



March 5, 2018

Centers for Medicare & Medicaid Services (CMS)
7500 Security Blvd
Baltimore, MD 21244

Submitted via: www.regulations.gov

Re: Comments on Advance Notice of Methodological Changes for Calendar Year (CY) 2019 for Medicare Advantage (MA) Capitation Rates, Part C and Part D Payment Policies and 2019 draft Call Letter

Insmmed appreciates the opportunity to comment on the Advance Notice of Methodological Changes for Calendar Year (CY) 2019 for Medicare Advantage (MA) Capitation Rates, Part C and Part D Payment Policies and 2019 Draft Call Letter. Insmmed is a global biopharmaceutical company focused on the unmet needs of patients with rare diseases. Our lead product candidate is amikacin liposome inhalation suspension (ALIS) (formerly known as liposomal amikacin for inhalation), which is in late-stage development for adult patients with nontuberculous mycobacteria (NTM) lung disease who have not responded to other therapy which is caused by Mycobacterium avium complex (MAC), a rare and often chronic infection that can cause irreversible lung damage and can be fatal. Our earlier clinical-stage pipeline includes INS1007 and INS1009. INS1007 is a novel oral, reversible inhibitor of dipeptidyl peptidase 1 (DPP1), an enzyme responsible for activating neutrophil serine proteases, which are implicated in the pathology of chronic inflammatory lung diseases, such as non-cystic fibrosis (non-CF) bronchiectasis. INS1009 is an inhaled nanoparticle formulation of a treprostinil prodrug that may offer a differentiated product profile for rare pulmonary disorders, including pulmonary arterial hypertension (PAH).

Insmmed's comments on the 2019 Advance Notice and Draft Call Letter are provided below.

Insmmed supports CMS's efforts to continue to monitor and improve the Medicare program. CMS has a long history of reviewing formularies and has excelled at managing the program by adapting and instituting appropriate program updates as the healthcare and prescription drug landscapes have evolved. Insmmed believes CMS ought to increase their focus on access to therapies with Qualified Infectious Disease Products (QIDP) designation by the Food and Drug Administration (FDA). CMS takes an active interest in specific needs of the Medicare population, and to ensure Medicare beneficiaries are provided the safest medications, CMS should promote appropriate coverage of and access to QIDPs among Part D plans.

QIDP Background

The QIDP designation, created as part of the Generating Antibiotics Incentives Now (GAIN) Act, was created to incentivize the development and commercialization of much-needed, novel antibiotics.¹ FDA recognized this as

¹ Food and Drug Administration Safety and Innovation Act, Pub. L. No. 112-144, §§ 801 et seq., 126 Stat. 993, 1077 (2012). Available at: <https://www.congress.gov/112/plaws/publ144/PLAW-112publ144.pdf>

a need due to the growing number of disease resistant antibiotics and lack of new antibiotics in development to replace those

that had become ineffective due to resistance. The GAIN provision requires FDA to take certain steps to encourage drug sponsors to develop antibiotics, for example, as part of the QIDP designation, the FDA's review of the drug application is expedited and QIDP products qualify for an additional five years of marketing exclusivity to be added to exclusivities already granted by the Food, Drug, and Cosmetic Act.²

For a drug product to be designated a QIDP, the sponsor is required to demonstrate that the drug is an "antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections."³ A 2018 analysis found that the FDA has granted QIDP designation to 147 products, of which 12 have been approved (9 of the 12 QIDPs were approved for one or more indications).⁴

FDA Drugs Approved with the QIDP, as of October 2016 ^{5,6}		
Drug name and sponsor	Approval date	Indication
Dalvance (dalbavancin hydrochloride) Allergan, Inc.	May 23, 2014	Antibacterial to treat acute bacterial skin and skin structure infections
Sivextrob (tedizolid phosphate) for tablet and injection Merck & Co., Inc.	June 20, 2014	Antibacterial to treat acute bacterial skin and skin structure infections
Orbactiv (oritavancin diphosphate) The Medicines Company	Aug. 6, 2014	Antibacterial to treat acute bacterial skin and skin structure infections
Zerbaxa (ceftolozane and tazobactam) Merck & Co., Inc.	Dec. 19, 2014	Antibacterial to treat complicated intra-abdominal infections, in combination with metronidazole, and complicated urinary tract infections, including pyelonephritis
Avycaz (ceftazidime and avibactam) Allergan, Inc.	Feb. 25, 2015	Antibacterial to treat complicated intra-abdominal infections in combination with metronidazole, and complicated urinary tract infections in patients who

² Woodcock, J. U.S. Food & Drug Administration. Three encouraging steps towards new antibiotics. September 23, 2014. Available at: <https://blogs.fda.gov/fdavoices/index.php/tag/qualified-infectious-disease-product-qidp/>

³ Food and Drug Administration Safety and Innovation Act. Pub. L. 112–144, title V, § 508, July 9, 2012, 126 Stat. 1045. Available at: <https://www.gpo.gov/fdsys/pkg/USCODE-2012-title21/pdf/USCODE-2012-title21-chap9-subchapV-partA-sec355f.pdf>

⁴ Pink Sheet. US FDA Joins Chorus Of Concerns About Results of GAIN Act. February 5, 2018. Available at: <https://pink.pharmaintelligence.informa.com/PS122454/US-FDA-Joins-Chorus-Of-Concerns-About-Results-Of-GAIN-Act>

⁵ Ibid.

⁶ U.S. National Library of Medicine. Daily Med. Available at: <https://dailymed.nlm.nih.gov/dailymed/index.cfm>

		have limited or no alternative treatment options, including acute pyelonephritis
Cresemba [®] (isavuconazonium sulfate) for capsule and injection Astellas Pharma U.S., Inc.	Mar. 6, 2015	Antifungal to treat adults with two types of invasive fungal infections (aspergillosis and invasive mucormycosis)
Baxdela (delafloxacin meglumine) for tablet and injection Melinta Therapeutics	June 19, 2017	Indicated in adults for the treatment of acute bacterial skin and skin structure infections.
Vabomere (meropenem and vaborbactam) Rempex Pharmaceuticals	August 29, 2017	Indicated for the treatment of adults with complicated urinary tract infections (cUTI) including pyelonephritis caused by: <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> , and <i>Enterobacter cloacae</i> species complex.
Solosec (secnidazole granules) Symbiomix Therapeutics	September 17, 2017	Indicated for the treatment of bacterial vaginosis in adult women.

Inter-Agency Support

The FDA is incentivizing the development of antibiotics to treat drug-resistant pathogens, but CMS has not modernized its publicly stated approach for coverage and access requirements for anti-infectives beyond the minimal standards. Janet Woodcock, M.D., Director of FDA's Center for Drug Evaluation and Research notes it is critical for healthcare providers to prescribe QIDP products once approved,⁷ and while the FDA is committed to this new designation, it is equally important for CMS to ensure access for these products as they come to market. Coverage requirements in Part D, except for the protected classes, are a minimum of 2 drugs per category/class.⁸ In addition to this explicit requirement, CMS also establishes additional coverage protocols and plan formulary review through its use of clinical appropriateness and non-discrimination reviews. CMS should ensure accessibility of QIDPs on formularies, whether through explicit requirements for plans or by the reviews the agency performs for clinical appropriateness and non-discrimination.

⁷ Woodcock, J. U.S. Food & Drug Administration. Three encouraging steps towards new antibiotics. September 23, 2014. Available at: <https://blogs.fda.gov/fdavoices/index.php/tag/qualified-infectious-disease-product-qidp/>

⁸ CMS. Medicare Prescription Drug Benefit Manual. January 2016. Available at: <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Part-D-Benefits-Manual-Chapter-6.pdf>



Health and Economic Burden

With more than 2 million people sickened every year in the U.S. with antibiotic resistant infections and at least 23,000 people who die each year as a direct result,⁹ it is clear antibiotic resistance is a major public health problem. Antibiotic resistance can have many negative downstream effects, such as enhancing virulence, causing a delay in therapy administration, creating an increased need for surgery, and increasing treatment costs.^{10,11} For example, a study of hospital costs associated with antibiotic-resistant gram-negative bacteria found that resistance was associated with 29.3% higher total hospital costs and 23.8% increased length of stay compared to the costs and length of stay for infections caused by susceptible gram-negative pathogens.¹² A separate study measured the direct patient impact and found that patients with antibiotic resistant infections have higher costs by approximately \$6,000–\$30,000 compared to patients with infections due to antimicrobial-susceptible organisms.¹³ The CDC has estimated the annual domestic impact of antibiotic-resistant infections to the U.S. economy to be \$20–\$30 billion in excess of direct healthcare costs.¹⁴

While Medicare Advantage (MA) plans have a more inherent incentive to cover these medications as they are responsible for A (hospital insurance) and B (medical care incident to a physician service), Insmmed is particularly concerned about access in standalone Prescription Drug Plans (PDPs). Because standalone PDPs do not face the financial risk of medical expenses, they may be less likely to provide favorable formulary coverage for these products. PDPs currently serve as the avenue for most beneficiaries who are enrolled in Part D to receive appropriate antibiotics, which makes it especially important for CMS to ensure coverage in this market. Additionally, comprehensive coverage and access can help drive adherence, which CMS identifies as a contributing factor to better health outcomes and lower costs. As the agency notes in the 2019 Advance Notice and Draft Call Letter, “We believe that...medication adherence can also produce medical spending offsets, which could lead to government and taxpayer savings in the trust fund, as well as beneficiary savings in the form of reduced premiums.”¹⁵

⁹ Department of Health and Human Services, Centers for Disease Control and Prevention, Antibiotic Resistance Threats in the United States, 2013. Atlanta, Ga. April 2017. Available at: <http://www.cdc.gov/drugresistance/threat-report-2013/>

¹⁰ Cosgrove S, Carmeli Y. The Impact of Antimicrobial Resistance on Health and Economic Outcomes. Clinical Infectious Diseases. 2003; 36:1433–1437. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12766839>

¹¹ Cosgrove, S. The Relationship between Antimicrobial Resistance and Patient Outcomes: Mortality, Length of Hospital Stay, and Health Care Costs. Clinical Infectious Diseases, 2006; 42:82–89, Available at: <https://doi.org/10.1086/499406>

¹² Mauldin, P, Salgado, C, Hansen, Ida. Attributable Hospital Cost and Length of Stay Associated with Health Care-Associated Infections Caused by Antibiotic-Resistant Gram-Negative Bacteria. Antimicrobial Agents Chemotherapy. 2010; 54:109–115. Available at: <http://aac.asm.org/content/54/1/109.full#ref-7>

¹³ Cosgrove, S. The Relationship between Antimicrobial Resistance and Patient Outcomes: Mortality, Length of Hospital Stay, and Health Care Costs. Clinical Infectious Diseases, 2006; 42:82–89. Available at: <https://doi.org/10.1086/499406>

¹⁴ Executive Office of the President, President’s Council of Advisors on Science and Technology, Report to the President on Combating Antibiotic Resistance, Washington, D.C.: September 2014. Available at: <https://www.cdc.gov/drugresistance/pdf/report-to-the-president-on-combating-antibiotic-resistance.pdf>

¹⁵ CMS. Medicare Program; Contract Year 2019 Policy and Technical Changes to the Medicare Advantage, Medicare Cost Plan, Medicare Fee-for-Service, the Medicare Prescription Drug Benefit Programs, and the PACE Program. November 2017. <https://s3.amazonaws.com/public-inspection.federalregister.gov/2017-25068.pdf>



Insmmed supports the FDA's focus on innovative antibiotic agents and incenting their development, but CMS must provide inter-agency support and ensure coverage of and access to these products. We encourage CMS to think more holistically around coverage criteria and require non-discrimination tests for plans in this emerging category/class. We recommend CMS align coverage policies and criteria with other agency priorities, such as reducing antibiotic resistance, particularly because of the clinical need and potential overall cost savings to the Medicare program.

Insmmed appreciates the opportunity to comment on the Draft 2019 Advance Notice and Call Letter. We look forward to working with CMS to improve coverage of QIDPs and ensure continued beneficiary access to high quality care.

Sincerely,

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Insmmed Incorporated