Food and Drugs Authority (FDA)

Public Assessment Report (PAR)

Cecolin Vaccine
(Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine (Escherichia coli))

AVCR013/23

Xiamen Innovax Biotech Co., Ltd., China

PART 1: ABSTRACT

Cecolin (Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine (Escherichia coli)) is a mixture of two aluminum hydroxide adjuvant-absorbed recombinant L1 capsid proteins of human papillomavirus (HPV) type-16 and type-18 each self-assembled into virus like particles (VLPs). The HPV-16 and HPV-18 L1 antigens are expressed in Escherichia coli by recombinant DNA technology. Cecolin is manufactured at Xiamen Innovax Biotech Co., Ltd. No. 52, Shanbianhong East Road, Haicang District, Xiamen City, Fujian Province, China 361027.

The Food and Drugs Authority's Guidelines for the registration of human vaccines defines specific evaluation mechanisms for vaccines with stringent standards for quality, safety, and efficacy.

The marketing authorization of Cecolin vaccine by the FDA is based on reliance pathway in which there was an abridged review of Module 1 to Module 5 of submitted Common Technical Document (CTD) dossier to ascertain the quality, safety, efficacy and sameness of Cecolin vaccine prequalified by WHO.

All accepted presentations of Cecolin have been shown in Part 2 of this report. The approved Patient Information Leaflet (PIL), Summary of Product characteristics (SmPC) and the approved labelling have been presented in Part 3, Part 4 and Part 5 respectively.

Scientific discussion on the quality, nonclinical and clinical aspects of Cecolin has been presented in Part 6 of this report.

The detailed steps taken to approve Cecolin by the FDA have been presented in Part 7 of this report.

No action or steps have been taken following the marketing authorization of Cecolin.

PART 2: ACCEPTED PRESENTATIONS

FDA Registration Number	Brand Name	Strength	Pharmaceutical Form	Route of Administration	Immediate Packaging	Content (concentration)	Pack size
FDA/HVC/241-06011	Cecolin	1*	Suspension for injection.	Intramuscular	Glass vial	1*	Carton of 10 single-dose vial

1*= Each dose of 0.5 mL Contains:

- Recombinant human papillomavirus type 16 L1 protein 40µg
- Recombinant human papillomavirus type 18 L1 protein 20µg

PART 3: PATIENT INFORMATION LEAFLET (PIL)

Refer to Part 4 for the Summary of Product Characteristics (SmPC) which suffices in the case of vaccines.

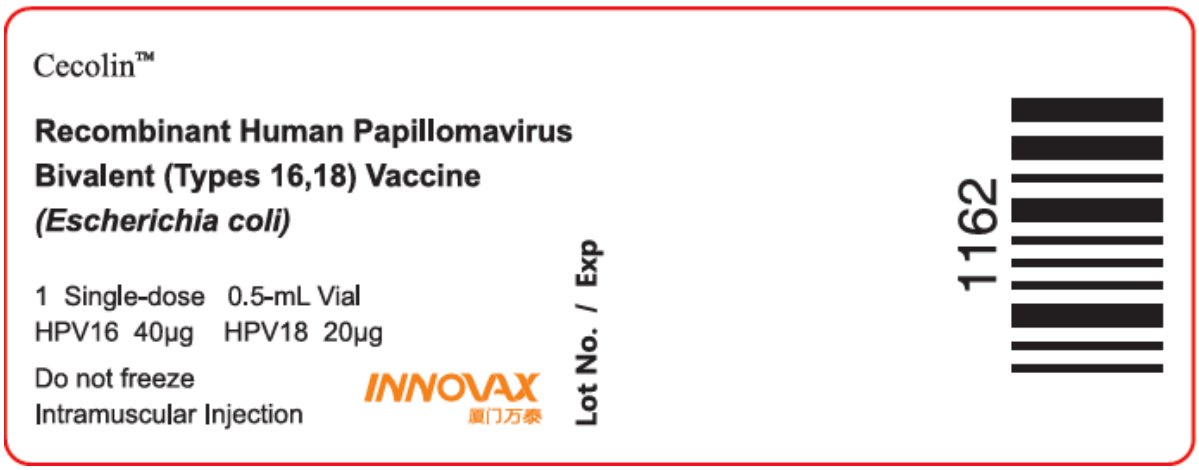
PART 4: SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

Refer to the FDA website below for the SmPC

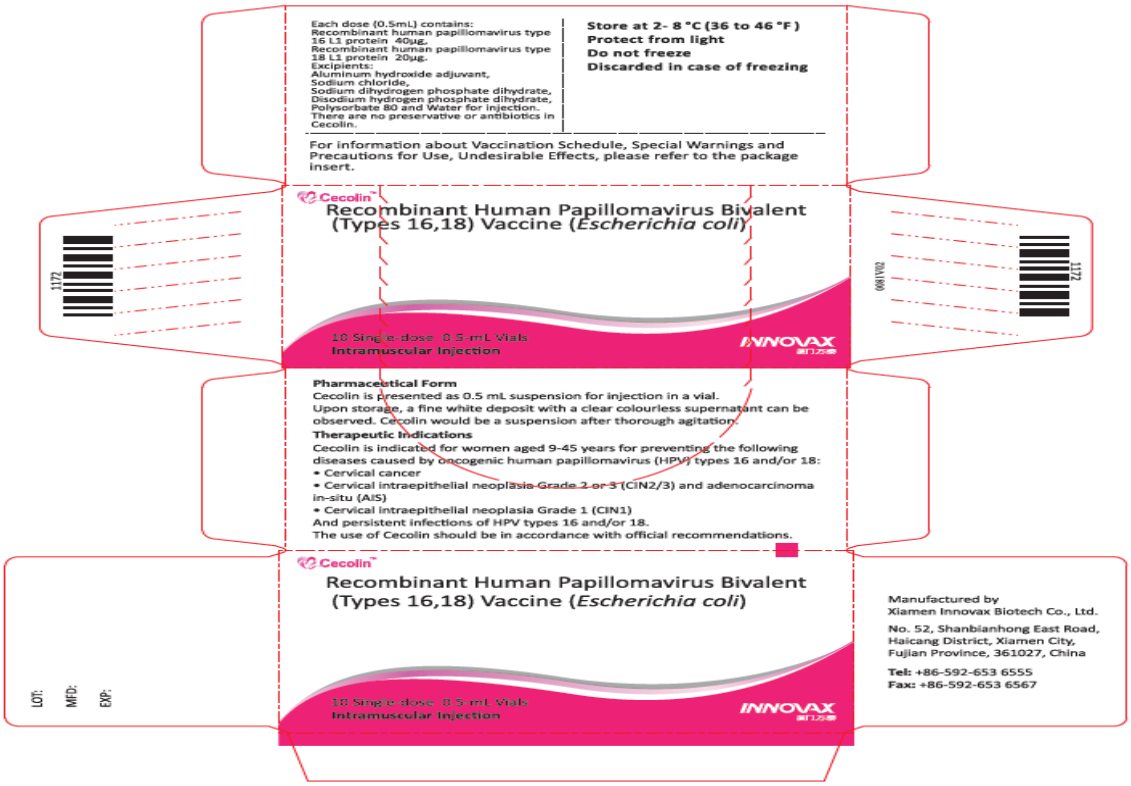
https://www.fdaghana.gov.gh/img/smpc/SmPC%20for%20Cecolin%20Vaccine.pdf

PART 5: LABELLING

Primary label



Secondary label



PART 6: SCIENTIFIC DISCUSSION

6.0. About the Product: General information:

- **Name of vaccine:** Cecolin (Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine (Escherichia coli))
- **Therapeutic indication**: Cecolin is indicated for women aged 9-45 years. Cecolin is used for preventing the following diseases caused by oncogenic human papillomavirus (HPV) types 16 and/or 18: Cervical cancer; Cervical intraepithelial neoplasia Grade 2 or 3 (CIN2/3) and adenocarcinoma in-situ (AIS); Cervical intraepithelial neoplasia Grade 1 (CIN1), and persistent infections of HPV types 16 and/or 18.
- **Manufacturer**: Xiamen Innovax Biotech Co., Ltd. No. 52, Shanbianhong East Road, Haicang District, Xiamen City, Fujian Province, China 361027
- **Local agent**: Imperial Health Sciences Ghana ltd No.3 Pretoria Road,Meridian Business Park , Free Zones, Enclave- Tema, Ghana
- **Pharmaceutical form:** Suspension for injection. Upon storage, a fine white deposit with a clear colourless supernatant can be observed. Would be a suspension after thorough agitation.

- **Storage:** Cecolin must be stored at 2°C to 8°C (36ºF and 46ºF) and protected from light. DO NOT FREEZE. Discard if vaccine has been frozen.
- **Shelf:** 36 months
- **Product presentation:** Cecolin is supplied as a carton of ten single-dose vial (size: 2 mL, type I borosilicate glass, with a rubber butyl stopper)

6.1 Drug Substance (DS)

6.1.1 Manufacturer

Xiamen Innovax Biotech Co., Ltd. No. 52, Shanbianhong East Road, Haicang District, Xiamen City, Fujian Province, China 361027

6.1.2 Manufacturing Process

The manufacturing of the Recombinant Human Papillomavirus Bivalent (Types 16, 18) bulk drug substance consists of three-stage fermentation which include shake-flask culture, seed fermentation and production fermentation, harvesting and purification of HPV 16 & HPV 18 Antigen Bulk.

6.1.3 Stability

Based on the stability data submitted, the purified HPV 16 antigen bulk is stored in the disposable liquid storage bags at 5±3°C for up to 4 weeks, and the purified HPV 18 antigen bulk is stored in the glass bottles for up to 2 months.

6.2 Drug Product (DP)

6.2.1 DP Manufacturer

Xiamen Innovax Biotech Co., Ltd. No. 52, Shanbianhong East Road, Haicang District, Xiamen City, Fujian Province, China 361027

6.2.2 Manufacturing Process

The manufacturing processes preparation of aluminum hydroxide adjuvant, adsorbed HPV16 antigen bulk, preparation for adsorbed HPV18 antigen bulk, preparation of HPV16/18 bivalent vaccine final bulk, filling and visual inspection and packaging.

6.2.3 Stability

Based on the stability data submitted, Cecolin has a shelf life of 36 months under the storage condition of 5±3°C.

6.3 Non-clinical Aspects

6.3.1 Pharmacology

The following primary pharmacodynamic nonclinical studies were conducted and submitted by Marketing Authorization Holder for which data submitted for these studies are considered satisfactory.

- Humoral Response in Mice Immunized with Recombinant HPV 16/18 Bivalent Vaccine
- Humoral response in Rats Immunized with Recombinant HPV 16/18 Bivalent Vaccine
- Humoral response in Rhesus Monkeys Immunized with Recombinant HPV 16/18 Bivalent Vaccine

6.3.2 Toxicology studies

- Acute Toxicity Study of Intramuscular Injection of Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine (Escherichia. coli) in Rats

- Immunotoxicity Study of Repeated Intramuscular Injection of Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine (Escherichia. coli) in Rats

- General Reproductive Toxicity Study (Phase I) of Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine (Escherichia. coli) (in Rats)

- Phase II Reproductive Toxicity Study of Intramuscular Injection of Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine (Escherichia. coli) in Rats

- Muscle Irritation Study of Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine (Escherichia. coli) in Japanese White Rabbits

- Systemic Allergy Study of Recombinant Human Papillomavirus Bivalent (Types 16, 18) Vaccine (Escherichia. coli)

6.4 Clinical Aspects

The Marketing Authorization Holder claimed that the clinical studies were performed in accordance with Good Clinical Practice and all applicable regulatory requirements, including, where applicable, the Declaration of Helsinki.

The clinical study below was conducted and submitted by Marketing Authorization Holder for which data submitted for this study is considered satisfactory for clinical safety and efficacy of Cecolin vaccine.

- Study Report of Phase I Clinical Study of Recombinant Bivalent Human Papillomavirus (Types 16, 18) Vaccine (Escherichia. coli).

- Study Report of A Phase II Clinical Study of Recombinant Bivalent Human Papillomavirus (Types 16, 18) Vaccine (Escherichia. coli)

- A Phase III Clinical Study of A Bivalent Human Papillomavirus (Type 16, 18) Recombinant Vaccine (E.Coli)

- A Bridging Study of a Bivalent Human Papillomavirus (Type 16, 18) Recombinant Vaccine (E.Coli) in Healthy Female Subjects Aged 9-17 years

Part 7: Steps taken for registration

7.1 Submission of the Dossier

The local agent – Imperial Health Sciences Ghana Ltd – representing Xiamen Innovax Biotech Co., Ltd. No. 52, Shanbianhong East Road, Haicang District, Xiamen City, Fujian Province, China 361027, submitted application to the Food and Drugs Authority (FDA) for the registration of Cecolin vaccine.

The following are steps taken for the registration of Cecolin vaccine.

Receipt of application	• 6th October 2023
Acknowledgement of Application	• 20th November 2023
Date of Assessment	• 20th February 2024-18th March 2024
Date of Registration meeting	• 24th May 2024
Date of Approval	• 13th June 2024

7.2 Legal basis

The legal basis for the receipt, evaluation, and registration of product is provided below:

- Section 118 (1) of the Public Health Act, 2012, Act 851
- FDA Reliance Policy (FDA/GEN/GDL - 04/02)
- Guidelines for registration of human vaccines (FDA/VBP/GDL-05/03)
- SOP for evaluation and registration of a Biological Product application (FDA/VBP/SOP -01).
- SOP for good review practices - Biological Product dossier evaluation (FDA/VBP/SOP -05)

This application was reviewed via the FDA Reliance registration pathway

Part 8: Steps taken following registration.

No action or steps have been taken following marketing authorization of Cecolin vaccine.