



Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY

**MEDICINES RECOMMENDED FOR MINOR INCLUSION IN THE PHILIPPINE
NATIONAL FORMULARY (PNF)**

The Health Technology Assessment Council (HTAC) has already finished the assessment and initial deliberation on applications for minor inclusion (i.e., additional strength, immediate packaging, net content) of health technologies currently listed in the PNF. The HTAC hereby issues the following preliminary recommendation for following drugs:

Drug	Preliminary HTAC Recommendation
0.1% Sodium Hyaluronate (15mL)	<p>Recommended for coverage and inclusion in the PNF</p> <p>HTAC noted that the 5 mL package size of Sodium Hyaluronate 0.1% (Annex A) is already included in the Philippine National Formulary. Considering that the request is for the 15 mL package size of Sodium Hyaluronate 0.1%, there is no question to its efficacy as this is merely a higher volume of the same product. For the 15 mL package size, preservative efficacy is good until 28 days to control microbial contamination during patient use. Physico-chemical stability is good until 90 days from opening the container.</p> <p>The 15 mL package at Php 325.00/bottle is cheaper than the currently listed 5 mL package at Php 339.00/bottle, volume per volume.</p>
2.5% Peritoneal Dialysis Solution (2L and 5L)	<p>Recommended for coverage and inclusion in the PNF</p> <p>The use of 2.5% Peritoneal Dialysis (PD) Solution (Annex B) allows better ultrafiltration without exposing the patient to a higher glucose load as in the case of using 4.25% PD Solution. Also, 2.5% PD Solution is chemically equivalent with the currently-listed preparation 2.3% PD Solution. It was noted that 2.5% PD Solution was previously listed in 2006 PNDF, Volume II, 3rd Edition and delisted not for safety concerns, but due to the manufacturer's commercial exit in the Philippines.</p> <p>The costing analysis showed that it is cheaper in terms of the total cost per year per patient compared to 2.3% PD solution with a price difference on the total cost per year per patient of Php 820.00 for the 2L-preparation and Php 146,149.34 for 5L-preparation.</p> <p>The cost per dosage unit for 2L is Php 190.00 and Php 481.57 for 5L of 2.5% PD Solution.</p>

The HTAC hereby makes public the **preliminary recommendation** attached in the Summary of Evidence with supporting studies informing their recommendation.

All comments, inputs and/or appeals may be submitted until **09 March 2021** for the consideration of the HTAC through email at hta@doh.gov.ph. Kindly note that appeals will no longer be entertained after the prescribed deadline.

A handwritten signature in black ink, appearing to read 'A. Guerrero', is positioned above the printed name.

ANNA MELISSA S. GUERRERO, MD, MPH (HTA)
Head
Health Technology Assessment Unit

Annex A. Summary of Evidence of 0.1% Sodium Hyaluronate (15ml)

Section 1. General Information on the Proponent and the Proposed Inclusion

PROPONENT/S	Asian Eyes Optical Incorporated
GENERIC NAME	Sodium Hyaluronate 0.1%
BRAND NAME (if any)	Avizor Lacrifresh Moisture
THERAPEUTIC CLASSIFICATION	Ophthalmic Solution
FOR LISTED MEDICINES:	
· Current Dosage Strength	0.1% (1mg/mL)
· Proposed Dosage Strength	0.1% (1mg/mL)
· Current Immediate Packaging	5 ml per bottle
· Proposed Immediate Packaging	15 ml per bottle
MANUFACTURER	Avizor S.A. (Spain)
IMPORTER/TRADER	Asian Eyes Optical Incorporated
DISTRIBUTOR	Asian Eyes Optical Incorporated

Section 2. Summary of Evidence Reviewed

The new immediate packaging of the medicine:	Remarks/Evidence
1. Has good quality	<p>0.1% Sodium Hyaluronate (Lacrifresh) has a valid Certificate of Product Registration with the Philippine FDA, assuring the public of its quality.</p> <p>Further, study on the shelf-life demonstrates product stability with stable physicochemical properties up to 90 days</p>
2. Has proven safety based on sound evidence	<p>Certificate of Good Manufacturing Process (cGMP) (the ISO certification of Avizor in Spain authenticated by Philippine Consulate of Madrid) was submitted as equivalent of FDA cGMP</p> <p>Preservation of product sterility was shown based on study of shelf-life antimicrobial preservative simulation use.</p>
3. Has proven efficacy for the stated indication based on sound evidence	<p>Given that the same dosage strength is already listed in the PNF, same efficacy was noted.</p> <p>Further, a letter from the President of Philippine Cornea Society supports the minor inclusion of 15 mL preparation of Sodium Hyaluronate 0.1% eye drops in the PNF as an effective and economical ocular lubricant.</p>
4. Has favorable cost-effectiveness analysis	<p>The total cost per treatment course of three months per patient for using the 15 mL-preparation (Php 1,169.96) is lower than the total cost per year per patient of the currently-listed 5 mL-preparation (Php 3,661.2) with a price difference of PhP 2, 491.24. Please refer to the costing table below.</p>

Section 3. Costing Table

PARAMETER	PROPOSED INCLUSION <i>0.1% Sodium Hyaluronate 15 mL bottle</i>	CURRENTLY LISTED IN THE PNF <i>0.1% Sodium Hyaluronate 5 mL bottle</i>
COST PER DOSAGE UNIT (in PhP)	Php 1.0833 per drop (Lacrifresh at 325.00Php/bottle)	Php 3.3900 per drop (Hialid at 339.00Php/bottle)
NUMBER OF DOSAGE UNITS PER UNIT COURSE	Approximately 300 drops per 15 ml	Approximately 100 drops per 5 ml
TOTAL DIRECT COST PER PATIENT PER TREATMENT COURSE (in PhP)*	Php 1,169.96 (54 ml over 3 months or 1080drops)	Php 3,661.2 (54 ml over 3 months or 1080 drops)
ADDITIONAL COST PER PATIENT PER TREATMENT COSTS: (n PhP) a. Implementation costs: (cost of drug administration, monitoring, additional diagnostic services, additional equipment, travel, caregiver, etc.) b. Intervention costs: (management of adverse drug reactions)	n/a	n/a
TOTAL COST PER PATIENT PER TREATMENT COURSE (in PhP)	Php 1,169.96 (54 ml over 3 months or 1080drops)	Php 3,661.2 (54 ml over 3 months or 1080 drops)
EXPECTED NUMBER OF PATIENT-TREATMENT COURSES PER YEAR	3 month courses per year	3 month courses per year
TOTAL SAVINGS	PhP 2, 491.24	

Annex B. Summary of Evidence of 2.5% Peritoneal Dialysis Solution (2L and 5L)

Section 1. General Information on the Proponent and Proposed Inclusion

Proponent/s	National Kidney and Transplant Institute (NKTII)
	Philippine General Hospital (PGH)
Generic Name	Peritoneal Dialysis Solution with 2.5% Dextrose
Brand Name (If Any)	Dianeal PD2
Therapeutic Classification	Peritoneal Dialysis Solution
For Listed Medicines:	
• Current Dosage Strength/S	Peritoneal Dialysis Solution with 2.3% and 4.25% Dextrose
• Proposed Dosage Strength	Peritoneal Dialysis Solution with 2.5% Dextrose
• Current Net Liquid Content	2,000 mL and 5,000 mL
• Proposed Net Liquid Content	2,000 mL and 5,000 mL
• Current Immediate Packaging	Bottles/Bag
• Proposed Immediate Packaging	Bottles/Bag
PNF Listed Indication	Correct acid and electrolyte imbalance, and fluid overload; remove metabolites in renal failure
Manufacturer	Baxter Healthcare Philippines, Inc.
Importer/Trader	N.A.
Distributor	Baxter Healthcare Philippines, Inc.

Section 2. Summary of Evidence Reviewed

The new dosage of the medicine:	Remarks/Evidence
1. Has good quality	Baxter 2.5% Peritoneal Dialysis Solution has a Certificate of Product Registration (CPR) with the Philippine Food and Drug Administration (FDA), assuring the public of its quality. The CPR Registration Numbers for 2L and 5L of 2.5% Peritoneal Dialysis Solution are DR-XY22538 and DR-XY26535, respectively.
2. Has proven safety based on sound evidence	Dextrose 1.5%, 2.5%, and 4.25% (2L and 5L) were part of 2006 Philippine National Drug Formulary (PNDF) Volume II, 3rd edition. This establishes the recognition of the product's safety and efficacy by the Department of Health. The product was delisted from PNDP due to the company's commercial exit from the Philippines and not for any safety reason.

	<p>However, during this period of commercial exit (till July 2018), Baxter Dianeal continued to be available for legacy patients and had maintained active registration with the Food and Drug Administration.</p> <p>Dianeal has been sold over 1.5 billion bags worldwide. With an average of 4 bags for treatment dose, estimated more than 13.7 million of treatments-months have been performed. Cumulatively, from initial worldwide commercialization on 27 Sep 1978 to 30 Sep 2019, a total of 184,069 initial adverse event reports were received from worldwide reporting sources for all Dianeal solutions (1.5%, 2.5%, 4.25%).</p> <p>There was no product recall being taken in the reporting interval for safety reasons for the Philippines since its availability in 1998.</p>
<p>3. Has proven efficacy for the stated indication based on sound evidence</p>	<p>According to the International Society for Peritoneal Dialysis (ISPD) Guidelines, 1.5%, 2.5%, and 4.25% Peritoneal Dialysis Solutions for acute PD are equivalent if glucose is measured. Globally it is well accepted that PD with Dextrose Hydrus 1.5%, 2.5% and 4.25% (the US Pharmacopeia compliant products) are the same as PD with glucose anhydrous 1.36%, 2.27% and 3.86% (European Pharmacopoeia compliant products).</p> <p>To be compliant with the regulations, the PD Solutions available in the US (both from Baxter and FMC) are labeled as Dextrose 2.5% (Dextrose Hydrus 2.5%) and the PD Solutions available in the Europe (both from Baxter and FMC) are labeled as Glucose 2.27% (Glucose anhydrous 2.27%). The PD Solutions available in the US and Europe are the same. The only difference is the way of labeling.</p> <p>Baxter PD Solution available in the Philippines contains Dextrose Hydrus 2.5% which is equivalent to 22.7g of Dextrose Anhydrous (Glucose anhydrous) per 100ml of the solution. FMC's PD Solution contains Glucose monohydrate 25g (Dextrose Hydrus 25g) which is equivalent to 22.7g of Glucose anhydrous per 100ml of PD Solution. Hence, both Baxter and FMC products are equivalent in terms of glucose concentration and both contain 22.7g of glucose anhydrous per 100ml of PD solution.</p> <p>References:</p> <ol style="list-style-type: none"> 1. Cullis et al. ISPD Guidelines/Recommendations: Peritoneal Dialysis for Acute Kidney Injury. Peritoneal Dialysis International, Vol. 34, pp. 494-517 2. USP & NF, Official as of 1-May-2020; Printed from: https://online.uspnf.com/uspnf/document/1_GUID-FC34A2DF-4370-4A76-A3B0-C1AC567553C2_5_en-US 3. European Pharmacopoeia 10.0, pg. 2758. <p>Published clinical practice guidelines for end-stage renal disease include treatment algorithms using 2.5% and 2.3% Peritoneal Dialysis Solutions.</p> <p>References:</p> <ol style="list-style-type: none"> 1. Canadian Society of Nephrology Guidelines/Recommendations - Clinical Practice 2. Guidelines and Recommendations on Peritoneal Dialysis Adequacy 2011, Peritoneal Dialysis International, Vol. 31, pp. 218-239. 3. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Peritoneal Dialysis Adequacy, 2000. Am J Kidney Dis 37:S65-S136, 2001 (suppl 1). 4. Renal Association Clinical Practice Guideline on peritoneal dialysis in adults and children Woodrow et al. BMC Nephrology (2017) 18:333. 5. Renal replacement therapy and conservative management. NICE guideline Published: 3 October 2018 www.nice.org.uk/guidance/ng107. <p><i>*Guidelines 1&2 are from North America; therefore uses 2.5%. Guideline 3 is from Europe, therefore uses 2.27% (European Pharmacopeias require all peritoneal dialysis labels to be in anhydrous form)</i></p>

4. Has favorable cost-effectiveness analysis	The total cost per year per patient for using 2.5% PD solution (Baxter) is lower compared to the total cost per year per patient of the currently-listed preparation 2.3% PD solution (Fresenius Kabi) with a price difference on the total cost per year per patient of Php 820.00 for the 2L-preparation and Php 146,149.34 for 5L-preparation. Please see the costing table below for more information.
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Section 3. Costing table for 2L 2.5% (proposed HT for inclusion) VS 2L 2.3% (For Manual PD)

PARAMETER*	PROPOSED INCLUSION 2L 2.5% Peritoneal Dialysis Solution	CURRENTLY LISTED IN THE PNF 2L 2.3% Peritoneal Dialysis Solution
COST PER DOSAGE UNIT (in PhP)	190.00	190.00
NUMBER OF DOSAGE UNITS PER UNIT COURSE	3 bags per day (lifetime therapy)	3 bags per day (lifetime therapy)
TOTAL DIRECT COST PER PATIENT PER TREATMENT COURSE (in PhP)	570.00 (3 Bags/day)	570.00 (3 Bags/day)
ADDITIONAL COST PER PATIENT PER TREATMENT COSTS: (n PhP) a. Implementation costs: (cost of drug administration, monitoring, additional diagnostic services, additional equipment, travel, caregiver, etc.) b. Intervention costs: (management of adverse drug reactions)	1. Disinfection cap 15.60/cap 3 caps/day 2. Transfer set (extension catheter) 1,009/set. 2 Transfer set/annum. Annual charges = 2,018 Other charges vary from hospital to hospital.	1. Disinfection cap 16.00/cap 3 caps/ day 2. Extension catheter 1200/set. 2 Transfer set/annum. Annual charges = 2,400 Other charges vary from hospital to hospital.
TOTAL COST PER PATIENT PER TREATMENT COURSE (in PhP)	3 bags per day = 570 3 disinfection cap= 46.80 Transfer set= 5.52 <u>Total per diem= 622.33</u> <u>Total per tranche (every 2 weeks) =8,712.60</u>	3 bags per day = 570 3 disinfection cap= 48.00 Transfer set= 6.58 <u>Total per diem = 624.58</u> <u>Total per tranche (every 2 weeks) = 8,744.05</u>
EXPECTED NUMBER OF PATIENT-TREATMENT COURSES PER YEAR	365 days/ year 26 tranches/year (maintenance therapy)	365 days/ year 26 tranches/year (maintenance therapy)
Total cost per patient per year (in Php)	227,150	227,970.00
Price difference on total cost per year patient per year (in Php) (Total cost per patient per year of currently listed product - Total cost per patient per year of proposed inclusion)	820.00	

* Cost of medicine based on suggested retail price (SRP) as of 18 December 2020.

** One tranche = 2 weeks. Philhealth reimburses peritoneal dialysis per tranche.

Section 4. Costing table for 5L 2.5% (proposed HT for inclusion) VS 5L 2.3% (For Automated PD)

PARAMETER*	PROPOSED INCLUSION 5L 2.5% Peritoneal Dialysis Solution	CURRENTLY LISTED IN THE PNF 5L 2.3% Peritoneal Dialysis Solution
COST PER DOSAGE UNIT (in PhP)	481.57	550.00
NUMBER OF DOSAGE UNITS PER UNIT COURSE	2 bags per day (lifetime therapy)	2 bags per day (lifetime therapy)
TOTAL DIRECT COST PER PATIENT PER TREATMENT COURSE (in PhP)	963.14 (2 Bags/day)	1,100.00 (2 Bags/Day)
ADDITIONAL COST PER PATIENT PER TREATMENT COSTS: (n PhP) a. Implementation costs: (cost of drug administration, monitoring, additional diagnostic services, additional equipment, travel, caregiver, etc.) b. Intervention costs: (management of adverse drug reactions)	1. Disinfection cap 00.00/cap per day 2. HomeChoice Automated PD set (Cassette or Cyclor set) 504.00/set. 1 Cassettee per day. 3. Transfer set (extension catheter) 917.28/set. 2 Transfer set per annum. Annual charges = 1,834.56 Other charges vary from hospital to hospital.	1. Disinfection cap 16.00/cap per day 2. Cyclor set 750.00/set. 1 Cyclor Set per day. 3. Extension catheter 1200/set. 2 Transfer set per annum. Annual charges = 2,400 Other charges vary from hospital to hospital.
TOTAL COST PER PATIENT PER TREATMENT COURSE (in PhP)	2 Bags = 963.14 1 Cyclor set = 504.00 1 Disinfection cap = 00.00 Transfer set = 5.03 <u>Total per diem = 1,472.17</u> <u>Total per tranche= 20, 610.33</u>	2 Bags = 1,100.00 1 Cyclor set = 750.00 1 Disinfection cap = 16.00 Transfer set = 6.58 <u>Total per diem= 1872.58</u> <u>Total per tranche= 26,216.05</u>
EXPECTED NUMBER OF PATIENT-TREATMENT COURSES PER YEAR	365 days/ year 26 tranches/year (maintenance therapy)	365 days/ year 26 tranches/year (maintenance therapy)
Total cost per patient per year (in Php)	537,340.66	683,490.00
Price difference on total cost per year patient per year (in Php) (Total cost per patient per year of currently listed product - Total cost per patient per year of proposed inclusion)	146,149.34	

* Cost of medicine based on suggested retail price (SRP) as of 18 December 2020.

** One tranche = 2 weeks. Philhealth reimburses peritoneal dialysis per tranche.