Republic of the Philippines

DEPARTMENT OF SCIENCE AND TECHNOLOGY

BAGONG PILIPINAS

CALL FOR STAKEHOLDER COMMENTS ON THE PRELIMINARY RECOMMENDATION OF THE HEALTH TECHNOLOGY ASSESSMENT (HTA) COUNCIL ON *CEFTAROLINE FOSAMIL (600 mg powder for concentrate for solution for injection) IN THE TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA (CAP) IN CHILDREN*

Published as of 24 April 2025

As of 24 April 2025, the Health Technology Assessment (HTA) Council has completed the evidence appraisal on the assessment of ***ceftaroline fosamil* (600 mg powder for concentrate for solution for injection)** for possible government financing.

As such, the HTA Council hereby makes public its **preliminary assessment** that it **does not recommend the government financing of *ceftaroline fosamil*** for the treatment of community-acquired pneumonia (CAP) in the **pediatric population**, for stakeholder feedback/comments.

Kindly be apprised that the assessment on this health technology covers both the pediatric and adult population, **but a separate recommendation will be released for the adult population.** The population, intervention, comparator, and outcomes (PICO) set by the HTA Council for the said evaluation are shown in the table below, for your reference:

Population	Hospitalized patients of different ages (i.e., adults, adolescents, and children over the age of two months) with moderate to severe community-acquired pneumonia (CAP)	
Intervention	Ceftaroline fosamil 600 mg powder for concentrate for solution for injection	
Comparator	Ceftriaxone (2g q24hr)* OR Cefotaxime (1–2 g IV q8hr)* OR Ampicillin/sulbactam (1.5g q6hr)* OR PLUS Macrolide (e.g., Azithromycin* OR Clarithromycin* OR Erythromycin**) *For moderate-risk and high-risk CAP **For high-risk CAP only Ceftriaxone monotherapy, OR Ceftriaxone with Vancomycin	
Outcomes	**Efficacy/Effectiveness** 1. Clinical cure rates 2. All-cause mortality (cumulative incidence/ proportion) 3. Mortality rate as treatment failure 4. Length of hospital stay (in days) 5. Length of time to achieve clinical response	**Safety** 1. Adverse events 2. Serious adverse events 3. Discontinuation because of adverse events 4. Death

Pneumonia ranks as the fourth leading cause of death in the Philippines in 2024 causing 6.5% of all deaths (Philippine Statistics Authority, 2024a). Globally, intensive care unit (ICU) patients with severe

pneumonia have a 23% mortality rate (Regunath & Oba, 2024). Among children under five years old, pneumonia was the leading cause of mortality in children in 2022 (9.9 per 100,000) (Department of Health, 2022). Specifically, it is ranked as the third and second leading cause of death among children aged 5–9 and 10–14 years old, respectively. Focusing on the pneumonia of interest in the research question, CAP is the eighth leading cause of mortality and the top infectious cause of death. In developing countries, the incidence of CAP is 0.29 cases per child-year (Cardinale et al., 2013), with the Philippines reporting 10,500 cases per 100,000 children under five years old (Song et al., 2016).

The potential pathogens that commonly cause CAP among children and adolescents include *Streptococcus pneumoniae*, *Haemophilus influenzae* type b, *Staphylococcus aureus, Klebsiella pneumoniae*, non-typeable *H. influenzae*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*. Among these, *S. pneumoniae* (30–50%) and *H. influenzae type* b (10–30%) are considered the most common causative organisms (NAG 2017). Meanwhile, *S. aureus, K. pneumoniae, M. pneumoniae and C. pneumoniae* are the less common pathogens. *Refer to Annex A* for a tabulated summary of the Antimicrobial Resistance Surveillance Program (ARSP) 2023 resistance data to antimicrobial agents tested (i.e., antibiotics that are of the same line of treatment as ceftaroline fosamil).

It was noted that the resistance data were not specific to CAP. No ARSP data is available on the resistance profiles of *M. pneumoniae* and *C. pneumoniae*, as these are not routinely tested. Currently, there is no local data available on the resistance of CAP-causing pathogens to ceftaroline fosamil, as the Research Institute for Tropical Medicine (RITM) does not routinely test for it, due to the following reasons: (1) in adherence to the recommendations of the Clinical and Laboratory Standards Institute (CLSI), which prioritizes testing of commonly used antibiotics (ceftaroline is a highly specialized agent typically reserved for infections caused by extensively drug-resistant or pan-resistant strains) and (2) ceftaroline antibiotic discs and Epsilometer-tests are not available locally (RITM, 2025). It is also important to note that most of the isolates reported in the 2023 ARSP database (n=117,398) were from adults aged 20–64 years (~40–60%). Only about 2% to 10% of isolates were from individuals aged 19 years and below, limiting pediatric-specific resistance data. Moreover, no local data was found that reports case fatality rates (CFR) of pediatric CAP disaggregated by bacterial pathogens. However, a 2018 local study on hospitalized adult patients (≥14 years old) with CAP reported the following CFRs by pathogen: *K. pneumoniae* (2.06%), *H. influenzae* (1.12%), *S. pneumoniae* (0.93%), and *S. aureus* (0.75%).

Acknowledging the significant burden of CAP in the country and the growing concerns on antimicrobial resistance, the HTA Council recognizes the importance of evaluating treatment options. However, the HTA Council hereby releases its **preliminary assessment that it does not recommend the government financing of *ceftaroline fosamil* for the treatment of CAP in the pediatric population** based on the following reasons:

- In terms of **clinical efficacy/effectiveness**, two (2) of the six (6) RCTs included in the systematic review involve the pediatric population. There is no available evidence for the outcomes *mortality rate as treatment failure, length of hospital stay (in days)* and *length of time to achieve clinical response in the pediatric population.* Meanwhile, for outcomes with available evidence, the results are as follows:
    - There is **inconclusive evidence** between ceftaroline fosamil and ceftriaxone with or without vancomycin in terms of clinical cure rates at end of treatment (EOT) and clinical cure rates at test of cure (TOC) [both with *moderate certainty of evidence*].
    - There is **inconclusive evidence** between ceftaroline fosamil and ceftriaxone in terms of all-cause mortality [*low certainty of evidence*].
- In terms of **clinical safety**, two (2) of the six (6) RCTs included in the systematic review involve pediatric populations. The results reveal that there were **inconclusive evidence** between ceftaroline fosamil compared to ceftriaxone with or without vancomycin for all outcomes: treatment-emergent AEs (TEAEs) *[low certainty of evidence]*, serious adverse events (SAEs) *[low certainty of evidence*], and discontinuation of drug from adverse events (AEs) [*moderate certainty of evidence*].
- Despite global production of ceftaroline fosamil since 2010, the clinical evidence on ceftaroline fosamil for children is limited to two (2) trials only (File et al., 2012). Upon review of the recommendations and guidelines of HTA agencies and ministries of health on the use of ceftaroline fosamil, the three (3) clinical practice guidelines scoped on pediatric CAP do not include ceftaroline fosamil in their recommendation. Specifically, ceftaroline fosamil is not included in the 2021 Pediatric Infectious Disease Society of the Philippines (PIDSP) guidelines for CAP in children aged 3 months to 18 years, nor in the 2023 DOH Omnibus Health Guidelines for children under 10 years old with nonsevere and severe CAP and for adolescents with CAP (severity not specified). The 2017 DOH-National Antibiotic Guidelines also did not mention in their

recommendation the use of ceftaroline fosamil for moderate to high-risk CAP in infants and children up to five years old. In addition, ceftaroline fosamil was removed in 2019 in the WHO Essential Medicines List (EML) after it did not meet the revised criteria for the inclusion of Reserve group antibiotics, which require a favourable benefit-risk profile and proven activity against "Critical Priority" or "High Priority" pathogens identified by the WHO Priority Pathogens List.

For the supporting evidence reviewed and discussed by the HTA Council in coming up with this preliminary recommendation, please refer to: **https://tinyurl.com/EvidenceCeftarolineFosamil.** All comments, inputs, and/or appeals on the above preliminary recommendation may be submitted until **24 April 2025 (Friday)**, for the consideration of the HTA Council, through email at hta@dost.gov.ph. Please use the prescribed form for appeals indicated in the official HTA Philippines website [https://hta.dost.gov.ph/appeals-2/]. **Appeals not following the prescribed format, and those submitted beyond the deadline shall not be entertained**.

Should you have any questions or concerns regarding the preliminary recommendation, please do not hesitate to contact us through the same email address or via telephone call at (02) 8837 2071 loc. 4100.

Thank you very much.

On behalf of the HTA Philippines:

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Annex A: ARSP 2023 Report of Resistance Rates of CAP-related Pathogens

Causative Agents of CAP in Children		No. of Isolates Tested	% Resistance rate to Antimicrobial Agents Tested						% of total isolates detected as MDR	% of total isolates detected as possible XDR
			Ceftriaxone	Cefotaxime	Ampicillin/Sulbactam	Azithromycin	Erythromycin	Vancomycin		
Most common	*S. pneumoniae*	427	(NM): 0.84% (M): 1.67%				7.62%	0.00		
	H. influenzae	390	0.59%	0.00%	10.96%	0.00%				
Less Common	*S. aureus*	7,834					11.94%	2.01%		
	K. pneumoniae	16,164	43.92%						57.7%	26.1%
	M. pneumoniae									
	C. pneumoniae									

Percentage of Resistant Isolates	≤ 5%	> 5 - 10%	> 10 - 30%	> 30%

Multidrug-resistant (MDR) = Acquired non-susceptibility to at least one agent in three or more antimicrobial categories (ARSP, 2023)
Extensively drug-resistant (XDR) = Non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (ARSP, 2023)
Possible Extensively drug-resistant (XDR) = In cases when incomplete panel of antimicrobials are tested (ARSP, 2013)