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Issued: March 25, 2025, Philadelphia, PA

Blujepa (gepotidacin) approved by US FDA for treatment of uncomplicated urinary tract infections (uUTIs) in female adults and pediatric patients 12 years of age and older

- *Blujepa* is the first in a new class of oral antibiotics for uUTIs in nearly 30 years
- Over half of all women experience a uUTI in their lifetime, with approximately 30% suffering from a recurrent episode
- Approval based on data from the pivotal phase III EAGLE-2 and EAGLE-3 trials

GSK plc (LSE/NYSE: GSK) today announced that the US Food and Drug Administration (FDA) has approved *Blujepa* (gepotidacin) for the treatment of female adults (≥ 40 kg) and pediatric patients (≥ 12 years, ≥ 40 kg) with uncomplicated urinary tract infections (uUTIs) caused by the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii* complex, *Staphylococcus saprophyticus* and *Enterococcus faecalis*.

Discovered by GSK scientists, *Blujepa* is a first-in-class oral antibiotic with a novel mechanism of action that is part of GSK's infectious diseases portfolio.

Tony Wood, Chief Scientific Officer, GSK, said: "The approval of *Blujepa* is a crucial milestone with uUTIs among the most common infections in women. We are proud to have developed *Blujepa*, the first in a new class of oral antibiotics for uUTIs in nearly three decades, and to bring another option to patients given recurrent infections and rising rates of resistance to existing treatments."

uUTIs are the most common infection in women, impacting up to 16 million women in the US annually.¹⁻⁴ Over half of all women are affected by uUTI in their lifetime,⁵ with approximately 30% suffering from at least one recurrent episode which can cause significant patient burden, including discomfort and restriction of daily activities.⁶ New treatments are needed as the number of uUTIs caused by drug-resistant bacteria is increasing which can result in higher treatment failure rates.⁷

Thomas Hooton, MD, Professor of Clinical Medicine, University of Miami School of Medicine said: "For many, uUTIs can be a burden that severely impacts daily life. With an increasing number of patients experiencing recurrent infections, there remains a clear need for continued research of antimicrobials to help address ongoing patient challenges and the strain on healthcare systems."

The approval is based on positive results from the pivotal phase III EAGLE-2 and EAGLE-3 trials which demonstrated non-inferiority to nitrofurantoin, one of the leading current standard of care options for uUTI, in female adults (≥ 40 kg) and pediatric patients (≥ 12 years, ≥ 40 kg) with a confirmed uUTI. In EAGLE-2, *Blujepa* demonstrated non-inferiority in therapeutic success which occurred in 50.6% (162/320) of participants compared to 47.0% (135/287) for nitrofurantoin (covariate-adjusted treatment difference 4.3%, 95% CI (-3.6, 12.1)). In EAGLE-3, *Blujepa* demonstrated statistically significant superiority versus nitrofurantoin (one-sided p-value 0.0003). Therapeutic success occurred in 58.5% (162/277) of participants compared to 43.6% (115/264) for nitrofurantoin (covariate-adjusted treatment difference 14.6%, 95% CI (6.4, 22.8)).

The safety and tolerability profile of *Blujepa* in the EAGLE-2 and EAGLE-3 phase III trials was consistent with previous trials. The most commonly reported adverse events (AEs) in *Blujepa* participants were gastrointestinal (GI). Diarrhea was the most common (16% of participants), followed by nausea (9%). Of the participants who reported GI AEs in the *Blujepa* group, the most common maximum severity was mild (69% Grade 1) and moderate (28% Grade 2). Participants with Grade 3 GI events accounted for 3% of all patients with GI events and occurred in <1% of all

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participants. There was one drug-related serious adverse event in each treatment arm (*Blujepa* and nitrofurantoin) across the two trials.

US commercial launch is planned in 2H 2025.

The development of *Blujepa* (gepotidacin) has been funded in part with federal funds from the US Department of Health and Human Services, Administration for Strategic Preparedness and Response, Biomedical Advanced Research and Development Authority (BARDA), under Other Transaction Agreement number HHSO100201300011C and with federal funds awarded by the Defense Threat Reduction Agency under agreement number HDTRA1-07-9-0002.

About *Blujepa* (gepotidacin)

Blujepa, discovered by GSK scientists, is a bactericidal, first-in-class triazaacenaphthylene antibiotic that inhibits bacterial DNA replication by a distinct binding site, a novel mechanism of action and for most pathogens, provides well-balanced inhibition of two different Type II topoisomerase enzymes. This provides activity against most target uropathogens (such as *Escherichia coli* and *Staphylococcus saprophyticus*), and *Neisseria gonorrhoeae*, including isolates resistant to current antibiotics. Due to the well-balanced inhibition for most pathogens, *Blujepa* target-specific mutations in both enzymes are needed to significantly affect susceptibility to *Blujepa*. Therefore, a lower potential for resistance development is expected. Efficacy and safety in patients have been demonstrated in uUTI and gonorrhea phase III clinical trials, including in patients with drug-resistant pathogens. **Please see full Prescribing Information including Medication Guide, [available here](#).**

About the EAGLE (Efficacy of Antibacterial Gepotidacin Evaluated) phase III program

The global phase III clinical program for *Blujepa* (gepotidacin) in adults and pediatric patients consists of three trials:

EAGLE-2 and EAGLE-3 (non-inferiority uUTI trials) compared the efficacy and safety of *Blujepa* (1,500mg administered orally twice daily for five days) to nitrofurantoin (100mg administered orally twice daily for five days) with 1531 and 1605 female adults and pediatric patients with uUTIs, respectively. Across both trials, the planned duration of follow-up for participants was approximately 28 days, and the primary endpoint, a stringent composite measure of efficacy, was the combined clinical and microbiological response at the Test-of-Cure (ToC) visit (days 10-13) in patients with qualifying uropathogens susceptible to nitrofurantoin.

EAGLE-1 (non-inferiority uncomplicated urogenital gonorrhea trial) compared the efficacy and safety of *Blujepa* to ceftriaxone plus azithromycin in 628 patients with uncomplicated urogenital gonorrhea caused by *N. gonorrhoeae*.

GSK in infectious diseases

GSK has pioneered innovation in infectious diseases for over 70 years, and the Company's pipeline of medicines and vaccines is one of the largest and most diverse in the industry, with a goal of developing preventive and therapeutic treatments for multiple disease areas or diseases with high unmet needs globally. Our expertise and capabilities in infectious disease strongly position us to help prevent disease and mitigate the challenge of antimicrobial resistance (AMR).

In antimicrobials, in addition to gepotidacin, GSK entered into an exclusive license agreement with Spero Therapeutics, Inc. in September 2022 to add tebipenem HBr, a late-stage antibiotic and potential treatment for complicated urinary tract infections (cUTIs), to the pipeline and are currently enrolling for PIVOT-PO, a phase III trial. In March 2023, GSK announced an exclusive license agreement with Scynexis for *Brexafemme* (ibrexafungerp tablets), a first-in-class antifungal for the treatment of vulvovaginal candidiasis (VVC) and reduction in the incidence of recurrent VVC.

BLUJEPA (gepotidacin) tablets, for oral use

Indication(s) and Important Safety Information (ISI)

INDICATION

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BLUJEPA is indicated for the treatment of female adult and pediatric patients 12 years of age and older weighing at least 40 kilograms (kg) with uncomplicated urinary tract infections (uUTI) caused by the following susceptible microorganisms: *Escherichia coli*, *Klebsiella pneumoniae*, *Citrobacter freundii* complex, *Staphylococcus saprophyticus*, and *Enterococcus faecalis*.

Usage to Reduce Development of Drug-Resistant Bacteria

To reduce the development of drug-resistant bacteria and maintain the effectiveness of BLUJEPA and other antibacterial drugs, BLUJEPA should be used only to treat infections that are proven or strongly suspected to be caused by bacteria.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

BLUJEPA is contraindicated in patients with a history of severe hypersensitivity to BLUJEPA

WARNINGS AND PRECAUTIONS

QTc Prolongation

A dose and concentration-dependent prolongation of the QTc interval has been observed with BLUJEPA. Avoid use of BLUJEPA in patients with a history of QTc prolongation or with relevant pre-existing cardiac disease, patients taking antiarrhythmic agents, and in patients receiving drugs that prolong the QT interval. Due to an increase in BLUJEPA exposure, avoid concomitant administration of BLUJEPA with strong CYP3A4 inhibitors, in patients with severe hepatic impairment (Child-Pugh Class C), and in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min)

Acetylcholinesterase inhibition

Dysarthria and other adverse reactions potentially attributed to acetylcholinesterase inhibition have been reported with BLUJEPA, an acetylcholinesterase inhibitor. Increased cholinergic effects can be associated with severe adverse effects including atrioventricular block, bradycardia, bronchospasm, seizures/convulsions, and vasovagal syncope. Monitor patients with underlying medical conditions that may be exacerbated by acetylcholinesterase inhibition and patients receiving succinylcholine-type neuromuscular blocking agents, systemic anticholinergic medications, or non-depolarizing neuromuscular blocking agents

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, have been reported in patients receiving BLUJEPA. If an allergic reaction to BLUJEPA occurs, discontinue the drug and institute appropriate supportive measures.

Clostridioides difficile-Associated Diarrhea

Clostridioides difficile Infection (CDI) has been reported with nearly all systemic antibacterial agents, including BLUJEPA. Evaluate patients who develop diarrhea

ADVERSE REACTIONS

The most common adverse reactions occurring in $\geq 1\%$ of patients are diarrhea, nausea, abdominal pain, flatulence, headache, soft feces, dizziness, vomiting, and vulvovaginal candidiasis

DRUG INTERACTIONS

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CYP3A4 Inhibitors: Avoid coadministration of BLUJEPA with strong CYP3A4 inhibitors due to increased gepotidacin exposure

CYP3A4 Inducers: Avoid coadministration of BLUJEPA with strong CYP3A4 inducers due to decreased gepotidacin exposure

CYP3A4 Substrates: Avoid coadministration of BLUJEPA with drugs that are extensively metabolized by CYP3A4 and have a narrow therapeutic window

Digoxin: Due to an increase in digoxin exposures, consider monitoring digoxin serum concentration, as appropriate, with concomitant administration of BLUJEPA

USE IN SPECIFIC POPULATIONS

Renal Impairment: Avoid use of BLUJEPA in patients with severe renal impairment with eGFR <30 ml/min, including those receiving dialysis

Hepatic Impairment: Avoid use of BLUJEPA in patients with severe hepatic impairment (Child-Pugh Class C)

About GSK

GSK is a global biopharma company with a purpose to unite science, technology, and talent to get ahead of disease together. Find out more at [gsk.com](https://www.gsk.com).

GSK inquires

Media:	Tim Foley	+44 (0) 20 8047 5502	(London)
	Sarah Clements	+44 (0) 20 8047 5502	(London)
	Kathleen Quinn	+1 202 603 5003	(Washington DC)
	Lyndsay Meyer	+1 202 302 4595	(Washington DC)
Investor Relations:	Constantin Fest	+44 (0) 7831 826525	(London)
	Annabel Brownrigg-Gleeson	+44 (0) 7901 101944	(London)
	James Dodwell	+44 (0) 20 8047 2406	(London)
	Mick Readey	+44 (0) 7990 339653	(London)
	Steph Mountifield	+44 (0) 7796 707505	(London)
	Jeff McLaughlin	+1 215 751 7002	(Philadelphia)
	Frannie DeFranco	+1 215 751 4855	(Philadelphia)

Cautionary statement regarding forward-looking statements

GSK cautions investors that any forward-looking statements or projections made by GSK, including those made in this announcement, are subject to risks and uncertainties that may cause actual results to differ materially from those projected. Such factors include, but are not limited to, those described in the "Risk Factors" section in GSK's Annual Report on Form 20-F for 2024.

Registered in England & Wales:

No. 3888792

Registered Office:

79 New Oxford Street
London
WC1A 1DG

References

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