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Health Technology Briefing
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Cabotegravir (long-acting intramuscular injection) with rilpivirine (long-acting intramuscular injection) for treating virologically suppressed HIV-1 infection in adolescents

Company/Developer	ViiV Healthcare UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 25399	NICE ID: Not available	UKPS ID: 674915

Licensing and Market Availability Plans

Currently in phase I/II clinical development.

Summary

Long-acting (LA) cabotegravir in combination with LA rilpivirine is being developed as a treatment for adolescents with virologically suppressed human immunodeficiency virus (HIV)-1. Virologically suppressed means that the amount of HIV in the blood is very low due to ongoing treatment. If left untreated, HIV-1 infection leads to the immune system becoming severely weakened, resulting in acquired immunodeficiency syndrome, a chronic and life-threatening condition. Adolescents with HIV-1 often face challenges in maintaining effective treatment, leading to worse health outcomes compared to adults. There is a need for new treatment options tailored to this age group to help improve long-term health and quality of life.

Cabotegravir works by blocking an important step that HIV needs to multiply, preventing the virus from integrating its genetic material into human cells. Rilpivirine helps stop the virus from making new copies of itself by interfering with an enzyme that HIV needs to reproduce. This treatment is a LA option given by intramuscular injections and offers a new, LA treatment option for adolescents living with HIV-1.

Proposed Indication

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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The treatment of virologically suppressed Human Immunodeficiency Virus (HIV) in adolescents (at least 12 years of age and weighing at least 35kg).[1]

Technology

Description

Cabotegravir (Vocabria, CAB) inhibits HIV integrase by binding to the integrase active site and blocking the strand transfer step of retroviral deoxyribonucleic acid (DNA) integration which is essential for the HIV-1 replication cycle.[2] As a result this prevents strand transfer of the viral genome into the host genome, and therefore replication of the virus.[3] Rilpivirine (Rekambys, RPV) is a diarylpyrimidine non-nucleoside reverse transcriptase inhibitor (NNRTI) of HIV-1 and it's activity is mediated by non-competitive inhibition of HIV-1 reverse transcriptase (RT). Rilpivirine does not inhibit the human cellular DNA polymerases α, β and γ.[4] Instead, rilpivirine's flexible structure around the aromatic rings allows the adaptation to changes in the non-nucleoside RT binding pocket, reducing the likelihood of viral mutations conferring resistance.[5]

LA cabotegravir 600 mg in combination with LA rilpivirine 900 mg intramuscular injections are currently in development for the treatment of adolescents aged 12-17 years with virologically suppressed HIV-1.[1] In the phase I/II trial (MOCHA, NCT03497676) participants in Cohort 1C (CAB LA only), participants receive an intramuscular injection of 600 mg at Week 4, followed by either 400 mg at Weeks 8 and 12 (Q4W dosing) or 600 mg at Weeks 4 and 8 (Q8W dosing). In Cohort 1R (RPV LA only), participants receive an intramuscular injection of 900 mg at Week 4, followed by either 600 mg at Weeks 8 and 12 (Q4W dosing) or 900 mg at Weeks 4 and 8 (Q8W dosing). In Cohort 2A (CAB LA + RPV LA after oral lead-in), participants receive 600 mg CAB LA + 900 mg RPV LA at Weeks 4 and 8, then every 8 weeks from Week 16. In Cohort 2B (CAB LA + RPV LA, no oral lead-in), participants receive 600 mg CAB LA + 900 mg RPV LA at Weeks 0 and 4, then every 8 weeks from Week 12. Throughout the clinical trial patients remained on their original antiretroviral treatments, but were not provided through the study.[1,6]

Key Innovation

There is an unmet need for adolescents aged 12-17 years with virologically suppressed HIV-1. This is highlighted by the evidence that suggests that adolescents with HIV have worse health outcomes along each step of the HIV care cascade worldwide compared with adults.[7] Advances in treatment mean HIV can be a manageable condition, but some people face challenges with taking daily oral regimens, including adherence, the daily reminder of HIV, and a fear of disclosure and associated stigma.[8] LA cabotegravir in combination with LA rilpivirine does provide a new treatment option for adolescents with virologically suppressed HIV-1.

Regulatory & Development Status

Oral cabotegravir is indicated in combination with oral rilpivirine for the short-term treatment of HIV-1 infection in adults and adolescents (at least 12 years of age and weighing at least 35 kg) who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen without present or past evidence of viral resistance to, and no prior virological failure with agents of the NNRTI and integrase inhibitor class for:[9]

- Oral lead-in to assess tolerability of cabotegravir and rilpivirine prior to administration of LA cabotegravir injection plus LA rilpivirine injection.
- Oral therapy for adults and adolescents who will miss planned dosing with cabotegravir injection plus rilpivirine injection.

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Cabotegravir and rilpivirine are not in phase II/III development for any other indication.[10]

Patient Group

Disease Area and Clinical Need

HIV is a virus that attaches itself to CD4 lymphocytes, which protect the body against various pathogens. Once attached, it enters the CD4 cells and uses them to make thousands of copies of itself. These copies then leave the CD4 cells, killing the cells in the process.[11] If left untreated, the immune system can weaken significantly, leading to acquired immunodeficiency syndrome (AIDS). AIDS is a chronic and potentially life-threatening condition.[12] Approximately two to six weeks after infection, flu-like symptoms of HIV begin which often includes fever, rash, sore throat and swollen glands, lasting for one to two weeks. After initial symptoms have dissipated, an asymptomatic phase occurs, and further symptoms may not present for many years. When the immune system becomes severely damaged, later stage symptoms include weight loss, chronic diarrhoea, night sweats, recurrent infections and serious illnesses.[13] The highest risk of HIV is among men who have unprotected sex with men, people who share needles for drug use, and those in high-prevalence areas.[11] Those with HIV that take their medication as prescribed will eventually reach a point of viral suppression where HIV is not detectable in their blood or genital secretions by even the most sensitive viral load testing methods currently available. However, this state of viral suppression can be reversed if a person loses access or stops taking the medication as prescribed.[14]

The most recent figures for adolescents with HIV, as reported in the Children's HIV and AIDS Reporting System (CHARS) annual report 2022-23, indicate that there are 301 children and young people in active paediatric care in England. Of these, 133 (44.2%) are aged 15 to 19 years.[15] In England, in 2023-2024 there were 3,000 finished consult episodes (FCE) for HIV (ICD10 code: B20-B24), resulting in 558 day cases and 20,171 FCE bed days.[16]

Recommended Treatment Options

There is no treatment option recommended by NICE for virologically suppressed HIV-1 infection in adolescents. The European AIDS Clinical Society (EAC) recommends the use of antiretroviral therapy in all children and adolescents with HIV irrespective of age, clinical stage, CD4 count and viral load.[17]

Clinical Trial Information

Trial	**MOCHA;** NCT03497676; Phase I/II Study of the Safety, Acceptability, Tolerability, and Pharmacokinetics of Oral and Long-Acting Injectable Cabotegravir and Long-Acting Injectable Rilpivirine in Virologically Suppressed HIV-Infected Children and Adolescents **Phase 1/2** - Active, not recruiting **Locations**: USA and other countries **Primary completion date:** 18 February 2023
Trial Design	Non-randomized, sequential assignment, open label
Population	N=168 (actual); participants with HIV-1 that are virologically suppressed; adolescents aged 12-17 years.

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Intervention(s)	• Cabotegravir (CAB) – administered either orally (30 mg tablet) or as a long-acting injectable (CAB LA) via intramuscular (IM) injection. • Rilpivirine (RPV) – administered either orally (25 mg tablet) or as a long-acting injectable (RPV LA) via IM injection.
Comparator(s)	No active comparator. All participants receive some form of Cabotegravir (CAB) and/or Rilpivirine (RPV) in either oral or long-acting injectable form. Additionally, all participants remained on their previous antiretroviral therapies, though these treatments were not provided through the study.
Outcome(s)	**Primary Outcome Measures:** Safety Outcomes (Adverse Events) • Proportion of participants with Grade 3 or higher AEs • Proportion of participants with serious AEs (SAEs) meeting ICH criteria • Proportion of participants with AEs leading to permanent discontinuation of study product • Proportion of participants who died due to AEs Pharmacokinetics (PK) Measures • Geometric Mean Area Under the Plasma Concentration-Time Curve (AUC) • Maximum Plasma Concentration (Cmax) • Pre-dose Concentration (C0) • Time of Maximum Concentration (Tmax) • Total Body Clearance (CL/F) See trial record for a full list of outcome measures.
Results (efficacy)	See trial record
Results (safety)	See trial record

Estimated Cost

The list price for cabotegravir is £1,197.02 for the bi-monthly intramuscular injection vial (excluding VAT) and £440.47 for the bi-monthly intramuscular injection vial of rilpivirine (excluding VAT).[18]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Cabotegravir with rilpivirine for the oral treatment of HIV-1 (GID-TA10604). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Cabotegravir for preventing HIV-1 in adults and young people (GID-TA11304). Expected date of issue to be confirmed.

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- NICE technology appraisal. Cabotegravir with rilpivirine for treating HIV-1 (TA757). January 2022.
- Quality standard. HIV testing: encouraging uptake (QS157). September 2017.

NHS England (Policy/Commissioning) Guidance

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Other Guidance

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- Children's HIV association (CHIVA). CHIVA Guidance on Transition for adolescents living with HIV. 2010 (updated August 2021).[20]
- St George's Healthcare National Health Service (NHS) trust. Paediatric HIV Guidelines. 2014.[21]

Additional Information

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