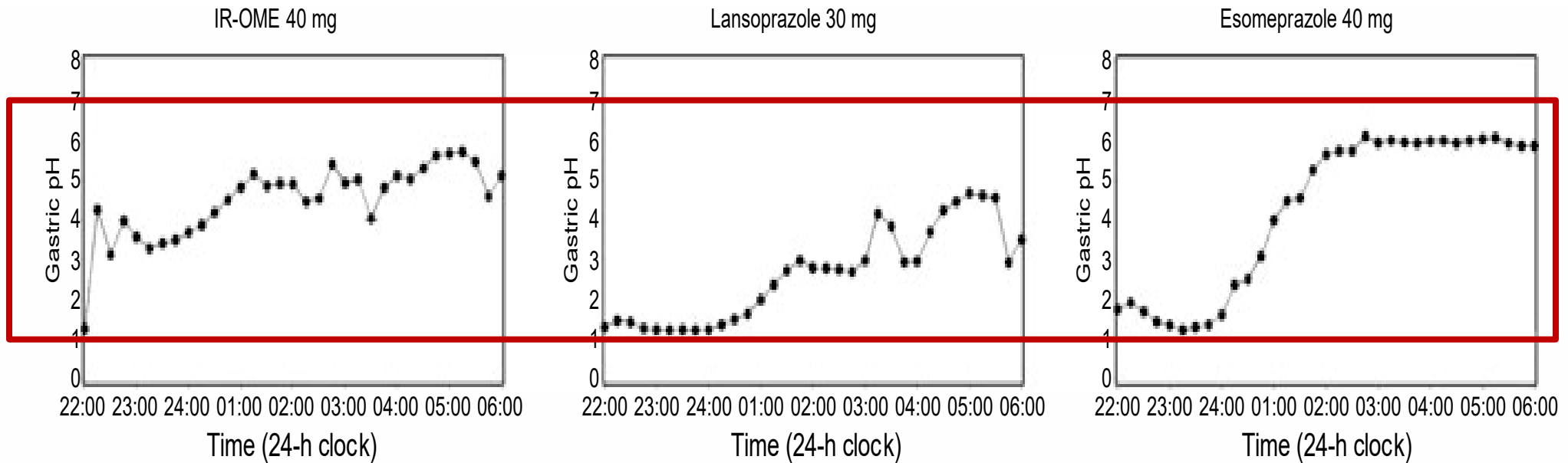


Figure 1. Median gastric pH during the night on day 7. Note: Each point represents the median pH during the 15-min interval.

## Pharmacodynamic Parameters of Proton Pump Inhibitors by Product Labeling

	Esomeprazole		Lansoprazole		Rabeprazole	Pantoprazole	
	40 mg	20 mg	30 mg	15 mg	20 mg	40 mg	20 mg
Time gastric pH > 4 (hours)	16.8	12.7	15.8	11.7	14.4	NA	NA
Percentage of time with gastric pH > 4	70%	53%	66%	49%	60%	NA	NA
Median gastric pH	4.9	4.1	4.9	4.0	3.5	3.8	2.9

NA = not available

Katz et al, ACG Clinical Guideline for the Diagnosis and Management of GERD. Am J Gastroenterol 2021

# ESMATAAC

## (PRODUCT KNOWLEDGE)

### Ingredients:

Esomeprazole magnesium 40 mg / 20mg Capsule

It is the S isomer of omeprazole resulting, in higher plasma levels than Omeprazole lead to better control of intragastric pH.

### Mode Of Action:

Esmatac as esomeprazole is PPI.

blocks the final step in gastric acid production.

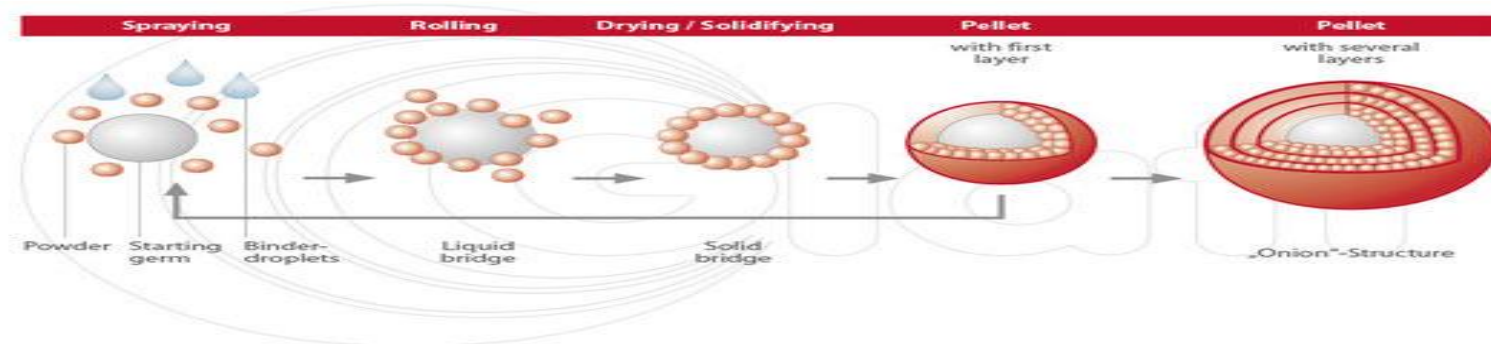
# ESMATAAC

## (PRODUCT KNOWLEDGE)

### Formulation:

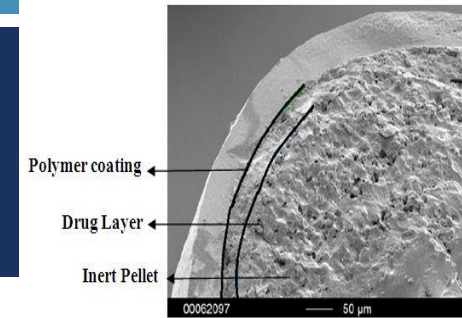
Delayed Release Enteric Coated Pellets.

Multiple – unit pellet system(MUPS)



Resulted in longer duration of effective concentration.

# ESMATAC



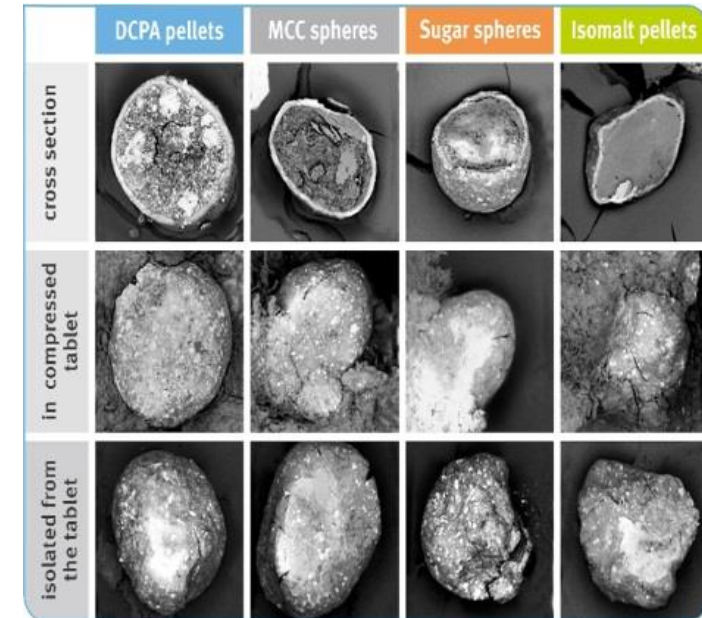
ESMATAC is formulated as delayed release enteric coated pellets of different sizes that gives it 4 main important characteristics:

1. **Gastric resistance** : Enteric coating ensures pellets bypass stomach and release the drug only in the intestine where absorption is optimal.
2. **Enhanced efficacy**: Pellets protects Esomeprazole from degradation by HCl, preserving therapeutic efficacy.
3. **Steady absorption**: the gradual release provides controlled plasma levels, allowing almost 24 Hrs symptoms management.
4. **Reduced side effects** : Pellets prevents premature Esomeprazole release and gastric lining irritation.

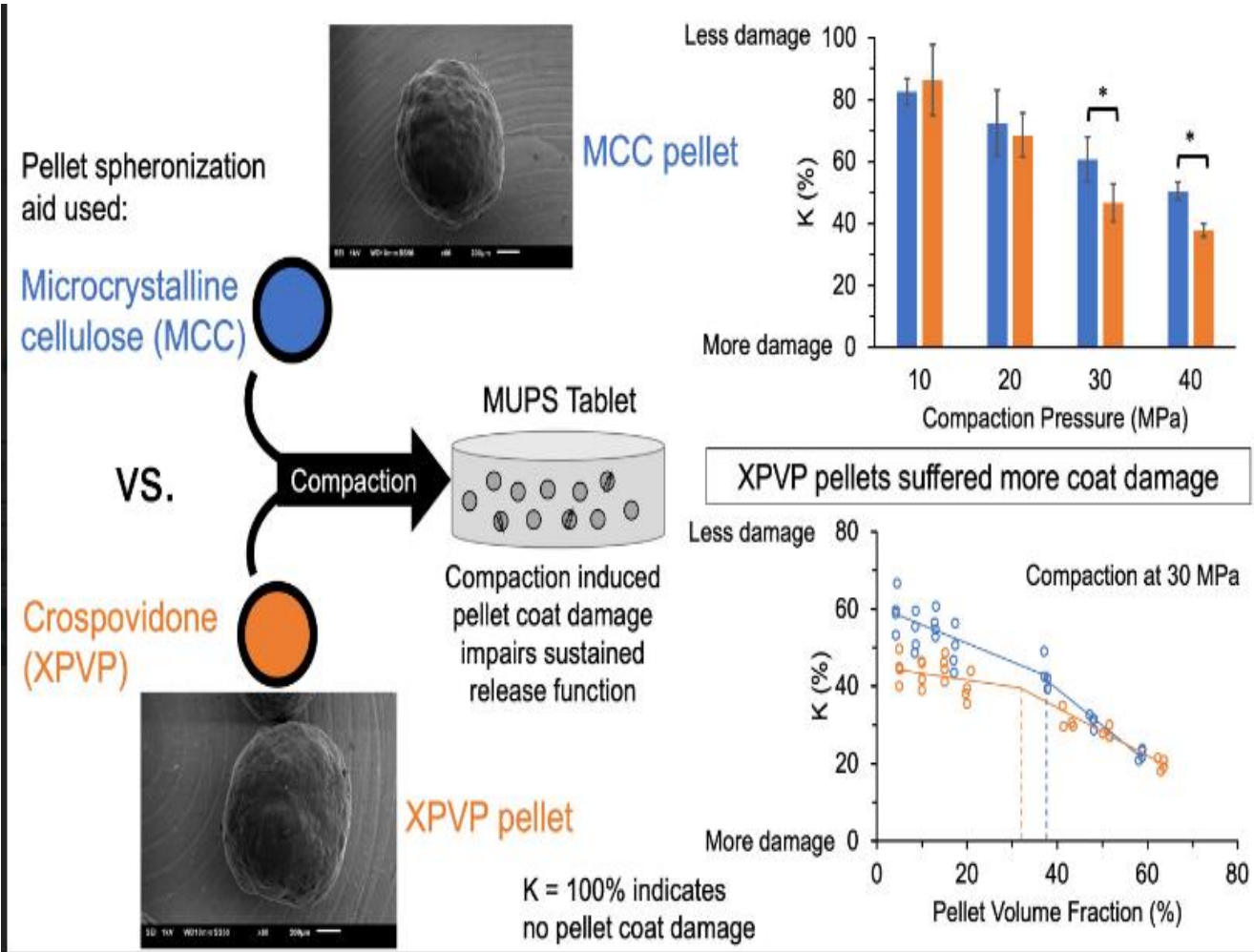
# TABLETED MUPS



- Compression pressure of tableting cause destruction of the polymer layer, which protects the active ingredient.
- No matter the compaction pressure, percentage of (10-20) of pellets is destroyed.
- ESMATAC is delivered in the optimum dosage form that ensures maximum control.



# TABLETED MUPS



# PHARMACOKINETICS

## **Absorption:**

- 90% after single oral dose of 40 mg capsule.

## **Metabolism:**

- Mainly hepatic.

## **Route of elimination:**

- Approximately 80% is excreted in urine and the remaining 20% is excreted in feces.

## **half-life:**

- 1-1.5 hours

# PRECAUTIONS

## **Effect of food:**

- Should be taken at least one hour before a meal.

## **Hepatic insufficiency:**

- No dose adjustment with mild & moderate Liver impairment but in sever case dose must not exceed 20mg.

## **Renal insufficiency:**

- Adjustment of dose is not required.

# PPI COMPLIANCE AND TIMING

- PPI: twice daily, 30-60 minutes before meals.
- Only 46% of patients dosed PPIs at appropriate times.
- 36% of physicians do not give any directions or give inappropriate directions to patients regarding timing of their PPI therapy.
- USA, study reported that 70% of primary care physicians and 20% of gastroenterologists encouraged patients to take their PPI at bedtime or believed timing to be unimportant.

-Van Soest et al. Persistence and adherence to PPI in daily clinical practice. *Aliment Pharmacol Ther.* 2006;24(2):377-385.

# SPECIAL POPULATION

## **Pregnancy:**

Category C

## **Lactating women:**

No study on lactating women so should not used during lactation.

## REBOUND ACID SECRETION

- Many people experience excess acid production when they stop using PPIs.
- It's recommended that you taper off the medication gradually.

# WARNING

## **Chronic treatment with PPI may**

- Decrease the absorption of Calcium
- Decrease absorption of vitamin B12.
- Decrease the absorption of iron.

# DRUG INTERACTION

## Acc.To metabolism:

- Esomeprazole is a competitive inhibitor of the enzyme CYP2C19, and may therefore interact with drugs that depend on it for metabolism, such as diazepam and warfarin;
- The concentrations of these drugs may increase if they are used concomitantly with esomeprazole.
- Conversely, clopidogrel (Plavix) is an inactive prodrug that partially depends on CYP2C19 for conversion to its active form; inhibition of CYP2C19 blocks the activation of clopidogrel, thus reducing its effects.

# DRUG INTERACTION

## **Acc. to acidic pH:**

- Drugs that depend on an acidic pH will be poorly absorbed such as Ketoconazole .
- Whereas drugs that are broken down in acidic pH will be absorbed to a greater extent than normal such as Erythromycin .

## INDICATIONS & DOSAGE

Indication	Dose
<b>GERD &amp; EE</b>	<b>40 MG once daily for 4-8 weeks.</b>
<b>Maintenance of healing of EE</b>	<b>20 mg once daily for 6 months.</b>
<b>H. Pylori eradication</b>	<b>40 mg twice daily for 14 days.</b>
<b>Zollinger – Ellison Syndrome</b>	<b>80 – 160 mg twice daily</b>
<b>Risk reduction of NSAIDs associated gastric ulcer.</b>	<b>20 mg once daily for 6 months.</b>

## ESOMEPRAZOLE AND FDA APPROVAL

- The US Food and Drug Administration approved esomeprazole magnesium for short-term use in children ages 1–11 years for the treatment of gastroesophageal reflux disease (GERD).

Randomized Controlled Trial > J Pediatr Gastroenterol Nutr. 2008 May;46(5):524-33.

doi: 10.1097/MPG.0b013e318176b2cb.

## Safety and tolerability of esomeprazole in children with gastroesophageal reflux disease

Mark A Gilger<sup>1</sup>, [Vasundhara Tolia](#), Yvan Vandenplas, Nader N Youssef, Barry Traxler, Marta Illueca

Affiliations – collapse

### Affiliation

<sup>1</sup> Baylor College of Medicine, Houston, TX, USA. [magilger@bcu.edu](mailto:magilger@bcu.edu)

PMID: 18493207 DOI: [10.1097/MPG.0b013e318176b2cb](https://doi.org/10.1097/MPG.0b013e318176b2cb)

Ref: <https://pubmed.ncbi.nlm.nih.gov/18493207/>



# SAFETY AND TOLERABILITY OF ESOMEPRAZOLE IN CHILDREN WITH GASTROESOPHAGEAL REFLUX DISEASE

## Study objective

- To evaluate safety, tolerability, and symptom improvement with once-daily esomeprazole in children with endoscopically proven gastroesophageal reflux disease (GERD).

## Patients and methods

- In this 8-week, multicenter, randomized, uncontrolled, double-blind study, children ages 1 to 11 years were stratified by weight to receive esomeprazole 5 or 10 mg (children <20 kg) or 10 or 20 mg (children ≥20 kg) once daily.

# SAFETY AND TOLERABILITY OF ESOMEPRAZOLE IN CHILDREN WITH GASTROESOPHAGEAL REFLUX DISEASE

## Study conclusion

- In children ages 1 to 11 years with endoscopically proven GERD, esomeprazole (at daily doses of 5, 10, or 20 mg) was generally well tolerated. The frequency and severity of GERD-related symptoms were significantly reduced during the active treatment period.

# ESOMEPRAZOLE AND FDA APPROVAL

## Dosage and administration:

### 1. Children aged 1-11 years

- Children <20 kg: receive esomeprazole 5 or 10 mg once daily.
- **Children  $\geq$ 20 kg: receive esomeprazole 10 or 20 mg once daily.**

### 2. Children aged 12-17 years

- Receive esomeprazole 20 or 40 mg once daily.

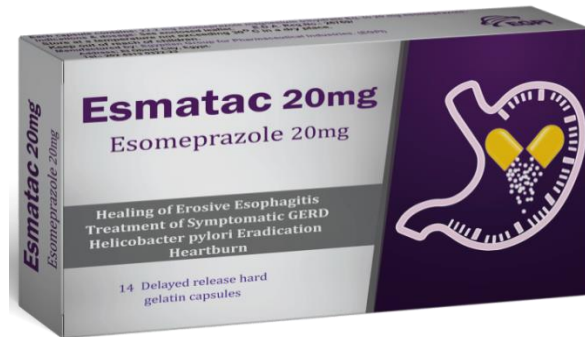
# TARGET CUSTOMERS

Specialty	Indications
PEAD/GP	GERD / Erosive esophagitis

## MESSAGE

- Dear Doctor, We are excited to introduce Esmatac 20 mg Capsules, an FDA-approved treatment for managing acid-related disorders in children aged 1–11 years.
- Esmatac 20mg is indicated for management of GERD symptoms and healing of Erosive esophagitis.
- Esmatac with its advanced enteric-coated pellet technology: Ensures delayed release for optimal acid suppression.
- Dosage: Children  $\geq 20$  kg: receive Esmatac 20 mg once daily for 8 weeks, the capsule to be added to yoghurt or juice.

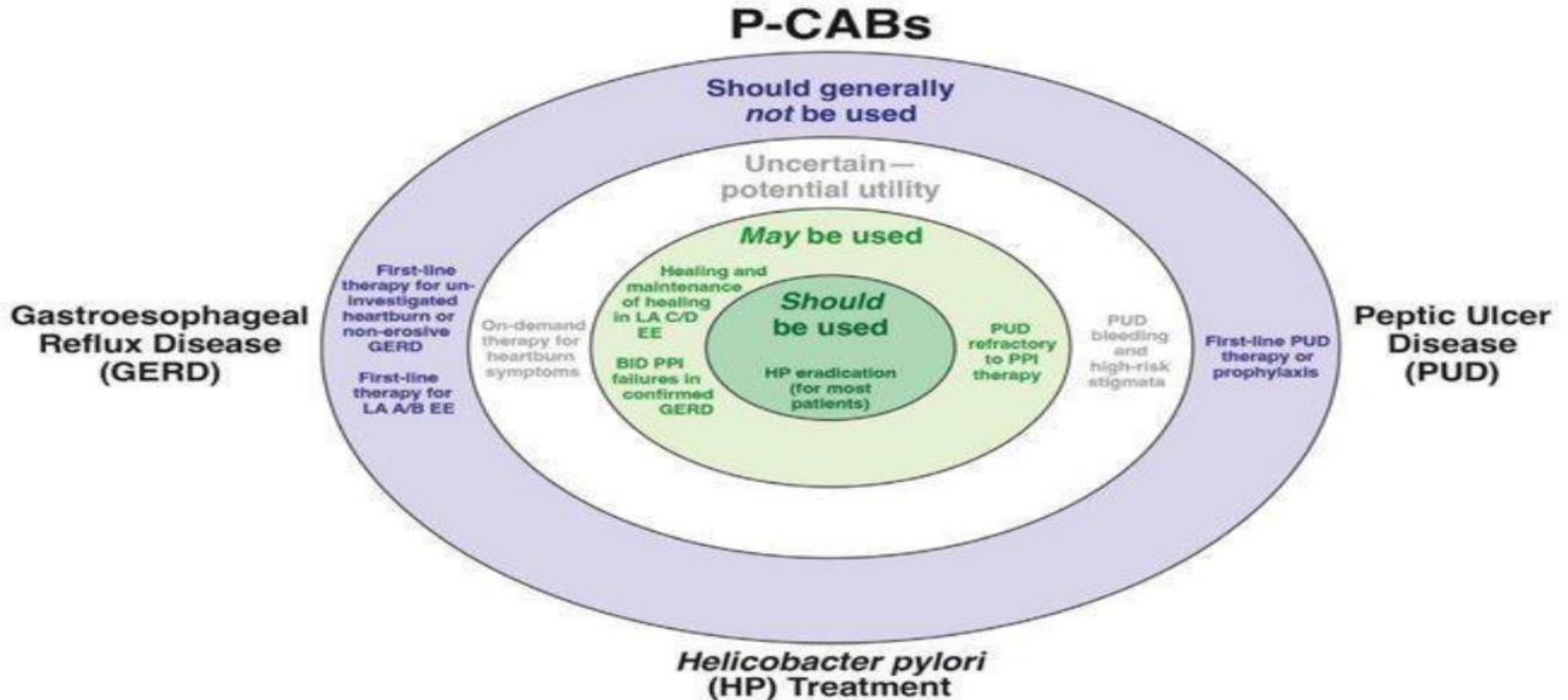
## PACKAGE & PRICE



**Esmatac 20**  
**Two strips**  
**55 L.E**



**Esmatac 40**  
**4 strips**  
**144L.E**

**AGA Clinical Practice Update on Integrating Potassium-Competitive Acid Blockers Into Clinical Practice: Expert Review**Amit Patel,<sup>1,2</sup> Loren Laine,<sup>3,4</sup> Paul Moayyedi,<sup>5</sup> and Justin Wu<sup>6</sup>

## PPIS MARKET MAT 8/2025

<b>138 player</b>	<b>Unit</b>	<b>PPG unit</b>	<b>MS unit</b>
<b>Grand total</b>	<b>104.5M</b>	<b>9%</b>	<b>100%</b>
<b>PANTOPRAZOLE</b>	<b>54.0M</b>	<b>12%</b>	<b>52%</b>
<b>OMEPRAZOLE</b>	<b>23.9M</b>	<b>1%</b>	<b>23%</b>
<b>ESOMEPRAZOLE</b>	<b>15.1M</b>	<b>8%</b>	<b>14%</b>
<b>VONOPRAZAN</b>	<b>7.5M</b>	<b>39%</b>	<b>7%</b>
<b>DEXLANSOPRAZOLE</b>	<b>2.1M</b>	<b>-6%</b>	<b>2%</b>
<b>RABEPRAZOLE</b>	<b>1.6M</b>	<b>-18%</b>	<b>2%</b>
<b>LANSOPRAZOLE</b>	<b>313.2K</b>	<b>-58%</b>	<b>0%</b>

# Market Overview

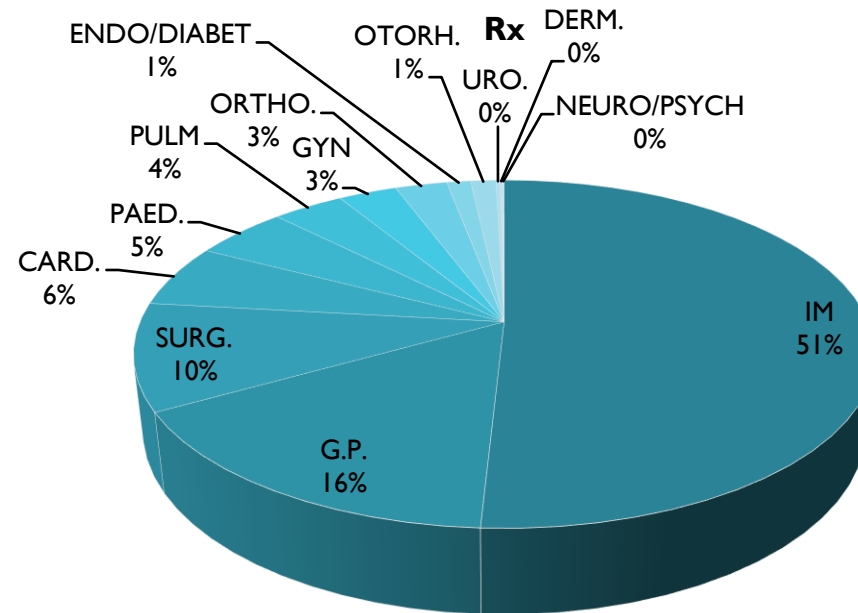
## Key Competitors — Profiles

Products	Unit	PPG unit	Rank unit	MS unit	Pack size	Company	Price
Nexicure	2M	31%	1	26.7%	20 Tab	Zeta pharma	152
Nexium	1.5M	-21%	2	19.1%	28 Tab	Astra	488
Esmorap	860K	-14%	3	11.0%	28 Cap	AUG	276
Ezogast	533K	22%	4	6.8%	28 Cap	Copad	320
FULPRAZAL	437K	35%	5	5.6%	14 Cap	Averroes	168
ESOVAXOLE	376K	3450%	6	4.8%	28 Cap	Biomed	192
EXEEDOGAST	295K	-8%	7	3.8%	20 Cap	Xeedia	168
AIG ESOMEPRAZOLE	237K	40%	8	3.0%	28 Cap	Planet cure	292
Esmatac	235K	8%	9	3.0%	28 Cap	EGPI	144

## PRICES OF MAIN COMPETITORS ESOMEPRAZOLE 40MG

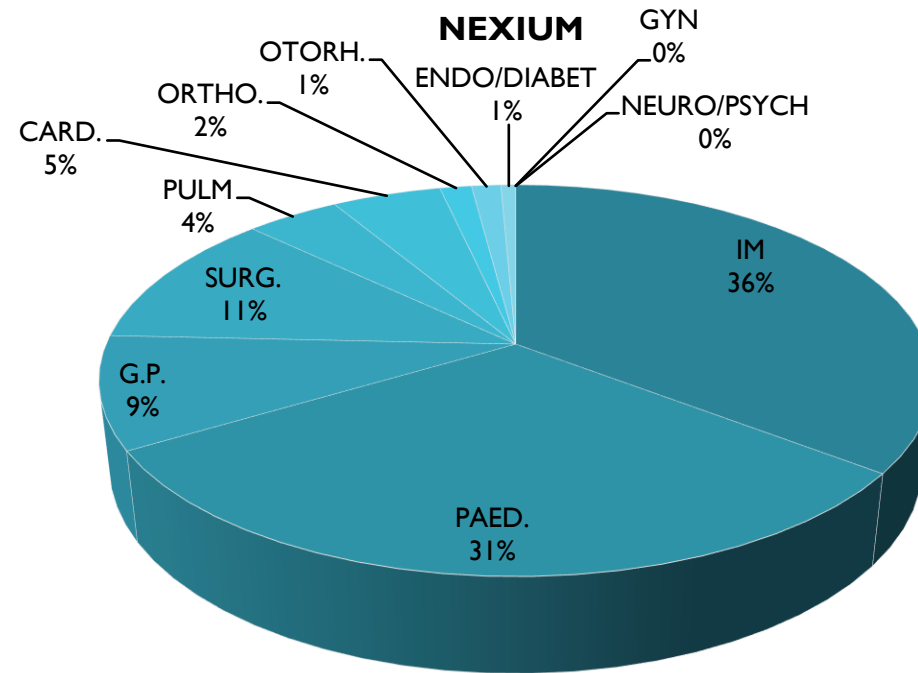
Product Name	Company	Pack	Price	Cost per tab-Cap
Nexium	AstraZeneca	28 tab	488	17,4
Ezogast	Copad	14 Cap	160	11,4
AIG Esomeprazole	Planet cure	28 cap	292	10,43
Esmorap	AUG Pharma	28 cap	276	9,85
Exeedogast	xeedia	20 Cap	168	8,4
Fulprazal	Averroes	14 Cap	118	8,4
Neximash	Mash Premiere	28 cap	220	7,85
Nexicure	Zeta Pharma	20 tab	152	7,6
Ardiximag	Acino	14 Tab	106	7,5
Esovoxole	Biomed	28 Cap	192	6,85
Esmatac	EGPI	28 cap	144	5,1

# RX ANALYSIS TOTAL PPI MARKET



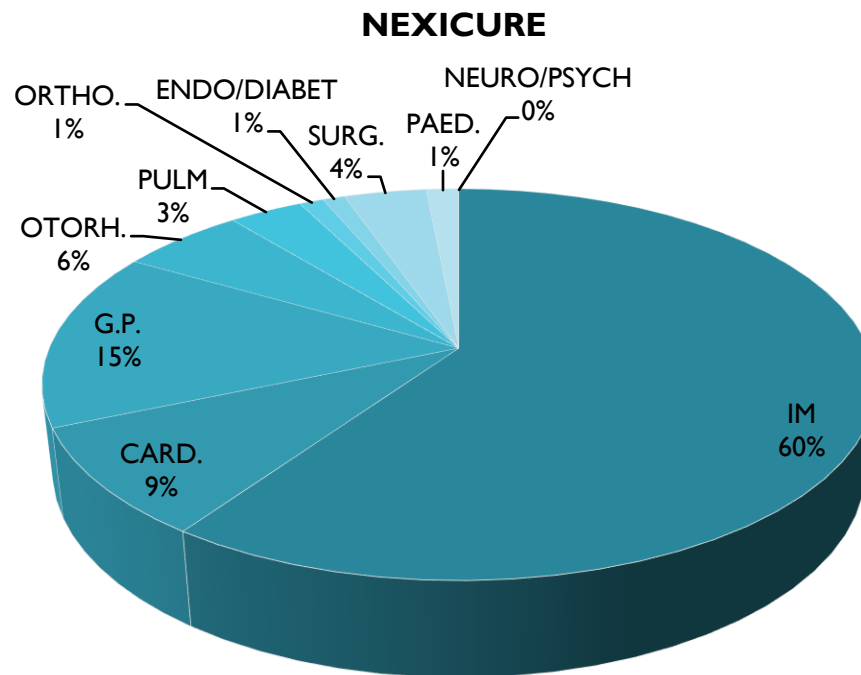
- Total number of Rx is 5.3M.
- IM & GP are occupying 67% of total prescribed PPIs.
- Data is for all dosage forms including vials and sachets, so it could be misleading regarding SG & PEAD.

# RX ANALYSIS TOTAL PPI MARKET



Total number 628 K Rx

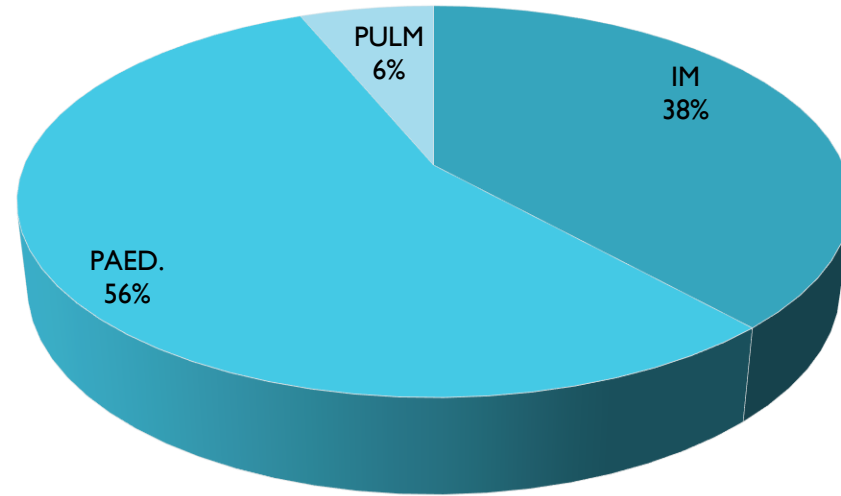
# RX ANALYSIS TOTAL PPI MARKET



Total number 189 K Rx

# RX ANALYSIS JUNE 2024 TOTAL PPI MARKET

## ESMATAAC



Total number 11 K Rx

## Target customers

Specialty	Indication 1	Indication 2	Indication 3
IM / GIT	EE / GERD	H. PYLORI	HEARTBURN
GP	HEARTBURN	H. PYLORI	EE / GERD
PULM	GERD		
ORTHO	PROPHYLAXIS	GERD	
SG	PROPHYLAXIS	GERD	
PH	HEARTBURN	GERD	

## ESMATAC CORE MESSAGE

Esmatac provides engineered relief for patients suffering from hyperacidity disorders by combining the superior acid control of esomeprazole with advanced MUPS technology. This ensures consistent drug absorption to cover 24hrs and improved patient adherence compared to conventional enteric-coated PPIs.



**Engineered Relief**

# Esmatac

Esomeprazole 20, 40 mg Capsule

(Delayed release enteric coated pellets)

## Engineered Relief

**Esmatac** capsules are made according to the same FDA standards as the original approved Esomeprazole, ensuring high quality and effectiveness.<sup>(1)</sup>



### Bioequivalence Study:

Showed that **Esmatac** and reference product deliver equivalent amount of Esomeprazole to the systemic circulation.



(1) FDA, Drug Approval Package, Application No.: 21-153 & 21-154, Approval Date: 2/20/2001

# Esmatac

Esomeprazole 20, 40 mg Capsule

(Delayed release enteric coated pellets)

## Engineered Relief

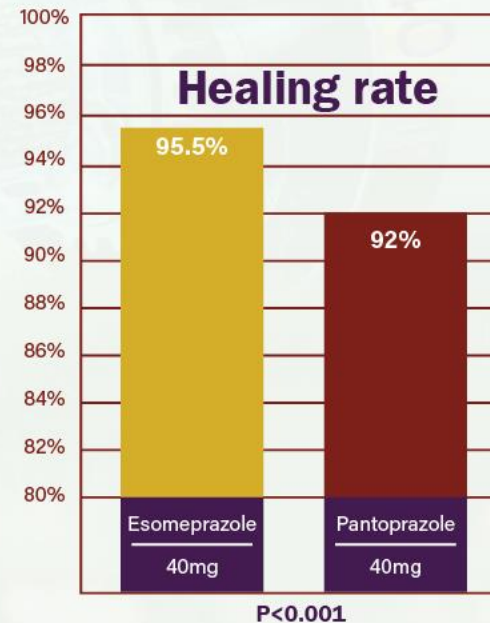
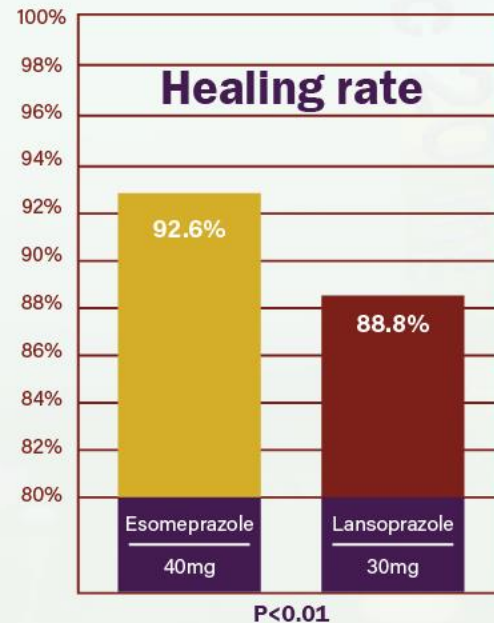
### Esmatac

Esomeprazole 40 mg

Has higher rate of healing in **Reflux Esophagitis (RE)** management (4-8 weeks) than other PPIs (Lansoprazole & Pantoprazole).



Data from six studies<sup>(2)</sup>



(2) Int J Clin Pract, 69 (7), 796-801 Jul 2015

# Esmatac

Esomeprazole 20, 40 mg Capsule

(Delayed release enteric coated pellets)

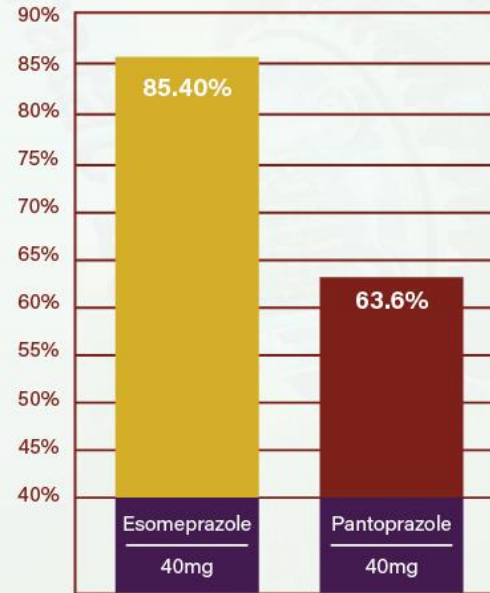
## Engineered Relief

### Esmatac

Esomeprazole 40 mg

Has better control of **nocturnal acidity** than Pantoprazole.<sup>(3)</sup>

The proportion of night time with intragastric pH > 4



(p=0.0002)

Thirty subjects were analysed, In a randomized, single-blinded trail for 5 days.

(3) Aliment Pharmacol Ther, 21 (8), 963-7 2005 Apr 15

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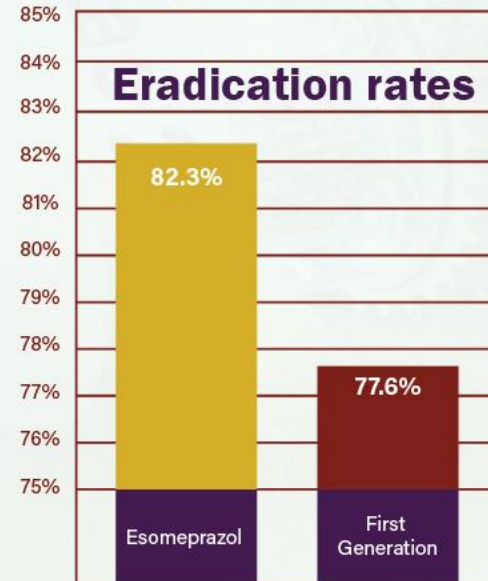
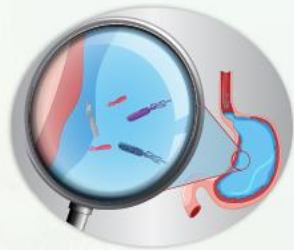
## Engineered Relief

### Esmatac

Esomeprazole 40 mg

Has higher **eradication rate** than first generation PPIs (Omeprazole-Lansoprazole-Pantoprazole) in the treatment of **Helicobacter pylori**.<sup>(4)</sup>

The meta-analysis (35 studies, 5998 patients)



Showed higher eradication rates for esomeprazole than for first-generation PPIs.

(4) Aliment Pharmacol Ther 2012; 36: 414-425 421<sup>a</sup> 2012 Blackwell Publishing Ltd

# Esmatac

Esomeprazole 20, 40 mg Capsule

(Delayed release enteric coated pellets)

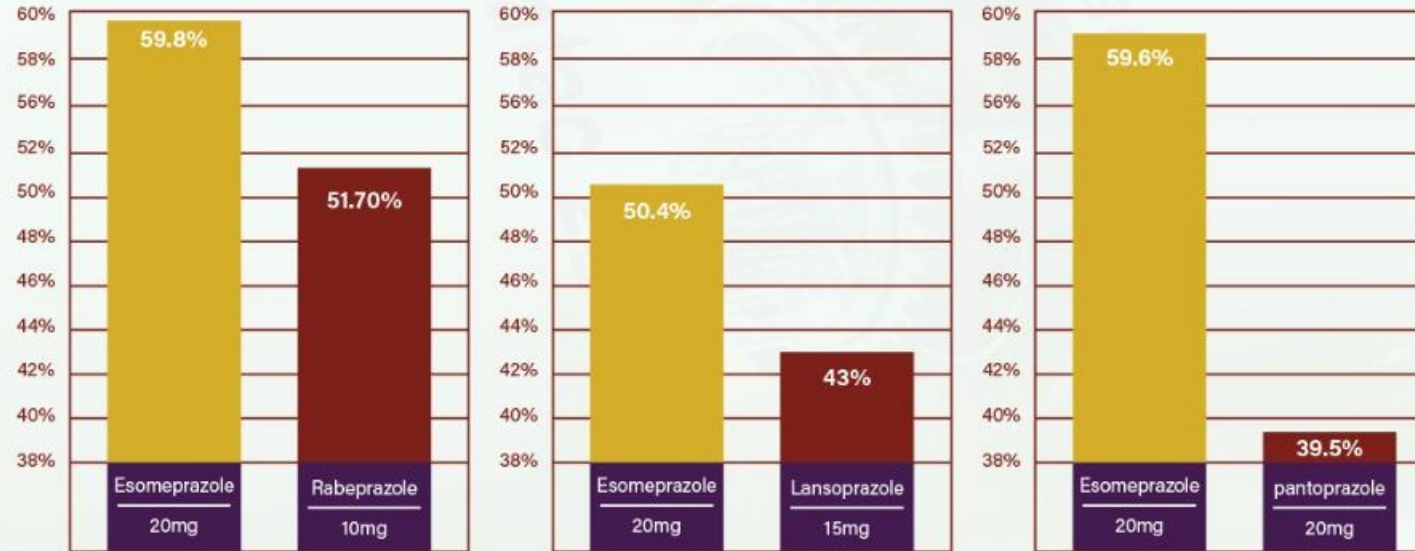
**Esmatac**

Esomeprazole 20 mg

**Engineered  
Relief**

As maintenance dose provided greater acid control than other PPIs.<sup>(5)</sup>

The main % of time with intragastric pH>4 on day 5



In a total of 108 Helicobacter pylori-negative healthy subjects, three standardised, randomized studies.

(5) Clin Drug Investig. 24 (1), 1-7 2004

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**Thank you**