

Surrey Heartlands Integrated Care System Area Prescribing Committee (APC)

Appendix 1: PPI cost and place in therapy

PPI	Formulation	Pack Size	Cost per 28 days	Traffic light classification	Patients with no swallowing difficulties	Patients with swallowing difficulties	Patients with enteral feeding tubes	Place in Therapy	Comments
Lansoprazole	15mg gastro-resistant capsules	28	£0.84	Green	Yes	Yes (see comments)	Yes (see comments)	1st line	Some capsules are licensed to be opened and have their contents mixed with water, apple/tomato juice, or sprinkled on soft food (e.g. yogurt, apple puree) to help people with swallowing difficulties. Some brands are licensed for enteral feeding tubes 14F or larger (check SPC)
Omeprazole	20mg gastro-resistant capsules	28	£0.84	Green	Yes	Yes (see comments)	Non-formulary	1st line	Most capsules can be opened, and granules dispersed in water (check individual SPC)
Omeprazole	10mg gastro-resistant capsules	28	£0.85	Green	Yes	Yes (see comments)	Non-formulary	1st line	Most capsules can be opened, and granules dispersed in water (check individual SPC)
Lansoprazole	30mg gastro-resistant capsules	28	£1.07	Green	Yes	Yes (see comments)	Yes (see comments)	1 st line	Some capsules are licensed to be opened and have their contents mixed with water, apple/tomato juice, or sprinkled on soft food (e.g. Yogurt, apple puree) to help people with swallowing difficulties. Some brands are licensed for enteral feeding tubes 14F or larger (check SPC)
Pantoprazole	20mg gastro-resistant tablets	28	£1.07	Green	Yes	Non-formulary	Non-formulary	2 nd line	Suitable for patients that cannot have animal-derived products
Pantoprazole	40mg gastro-resistant tablets	28	£1.11	Green	Yes	Non-formulary	Non-formulary	2 nd line	Suitable for patients that cannot have animal-derived products
Rabeprazole	10mg gastro-resistant tablets	28	£1.26	Green	Yes	Non-formulary	Non-formulary	2 nd line	Crushing is not recommended as stomach acid can destroy the active drug. Suitable for patients that cannot have animal-derived products.
Rabeprazole	20mg gastro-resistant tablets	28	£1.49	Green	Yes	Non-formulary	Non-formulary	2 nd line	Crushing is not recommended as stomach acid can destroy the active drug. Suitable for patients that cannot have animal-derived products.
Esomeprazole	20mg gastro-resistant capsules	28	£1.77	Green	Yes	Yes (see comments)	Yes (see comments)	3 rd line	Most (but not all) brands of esomeprazole tablets, capsules and granules for oral suspension are licensed for administration via gastric tubes. They will disperse in water for administration. For patients with fine-bore enteral tubes, consider switching to lansoprazole Fastabs®, which have smaller micro-granules.
Esomeprazole	40mg gastro-resistant capsules	28	£2.07	Green	Yes	Yes (see comments)	Yes (see comments)	3 rd line	Most (but not all) brands of esomeprazole tablets, capsules and granules for oral suspension are licensed for administration via gastric tubes. They will disperse in water for administration. For patients with fine-bore enteral tubes, consider switching to lansoprazole Fastabs®, which have smaller micro-granules.
Omeprazole	40mg gastro-resistant capsules	7	£2.60	Green	Yes	Yes (see comments)	Non-formulary	1st Line	Most capsules can be opened, and granules dispersed in water (check individual SPC)
Lansoprazole	15mg orodispersible tablets	28	£3.55	Green (R)	Non-formulary	Yes (see comments)	Yes (see comments)	1st line for restrictions	Restricted for use in adults with swallowing difficulties/cannot swallow tablets. Licensed for administration via nasogastric feeding tubes.
Esomeprazole	20mg gastro-resistant tablets	28	£4.75	Not for new initiation	Not for new initiation	Not for new initiation	Not for new initiation	Consider Switching to suitable alternative	
Esomeprazole	40mg gastro-resistant tablets	28	£4.77	Not for new initiation	Not for new initiation	Not for new initiation	Not for new initiation	Consider Switching to suitable alternative	

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Lansoprazole	30mg orodispersible tablets	28	£5.77	Green (R)	Non-formulary	Yes (see comments)	Yes (see comments)	1st line for restrictions	Restricted for use in adults with swallowing difficulties/cannot swallow tablets. licensed for administration via nasogastric feeding tubes.
Omeprazole	20mg gastro-resistant tablets	28	£6.80	Non-formulary	Non-formulary	Non-formulary	Non-formulary	Switch to suitable alternative	
Omeprazole	10mg gastro-resistant tablets	28	£8.48	Non-formulary	Non-formulary	Non-formulary	Non-formulary	Switch to suitable alternative	
Omeprazole	10mg dispersible gastro-resistant tablets	28	£9.30	Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary	Switch to suitable alternative	
Omeprazole	20mg dispersible gastro-resistant tablets	28	£13.92	Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary (see comments)	Switch to suitable alternative	Licensed for enteral feeding tubes however the granules in lansoprazole orodispersible tablets are smaller and therefore more appropriate to be used in enteral feeding tubes
Lansoprazole	30mg/5ml oral suspension	100ml	£17.01	Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary	Switch to suitable alternative	
Esomeprazole	10mg gastro-resistant granules sachets	28	£25.19	Green (R)	Non-formulary	Yes	Yes	3 rd line	Only for patients with dysphagia or enteral feeding tubes (6F or larger) when opening capsules is not clinically appropriate
Omeprazole	40mg gastro-resistant tablets	7	£27.2	Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary	Switch to suitable alternative	
Omeprazole	40mg dispersible gastro-resistant tablets	7	£27.92	Non-formulary	Non-formulary	Non-formulary	Non-formulary	Switch to suitable alternative	
Lansoprazole	15mg/5ml oral solution	100ml	£93.35	Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary	Switch to suitable alternative	
Lansoprazole	30mg/5ml oral solution	100ml	£123.05	Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary	Switch to suitable alternative	
Omeprazole	10mg/5ml SF Powder for Oral suspension	75ml	£212.92	Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary	Switch to suitable alternative	
Omeprazole	20mg/5ml SF Powder for Oral suspension	75ml	£412.00	Non-Formulary	Non-Formulary	Non-Formulary	Non-Formulary	Switch to suitable alternative	

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Branded PPI's	Zoton, Losec, Pariet, Nexium, Protium all formulations, all strengths			Non-Formulary Non-Formulary Non-Formulary Non-Formulary				Switch to suitable alternative	
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All licensed PPI's (with the exception of omeprazole oral powder for solution and other unlicensed PPI solutions) are equal in terms of clinical efficacy. The formulary recommendations are based primarily on cost. Where indicated for the purpose of administration through enteral feeding tubes, the size of the enteric coated granules in the formulation are also considered. The omeprazole powder for oral solution (and all other unlicensed PPI solutions) have not been selected as they have been demonstrated to be clinically inferior.

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Appendix 2: Summary of preferred PPI formulation for different patient requirements

Summary

- For people with no swallowing difficulties:
 - 1st Line: Lansoprazole capsules/Omeprazole capsules
 - 2nd line: Pantoprazole tablets (Suitable for patients that cannot have animal-derived products)
 - 2nd line: Rabeprazole tablets (Suitable for patients that cannot have animal-derived products)
 - 3rd line: Esomeprazole capsules – not for new initiation
- For patients who cannot swallow tablets/have swallowing difficulties:
 - 1st Line: lansoprazole orodispersible tablets
 - 2nd line: lansoprazole capsules/omeprazole capsules (opened, and granules dispersed in water/yoghurt/apple puree)
 - 3rd line: esomeprazole granule sachets
- For patients with enteral feeding tubes:
 - 1st line: lansoprazole orodispersible tablets
 - 2nd line: lansoprazole capsules
 - 3rd line: esomeprazole granule sachets

All other formulations are non-formulary for adults. See table for priority switching

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Appendix 3: Similarity between different drugs in class(2)

Table 2

Pharmacokinetic Properties of Proton Pump Inhibitors

	Omeprazole	Esomeprazole	Lansoprazole	Dexlansoprazole	Pantoprazole	Rabeprazole
Bioavailability, %	30-40	64-90	80-85	-	77	52
Time to peak plasma level (tmax, hr)	0.5-3.5	1.5	1.7	1-2, 4-5	2-3	2-5
Protein binding, %	95	97	97	96	98	96.3
Half-life, hr	0.5-1	1-1.5	1.6	1-2	1-1.9	1-2
Primary excretion	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic
Liver metabolism	CYP2C19	CYP2C19	CYP2C19	CYP2C19 CYP3A4	CYP2C19 CYP3A4	CYP2C19

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Appendix 4: Written communication from MHRA

From:

Hi there,

Application for an established medicine currently without traffic light classification

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I have long had an interest in the pharmaceuticals and pharmacology of Omeprazole oral suspension/ solution, and was surprised that this product has received a license, even though I accept that the unlicensed preparation was in use in significant quantities:

<https://www.medicines.org.uk/emc/product/11031/smpc>

Omeprazole is very acid labile and, the unlicensed solutions, there was more than 50% of the active ingredient lost to acid degradation before absorption (Northern Neonatal Formulary 2013 and earlier <https://www.wiley.com/en-gb/Neonatal+Formulary%3A+Drug+Use+in+Pregnancy+and+the+First+Year+of+Life%2C+7th+Edition-p-9781118819517>), and this despite giving neonates a significant dose of bicarbonate, sodium and potassium.

If the same theory is applied to adults, the amount of proportional buffer to the omeprazole by suspending it in an alkali, it is highly likely that the buffer solution will be diluted out in the much larger volume of stomach acid and therefore be even less bioavailable. It is also true that in this population the 'dose' of alkali, sodium and potassium is less clinically significant.

I am writing to you to enquire whether the manufacturers submitted any evidence for bioavailability specific to this formulation? I am in the process of writing a paper for the Area Prescribing Committee.

I have contacted Rosemont in June 2020 who informed me that the only information they have is that in the SPC. I have read the SPC very carefully and the evidence seems to be extrapolated as a 'me too' submission even though pharmaceutically it is such a different product.

I would be very grateful if I could be informed whether there was any additional basis for granting the license. If not, may I suggest that this is looked at again? There are two licensed products that should be used in preference – lansoprazole capsules which are licensed to be opened, and esomeprazole granules. These include enterically coated granules that protect the contents from the stomach acid.

Best regards.....

From: MHRA Customer Services <MHRACustomerServices@mhra.gov.uk>

Dear

Apologies for the delay in reply. We have reviewed your request and can provide the following information below. The approval of Omeprazole of 2 mg/ml Oral Suspension by the EU concerned member states (CMSs) was based on the assessment of the application by the reference member state (RMS), in this case, the Netherlands. As described in the public assessment report (PAR), the weakness of the supportive paediatric clinical study data in children under one year old was recognised by the RMS, that it was largely due the small number subjects investigated. This was acknowledged by the CMSs. However, in addition to the submitted study data, the decision by the member states to finally approve was in addition based on account of the experience with the innovator product. The applicant had demonstrated that the pharmacokinetic profile of the generic product is similar to the pharmacokinetic, pharmacodynamic, efficacy and safety profile of the reference product. In particular, the pharmacokinetic and pharmacodynamic data for young infants (<1 year) were supportive for omeprazole dosing recommendation of a milligram-per-kilogram weight basis in these patients.

Kind regards,

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Customer Service Centre

Medicines and Healthcare products Regulatory Agency

10 South Colonnade, Canary Wharf, London E14 4PU

info@mhra.gov.uk

Application for an established medicine currently without traffic light classification