Health Technology Briefing
October 2024

Clindamycin for treating bacterial vaginosis

Company/Developer	Organon

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 29891	NICE ID: Not available	UKPS ID: 671361

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Clindamycin phosphate vaginal gel is in clinical development for the treatment of bacterial vaginosis, which is a common cause of unusual vaginal discharge caused by a change in the natural balance of bacteria in the vagina. Around half of patients with bacterial vaginosis do not show any symptoms; when symptoms are present, the condition is characterised by a fishy-smelling vaginal discharge. This condition is not usually associated with soreness, itching, or irritation. Bacterial vaginosis has a high recurrence rate of around 50% within 1 year and can have a significant negative impact on quality of life for patients, in addition to a risk of serious health complications, such as pre-term labour and pelvic inflammatory disease. Also, adherence to current treatments can be poor as multiple doses are required. These factors highlight the need for more effective therapies for this indication.

Clindamycin phosphate vaginal gel is an antibiotic that works by stopping bacteria from making proteins they need to grow and multiply. It does this by attaching to a specific part of the bacteria's protein-making machinery (ribosome) and blocking its function. Clindamycin phosphate gel is administered as a single dose intravaginally and at body temperature transitions from liquid to gel, allowing it to stay in place and deliver medication effectively. If licenced, clindamycin phosphate vaginal gel will provide a novel treatment option for bacterial vaginosis.

Proposed Indication

Treatment of bacterial vaginosis (BV).[1]

Technology

Description

Clindamycin phosphate vaginal gel (Xaciato, DARE-BV1) is an antibacterial drug that inhibits bacterial protein synthesis by binding to the 23S RNA of the 50S subunit of the ribosome.[2] It impedes both the assembly of the ribosome and the translation process. The molecular mechanism through which this occurs is suggested to be due to clindamycin's three-dimensional structure, which closely resembles the 3'-ends of L-Pro-Met-tRNA and deacylated-tRNA during the peptide elongation cycle. In acting as a structural analogue of these tRNA molecules, clindamycin impairs peptide chain initiation and may stimulate dissociation of peptidyl-tRNA from bacterial ribosomes.[3] Clindamycin is predominantly bacteriostatic. Although clindamycin phosphate is inactive in vitro, rapid in vivo hydrolysis converts it to active clindamycin.[2]

Clindamycin phosphate vaginal gel is in clinical development for the treatment of bacterial vaginosis (BV). In the phase III clinical trial (NCT04370548), one dose of clindamycin phosphate vaginal gel, 2% (100mg clindamycin) was applied intravaginally.[1]

Key Innovation

BV can have a significant negative impact on a woman's quality of life and can have serious health implications; it can cause pre-term labour, pelvic inflammatory disease, and increased transmission of HIV and other sexually transmitted infections.[4] The combination of the risk of complications and likelihood for recurrence means that effective treatment options for BV are required.

Current treatments for BV often require multiple doses, meaning that adherence to treatment regimens can be onerous. Clindamycin phosphate vaginal gel only requires a single dose so could simplify the treatment process and improve patient compliance. Clindamycin phosphate vaginal gel also uses a novel thermosetting bioadhesive hydrogel formulation. This means it transitions from a liquid to a gel at body temperature, enhancing its ability to stay in place and deliver medication effectively.[5] If licensed, clindamycin phosphate vaginal gel will offer an additional treatment option for patients with BV.

Regulatory & Development Status

Clindamycin phosphate vaginal gel does not currently have marketing authorisation in the EU/UK for any indication.

Clindamycin phosphate vaginal gel is not in phase II/III development for any other indication.[6]

Clindamycin phosphate vaginal gel received FDA Fast Track designation in March 2020 for the treatment of BV in female patients aged 12 years and older.[7]

Patient Group

Disease Area and Clinical Need

BV is a common cause of unusual vaginal discharge that is characterised by an overgrowth of predominantly anaerobic organisms and a loss of lactobacilli. The vagina loses its normal acidity, and its pH increases to greater than 4.5.[8] The risk of developing BV is increased by being sexually active, the use of intrauterine devices and using perfumed products in or around the vagina.[8] Approximately 50% of women with BV are asymptomatic. When symptoms are present, BV is characterised by a fishy-smelling vaginal discharge. It is not usually associated with soreness, itching, or irritation.[8] It is common for BV to recur, usually within a few months.

Globally, the prevalence of BV ranges from 23 to 29% of women in the general population with significant variation by geographical region and race.[9] Reported prevalence rates in specific population sub-groups include 5% in a group of asymptomatic college students, 12% in pregnant women attending an antenatal clinic in the UK, and 30% in women undergoing termination of pregnancy.[10] BV is also more prevalent in Black women (45–55%) than in Caucasian women (5–15%).[11] In England, 2023-24, there were 764 finished consultant episodes (FCE) and 685 admissions for acute, subacute and chronic vaginitis (ICD-10 codes N76.0 and N76.1) which resulted in 705 FCE bed days and 154 day cases.[12]

Recommended Treatment Options

NICE recommend the following treatment options for BV:[13]

- Oral metronidazole 400 mg twice a day for 5 to 7 days
- For those who prefer topical treatment or cannot tolerate oral metronidazole:
  - Intravaginal metronidazole gel 0.75% once a day for 5 days (off-label for women aged younger than 18 years)
  - Intravaginal clindamycin cream 2% once a day for 7 days

Clinical Trial Information

Trial	**DARE-BVFREE**, NCT04370548; A phase 3 multi-center, double-blind, placebo-controlled, randomized study of DARE-BV1 in the treatment of bacterial vaginosis **Phase 3** - Completed **Location:** USA **Study completion date:** December 2020
Trial Design	Randomised, parallel assignment, quadruple masked, double blind, placebo controlled
Population	N = 307 (actual); female subjects with BV; aged 12 years and older
Intervention(s)	5g of clindamycin phosphate vaginal gel, 2 % (100mg) applied intravaginally
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: Number of patients with clinical cure at the Test of Cure (TOC) visit (day 21-30). [time frame: visit 3 day 21-30 post randomization] See trial record for full list of all outcomes
Results (efficacy)	See trial record
Results (safety)	See trial record

Estimated Cost

The cost of clindamycin phosphate vaginal gel is not yet known.

Relevant Guidance

NICE Guidance

NICE Clinical Knowledge Summary. Bacterial Vaginosis. July 2023.

NHS England (Policy/Commissioning) Guidance

No relevant guidance identified.

Other Guidance

- West of Scotland Sexual Health. Bacterial Vaginosis Guideline. 2021.[14]
- Sherrard, J., Wilson, J., Donders, G., Mendling, W., Jensen, J.S.. 2018 European (IUSTI/WHO) International Union against sexually transmitted infections (IUSTI) World Health Organisation (WHO) guideline on the management of vaginal discharge. 2018.[11]
- British Association for Sexual Health and HIV (BASHH). UK National Guideline for the management of Bacterial Vaginosis. 2012.[10]

Additional Information

References

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11 Sherrard J, Wilson J, Donders G, Mendling W, Jensen JS. 2018 European (IUSTI/WHO) International Union against sexually transmitted infections (IUSTI) World Health Organisation (WHO) guideline on the management of vaginal discharge. *Int J STD AIDS*. 2018;29(13):1258-72. Available from: https://doi.org/10.1177/0956462418785451.

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