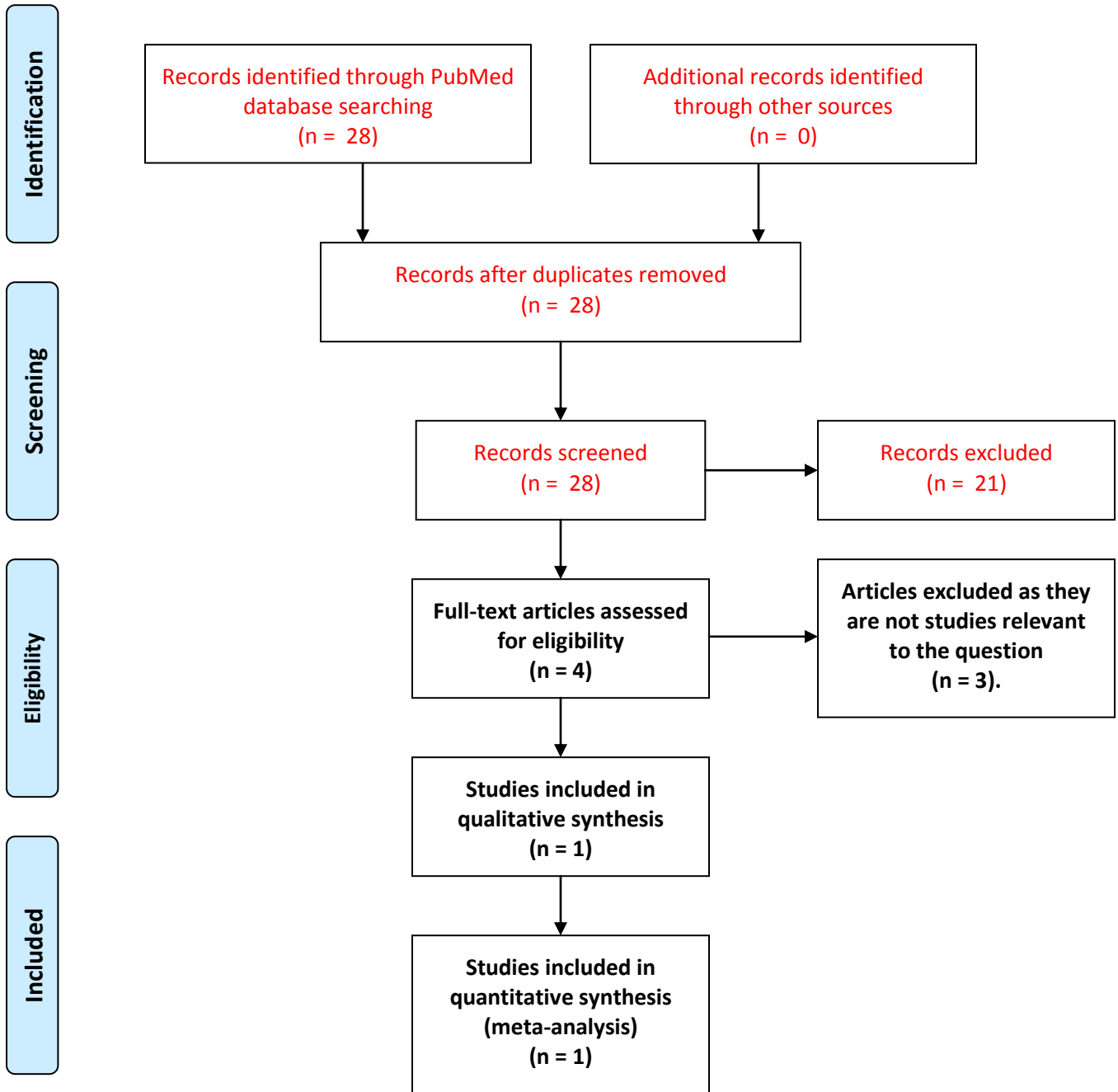




Republic of the Philippines  
Department of Health  
**OFFICE OF THE SECRETARY**

<b>Name of medicine (INN):</b>	Methoxypolyethylene glycol epoetin- beta 30ug, 50ug, 75ug, 100ug, 150ug, 200ug (SC/IV)
<b>Indication:</b>	For the treatment of anemia associated with chronic kidney disease (CKD)
<b>Date of deliberation:</b>	01 July 2015
<b>Recommendation:</b>	<b>DISAPPROVAL</b>
<b>Clinical evidence:</b>	<p>Based on the review of evidence, the Council found that there is similar incidence in the overall mortality (OR=0.81 (95%CI; 0.12 and 5.35)) and on the need for blood transfusion (OR=0.83 (95%CI; 0.17 and 4.15)) with the use of methoxy polyethylene glycol epoetin beta compared with regular epoetin beta. When compared with darbepoetin, similar incidence on overall mortality (OR=0.90 (95%CI; 0.59 and 1.40) and the need for blood transfusion (OR=0.94 (95%CI; 0.45 and 1.95) was likewise noted. Further, as regards the safety of the drug, the incidence of cardiovascular mortality, stroke, and hypertension is similar between methoxy polyethylene glycol epoetin beta compared with darbepoetin.</p> <p><i>(See Attachment for the full ERG evaluation)</i></p>
<b>Cost data:</b>	<p>The Council acknowledged the ERG report that methoxy polyethylene glycol epoetin beta and epoetin beta have similar efficacy and safety profiles, but the former is 3-4 times more expensive than the latter. It was noted that the two (2) products only differ in the frequency of dosing such that methoxy polyethylene glycol epoetin beta is administered once every two (2) weeks while epoetin beta is to be taken weekly, both for one (1) month. The Council requested the secretariat to correct the frequency of dosing reflected in the cost comparison table <i>(See Attachment)</i>.</p>
<b>Remarks:</b>	<p>The Secretary of Health has officially disapproved the proposal to include methoxypolyethylene glycol epoetin- beta in the PNF. There was no appeal received within the set deadline, thus the recommendation of the Council still remains.</p>

PRISMA Table



1. Among patients with chronic kidney disease and anemia, how safe is METHOXYPOLYETHYLENE GLYCOL EPOETIN BETA 200 mcg/0.3 mL Solution for Injection (IV/SC) pre-filled syringe [30ug, 50ug, 75ug, 100ug, 150ug, 200ug (SC/IV) compared with epoetin alfa in terms of adverse drug reactions? Local inflammatory reactions?

2. Among patients with chronic kidney disease and anemia, how cost-effective is METHOXYPOLYETHYLENE GLYCOL EPOETIN BETA 200 mcg/0.3 mL Solution for Injection (IV/SC) pre-filled syringe [30ug, 50ug, 75ug, 100ug, 150ug, 200ug (SC/IV) compared with compared with epoetin alpha?

**EVIDENCE TABLE 1**

NO	TITLE/ AUTHOR YEAR/JOURNAL	STUDY DESIGN	PARTICIPANT DESCRIPTION	INTERVENTION	RESULTS/OUTCOMES				GRADE OF EVIDENCE	REMARKS	
					EVENTS	Methoxy glycol epoetin beta		Epoetin beta or darbepoetin			
					(including adverse events)	No. of events *	Total # of patients	No. of events *			Total # of patients
1	Palmer et al. Cochrane Database Syst Rev. 2014	Meta-analysis	56 RCTs involving 15,596 patients with chronic kidney disease	Epoetin alfa vs. placebo	Need for blood transfusion					OR=0.07 (95%CI; 0.01 and 0.84)	
					All-cause mortality					OR=0.99 (95%CI; 0.14 and 6.86)	
				Epoetin beta vs. methoxy polyethylene glycol-epoetin beta	Need for blood transfusion					OR=0.83 (95%CI; 0.17 and 4.15)	
					All-cause mortality					OR=0.81 (95%CI; 0.12 and 5.35)	
				Darbepoetin alfa vs. methoxy polyethylene glycol-epoetin beta	Need for blood transfusion					OR=0.94 (95%CI; 0.45 and 1.95)	
					All-cause mortality					OR=0.90 (95%CI; 0.59 and 1.40)	
					Cardiovascular mortality					OR=0.69 (95%CI; 0.32 and 1.48)	
					Myocardial					OR=0.47 (95%CI; 0.06	

					infarction						and 3.65)
					Stroke						OR=1.33 (95%CI; 0.17 and 10.49)
					Hypertension						OR=0.94 (95%CI; 0.62 and 1.42)
					End-stage kidney disease						OR=1.83 (95%CI; 0.66 and 5.09)

\*group means with standard deviations may be reported if the data are continuous

**EVIDENCE TABLE 2: GRADE EVIDENCE PROFILE TABLE**

QUALITY ASSESSMENT							SUMMARY OF FINDINGS				Importance	
							No. of patients		Effect			Over-all Quality
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% CI)	Absolute MD		
Outcome: Need for blood transfusion												
1	Meta-analyses	None	None	None	None		Epoetin beta	Methoxy polyethylene glycol epoetin beta	0.83 (95%CI; 0.17 and 4.15)		High	Critical
Outcome: Need for blood transfusion												
1	Meta-analyses	None	None	None	None		Darbepoetin	Methoxy polyethylene glycol epoetin beta	0.94 (95%CI; 0.45 and 1.95)		High	Critical
Outcome: All-cause mortality												
1	Meta-analyses	None	None	None	None		Darbepoetin	Methoxy polyethylene glycol epoetin beta	0.81 (95%CI; 0.12 and 5.35)		High	Critical
Outcome: All-cause mortality												
1	Meta-analyses	None	None	None	None		Darbepoetin	Methoxy polyethylene glycol epoetin beta	0.90 (95%CI; 0.59 and 1.40)		High	Critical

**DETAILS REQUIRED FOR COST-EFFECTIVENESS ANALYSIS**

<p><b>PARAMETER</b> (Indicate information for intended recipient)*  <b><u>INTENDED RECIPIENT:</u></b></p>	<p><b>NEW MEDICINE OR PROPOSED NEW INDICATION/ FORMULATION/ ROUTE OF ADMINISTRATION</b></p>	<p><b>CURRENTLY LISTED MEDICINE FOR SAME INDICATION IN THE PNF</b>  <i>(*where there is no comparator medicine in the formulary, use the cost of the best existing standard of care)</i></p>	<p><b>REFERENCES</b></p>
<p>COST PER DOSAGE UNIT (in PhP) a. Proposed list price to the government b. Current prevailing market price</p>	<p>Methoxy polyethylene glycol epoetin beta (Mircera) 100 mcg inj (P7,400) 200 mcg inj (P14,000) 50 mcg inj (P3,800)</p>	<p>Epoetin alfa 4000IU pre-filled (P650)  Epoetin beta 5000IU pre-filled (P1,076.78)</p>	<p>Methoxy polyethylene glycol epoetin beta (Mircera) price from MIMS  Epoetin beta price from DPRI</p>
<p>NUMBER OF DOSAGE UNITS PER UNIT COURSE</p>	<p>2 x 50 mcg inj amps (once every 2 weeks)</p>	<p>4 x 5000IU syringe (weekly dose for one month)</p>	
<p>TOTAL DIRECT COST PER PATIENT PER TREATMENT COURSE (in PhP)</p>	<p>P 7,600 Monthly</p>	<p>P 4,308 Monthly</p>	
<p>ADDITIONAL COST PER PATIENT PER TREATMENT COURSE: (n PhP) a. Implementation costs: (cost of drug administration, monitoring, additional diagnostic services, additional equipment, travel, caregiver, etc.)</p>			
<p>TOTAL COST PER PATIENT PER TREATMENT COURSE (in PhP) Total Direct + Additional Costs</p>			
<p>ESTIMATED NUMBER OF PATIENTS WITH THE DISEASE/CONDITION WHO WILL USE THE MEDICINE</p>			
<p>QUALITY ADJUSTED LIFE YEARS (IF AVAILABLE)</p>			
<p>DISABILITY ADJUSTED LIFE YEARS (IF AVAILABLE)</p>			

## REVIEWERS' RECOMMENDATIONS

### Literature Search

- We searched PubMed database last February 2015 using the terms “epoetin beta” and “meta-analysis”. The yield was 28 articles. We reviewed the 28 articles and considered 7 articles for full text retrieval. However, only 4 full texts are available.
- Of the 4 full text articles reviewed, only one was included in this review. The article however is a 2014 Cochrane meta-analysis that included 56 studies involving 15,596 adult patients.
  - Palmer SC(1), Saglimbene V, Mavridis D, Salanti G, Craig JC, Tonelli M, Wiebe N, Strippoli GF. Erythropoiesis-stimulating agents for anaemia in adults with chronic kidney disease: a network meta-analysis. *Cochrane Database Syst Rev.* 2014 Dec 8;12:CD010590. doi: 10.1002/14651858.CD010590.pub2.

### Effectiveness/Efficacy

- All-cause mortality and need for blood transfusion was considered as the clinically relevant outcomes for the review. There was similar incidence in overall mortality in methoxy polyethylene glycol epoetin beta compared with regular epoetin beta (OR=0.81 (95%CI; 0.12 and 5.35). There was also similar incidence for the need for blood transfusion (OR=0.83 (95%CI; 0.17 and 4.15).
- Similarly, there was also similar overall mortality in methoxy polyethylene glycol epoetin beta compared with darbepoetin (OR=0.90 (95%CI; 0.59 and 1.40) as well as similar incidence on the need for blood transfusion (OR=0.94 (95%CI; 0.45 and 1.95). These too however were not statistically significant.

### Safety

- In terms of safety parameters like cardiovascular mortality, stroke, hypertension, the incidence of occurrence is similar between methoxy polyethylene glycol epoetin beta compared with darbepoetin.

### Summary of Review

- In summary we found methoxy polyethylene glycol epoetin beta to be similar in efficacy and safety compared to epoetin beta or darbepoetin.

### Cost Data (Cost-comparison table)

- In terms of cost, methoxy polyethylene glycol epoetin beta is 3-4 times more expensive than epoetin beta (P 15,200 vs. P 4,308 for monthly treatment)

### Overall Recommendation

- Overall, we found methoxy polyethylene glycol epoetin beta to be similar in efficacy and safety compared to epoetin beta but 3-4 times more expensive. Thus we don't have enough evidence or justification to include methoxy polyethylene glycol epoetin beta in the PNDF.

### References

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