



Republic of the Philippines
Department of Health
OFFICE OF THE SECRETARY

1 February 2023

DEPARTMENT CIRCULAR

No. 2023 - 0060

FOR: ALL CENTERS FOR HEALTH DEVELOPMENT, NATIONAL DRUG POLICY COMPLIANCE OFFICES, LEAGUES OF CITIES, PROVINCES AND MUNICIPALITIES, PROFESSIONAL HEALTH SOCIETIES, DIRECTORS OF BUREAUS AND REGIONAL OFFICES, BARMM MINISTER OF HEALTH, CHIEFS OF MEDICAL CENTERS AND SANITARIA, AND OTHER CONCERNED

SUBJECT: Health Technology Assessment Council (HTAC) Recommendation for the Inclusion of recombinant human erythropoietin (epoetin alfa) 4000 IU/mL solution for injection (IV/SC) 1mL pre-filled syringe for the management of chemotherapy-induced anemia in patients with non-myeloid disease in the Philippine National Formulary (PNF)

By virtue of Republic Act 11223, otherwise known as the Universal Health Care (UHC) Act, health technology assessment (HTA) shall be institutionalized as a fair and transparent priority-setting mechanism to provide financing and coverage recommendations on health technologies to be funded by the Department of Health (DOH) and the Philippine Health Insurance Corporation (PhilHealth).

Please be apprised that as of 24 January 2023, the Office of the Secretary approves the HTA Council recommendation to include **human erythropoietin (epoetin alfa) 4000 IU/mL solution or injection (IV/SC) 1mL pre-filled syringe** in the PNF on the basis of the following:

- Only the net volume of the pre-filled syringe that contains 4,000 IU of epoetin alfa was changed from 0.4mL to 1 mL. Both dosage formulations contain 4,000 IU of epoetin alfa; hence, the number of pre-filled syringes that will be consumed per dose (i.e. 150 units/kg/dose or 40,000 IU/dose) will not differ.
- The unit price of epoetin alfa, 4,000 IU/mL solution for injection (IV, SC) 1mL pre-filled syringe (Php 275.00, based on the provided procurement price by Jose B. Lingad Memorial Regional Hospital) is lower than the unit price of epoetin alfa, 4,000 IU/0.4 mL, pre-filled syringe (IV, SC) (Php 555.00 based on the 2022 DOH Drug Price Reference Index).
- Since the unit cost of the proposed dosage formulation is lower than the unit cost of the comparator (i.e., the currently listed form in the PNF) and there are no differences in the number of pre-filled syringes that will be consumed per patient per regimen, cost savings are expected with the use of the proposed epoetin alfa, 4000 IU/mL solution for injection (IV, SC), 1mL pre-filled syringe:
 - For an average adult patient with anemia due to concurrent myelosuppressive chemotherapy (60 kg* patient), the cost savings (per patient) associated with the use of the new formulation with new net content are the following:

- 150 units/kg/dose, thrice weekly dosing regimen: Php 20,160 for 8 weeks of treatment
- 40,000 units/week once weekly dosing regimen: Php 22,400 for 8 weeks of treatment
- For an average adult patient with anemia due to chronic kidney disease (50 kg* patient), the cost savings (per patient) associated with the use of the new formulation with new net content are the following:
 - 50 units/kg/dose, thrice weekly dosing regimen: Php 10,080 for 12 weeks of treatment
 - 100 units/kg/dose, thrice weekly dosing regimen: Php 20,160 for 12 weeks of treatment

**average weight of patients were based on consultation with medical societies (PSMO and PSHBT). Each pre-filled syringe is assumed for single-use only and should not be reused for the next dose. The remaining content of the PFS that will not be consumed will be discarded after use.*

Note that the cost savings would only prevail if the purchase price of the comparator is equal to the reference price in the DPRI.

- Compared to the unit price of the currently-listed epoetin alfa, 4,000 IU/ mL, vial form (Php 318.18 based on the 2022 DOH Drug Price Reference Index), the unit price of the proposed epoetin alfa, 4,000 IU/mL solution for injection (IV, SC) 1mL pre-filled syringe (Php 275.00) is still lower; hence, resulting in cost-savings.

For more details, you may refer to *Annex A* on the summary of evidence reviewed and *Annex B* on the costing analysis.

Kindly disseminate this to all concerned officials in your areas of responsibility so that they may be appropriately guided in their procurement activities. All are enjoined to ensure rational procurement, distribution, and use of health technologies in all government and private facilities.

Your full cooperation in this endeavor is expected and highly appreciated.

For your information and guidance.

By Authority of the OIC-Secretary of Health:


ATTY. CHARADE MERCADO GRANDE
 Assistant Secretary of Health
 Health Regulation Team

Annex A. Summary of Evidence Reviewed

The new net content of the medicine:	Yes	No	Remarks/Evidence
1. Has good quality	✓		Recombinant human erythropoietin (epoetin alfa) 4000 IU/mL solution for injection (IV/SC) 1mL pre-filled syringe has a valid Certificate of Product Registration with the Philippine Food and Drug Administration (FDA) assuring the public of its quality.
2. Has proven safety based on sound evidence	✓		<ol style="list-style-type: none"> 1. The active FDA CPR of Recombinant human erythropoietin (epoetin alfa) 4000 IU/mL solution for injection (IV/SC) 1mL pre-filled syringe certifies for the safety of the product. 2. Recombinant human erythropoietin (epoetin alfa) and its different dosage formulations are currently included in the Philippine National Drug Formulary (8th edition) which establishes the recognition of the product's safety by the Department of Health.
3. Has proven efficacy for the stated indication based on sound evidence	✓		<ol style="list-style-type: none"> 1. The active FDA CPR of Recombinant human erythropoietin (epoetin alfa) 4000 IU/mL solution for injection (IV/SC) 1mL pre-filled syringe certifies the efficacy of the product. 2. Recombinant human erythropoietin (epoetin alfa) and its different dosage formulations are currently included in the Philippine National Drug Formulary (8th edition) which establishes the recognition of the product's efficacy by the Department of Health.
4. Has favorable cost-effectiveness analysis	✓		The addition of the listing of Recombinant human erythropoietin (epoetin alfa) 4000 IU/mL solution for injection (IV/SC) 1mL pre-filled syringe in the PNF will result in cost-savings of Php 20,160 to Php 22,400 for patients with anemia due to concurrent myelosuppressive chemotherapy; and Php 10,080 to Php 20,160 for patients with anemia due to chronic kidney disease.
5. Other considerations			N/A

Annex B. Comparative costing analysis on the use of epoetin alfa, 4000 IU/0.4 mL, pre-filled syringe (IV, SC) vs epoetin alfa, 4000 IU/mL, pre-filled syringe (IV, SC)

Notes on the costing analysis:

- There was no difference in other medical costs associated with the use of the intervention and the comparator since only the net volume was proposed to be changed and not the dosing regimen.
- There was no definition indicated in the references used for the dosing regimen [i.e., Martindale 36th edition, Philippine National Formulary (PNF) and consultation with the Philippine College of Hematology and Transfusion Medicine (PCHTM)] on when to prescribe the dosing regimen of 150 units/kg/dose, thrice weekly and the alternative dosing regimen of 40,000 units/week, once weekly. For patient adherence, 40,000 IU/week dosing may be used as an alternative dosing regimen.
- The intervention is more affordable than the comparator due to significant differences in the total treatment regimen costs.
- There are four (4) total indications listed in the Philippine National Formulary (PNF) for epoetin alfa. The indication for chronic kidney disease (CKD) was also included in the costing analysis for the reason that aside from the indication of chemotherapy-induced anemia which was applied by the proponent, CKD is also considered to be vastly prevalent in the Philippine setting. On the other hand, indications such as anemia associated with HIV therapy and reduction of allogeneic RBC transfusion were excluded from the costing analysis.
- The total of expected number of users were not computed in the costing sheets due to the lack of data available specific for anemia due to concurrent myelosuppressive chemotherapy and anemia due to chronic kidney disease. Meanwhile, the intervention is notably more affordable as seen on the unit cost differences of the intervention and comparator but there was no justification given as to how epoetin alfa 4000 IU/mL is much cheaper than epoetin alfa 4000/0.4 mL.
- Each pre-filled syringe is for single-use only and should not be reused for the next dose. The remaining content of the PFS that will not be consumed will be discarded after use.

Indication 1: Management of chemotherapy-induced anemia in patients with non-myeloid malignant disease

Parameter	<i>Intervention</i>		<i>Comparator</i>	
	Epoetin Alfa 4000 IU/mL, pre-filled syringe (IV, SC)	Reference, Year	Epoetin Alfa 4000 IU/0.4mL, pre-filled syringe (IV, SC)	Reference, Year
Unit cost of medicine	Php 275.00/PFS	Jose B. Lingad Memorial Hospital	Php 555.00/PFS	<u>Drug Price Index 10th edition</u>

Number of dosage units per treatment course	<p>1. 150 Units/kg/dose: 60kg px x 150 units = 9,000 units (3 PFS) per dose</p> <p>OR</p> <p>2. 40,000 units/week = 10 PFS per once weekly dose</p>	<p><u>Martindale 36th Edition, Standard Therapeutic Guideline of Jose B. Lingad Memorial Regional Hospital</u></p> <p>Same dosing indicated in the PNF (8th Ed)</p> <p>Validated by PCHTM and PSHBT</p>	<p>1. 150 Units/kg/dose: 60kg px x 150 units = 9,000 units (3 PFS) per dose</p> <p>OR</p> <p>2. 40,000 units/week = 10 PFS per once weekly dose</p>	<p><u>Martindale 36th Edition, Standard Therapeutic Guideline of Jose B. Lingad Memorial Regional Hospital</u></p> <p>Same dosing indicated in the PNF (8th Ed)</p> <p>Validated by PCHTM and PSHBT</p>
Duration of Treatment	<p>1. 3 times weekly only until the chemotherapy course is completed</p> <p>OR</p> <p>2. Once weekly</p> <p>Continued for 8 weeks. If no response, there will be no benefit beyond the duration of treatment</p>	<p><u>Martindale 36th Edition, Standard Therapeutic Guideline of Jose B. Lingad Memorial Regional Hospital</u></p> <p>Validated by PCHTM and PSHBT</p>	<p>1. 3 times weekly only until the chemotherapy course is completed</p> <p>OR</p> <p>2. Once weekly</p> <p>Continued for 8 weeks. If no response, there will be no benefit beyond the duration of treatment</p>	<p><u>Martindale 36th Edition, Standard Therapeutic Guideline of Jose B. Lingad Memorial Regional Hospital</u></p> <p>Validated by PCHTM and PSHBT</p>
Total direct cost per patient per treatment course	<p>1. Php 275.00 x 9 PFS x 8 weeks = Php 19,800.00 for 8 weeks of treatment course</p> <p>2. Php 275.00 x 10 PFS x 8 weeks = Php 22,000.00 for 8 weeks of treatment course</p>		<p>1. Php 555.00 x 9 PFS x 8 weeks = Php 39,960.00 for 8 weeks of treatment course</p> <p>2. Php 555.00 x 10 PFS x 8 weeks = 44,400.00 for 8 weeks of treatment course</p>	

<p>Other medical cost associated with the use of the drug</p> <p>a. Implementation costs of drug administration (e.g. syringe, diluents) Monitoring (e.g. PT, PTT), additional diagnostic services</p> <p>b. Intervention costs: (management of adverse drug reaction)</p>	N/A	<p>Not computed. The other medical costs identified are the same (CBC determinations, diphenhydramine and paracetamol in case of allergy, and serum ferritin determination) and will cancel out since only the net content was changed, and not the dosing regimen.</p> <p>Both intervention and comparator do not require diluent or syringe.</p>	N/A	<p>Not computed. The other medical costs are the same (CBC determinations, diphenhydramine and paracetamol in case of allergy, and serum ferritin determination) and will only cancel out since only the net content was changed, not the dosing regimen.</p> <p>Both intervention and comparator do not require diluent or syringe.</p>
Incremental Cost	<p>1. 150 Units/kg/dose, thrice weekly: -P20,160.00</p> <p>2. 40,000 units/week, once weekly: -P22,400.00</p>			

Indication 2: Management of anemia due to chronic kidney disease

Parameter	Intervention Epoetin Alfa 4000 IU/mL, pre-filled syringe (IV, SC)	Reference, Year	Comparator Epoetin Alfa 4000 IU/0.4mL, pre-filled syringe (IV, SC)	Reference, Year
Unit cost of medicine	Php 275.00/PFS	Jose B. Lingad Memorial Hospital	Php 555.00/PFS	<u>Drug Price Index 10th edition</u>
Number of dosage units per treatment course	<p>50-100 units/kg/dose Average weight: 50 kg</p> <p>50 units*50 kg = 2500 units 100 units*50kg = 5000 units</p>	<p>Same dosing indicated in the PNF (8th Ed)</p> <p>Validated by PSHBT</p>	<p>50-100 units/kg/dose Average weight: 50 kg</p> <p>50 units*50 kg = 2500 units 100 units* 50kg= 5000 units</p>	<p>Same dosing indicated in the PNF (8th Ed)</p> <p>Validated PSHBT</p>

	1-2 PFS per dose		1-2 PFS per dose	
Duration of Treatment	3 times weekly; No response after 12th week: stop epoetin 1-2 PFS per dose, 3 doses a week 12 weeks = 36-72 PFS	Validated by PSHBT	3 times weekly; No response after 12th week: stop epoetin 1-2 PFS per dose, 3 doses a week 12 weeks = 36-72 PFS	Validated by PSHBT
Total direct cost per patient per treatment course	36-72 PFS*Php 275.00 Php 9,900-19,800		36-72 PFS*Php 555.00 Php 19,980-39,960	
Other medical cost associated with the use of the drug a. Implementation costs of drug administration (e.g. syringe, diluents) Monitoring (e.g. PT, PTT), additional diagnostic services b. Intervention costs: (management of adverse drug reaction)	N/A	Not computed. The other medical costs identified (CBC determinations, diphenhydramine and paracetamol in case of allergy, and serum ferritin determination) will cancel out since only the net content was changed, and not the dosing regimen. Both intervention and comparator do not require diluent or syringe.	N/A	Not computed. The other medical costs (CBC determinations, diphenhydramine and paracetamol in case of allergy, and serum ferritin determination) will only cancel out since only the net content was changed, not the dosing regimen. Both intervention and comparator do not require diluent or syringe.
Incremental cost	1. 50 Units/kg/dose, thrice weekly: -P10,080.00 2. 100 Units/kg/dose, once weekly: -P20,160.00			