Gynaia

INSTRUCTIONS FOR USE EPC

M6/PUL model V1.0.1 and PUV
model V1.0.1

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Label

Device Name	EPC
UDI	(01) 05430004729020 (8012) v1.0.1
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Contents	Instructions for use of EPC release v1.0.1
eIFU indicator	Hyperlink to the electronic instructions for use

Symbols

MD CE 2797 UK CA

Explanation of symbols

UDI	Unique Device Identifier = UDI-DI +UDI PI
	UDI-PI = Software version
	Date of manufacture / release date
	Manufacturer
	Consult instructions for use
MD	Medical Device

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WARNING — Decision-support only, not stand-alone.
EPC provides probabilistic risk estimates intended to support clinical assessment. The device is intended to be used as one component within a multi-step clinical assessment pathway and is not intended to be used in isolation

Device description

Intended Purpose	The EPC device, containing the M6/PUL model and PUV scoring system, is intended for use by EPC-trained specialist healthcare professionals as an aid providing a probabilistic risk estimate that informs clinical decision-making in the assessment of pregnancies of unknown location (PUL) and the assessment of pregnancies of uncertain viability (PUV). Based on selected biochemical variables, M6/PUL provides probability estimates for ectopic pregnancy (EP). M6/PUL is intended to be used as part of the two-step PUL triage protocol. Patients with an initial progesterone 2 nmol/L (0.63 ng/mL) or less can be stratified in the low risk group for EP. In these patients, running the M6/PUL model is optional. M6/PUL can be used with or without serum progesterone (M6P and M6NP). In case of intrauterine pregnancy, based on selected clinical and sonographic parameters, PUV provides probability estimates of a viable pregnancy or miscarriage. The outputs are intended to support, but not replace, established clinical management protocols and professional judgment. The device does not provide a diagnosis or prescribe or select a treatment, nor recommend a specific management action . The PUV scoring system is not intended for, and should not be used in, the diagnosis of miscarriage.
Intended user	EPC-Trained specialist health care professionals holding current Gynaia "Early Pregnancy training and certification" certificate
Patient target group	For PUL: women ≥ 16 years of age, in early pregnancy for whom the pregnancy cannot be located on transvaginal ultrasound scan. M6/PUL is intended to be used as part of the two-step PUL triage protocol. Patients with an initial progesterone 2 nmol/L (0.63

	ng/mL) or less can be stratified in the low risk group for EP. In these patients, running the M6/PUL model is optional. For PUV: women ≥ 15 years of age, with normally sited pregnancy inside the uterus, but with uncertainty about the viability (absence of an embryo or heartbeat) following transvaginal ultrasound scan
Contra indications	For PUL: - Patients under 16 - Initial β-hCG ≤ 25 IU/L - Serum hCG values obtained from different laboratories M6/PUL can be used with or without serum progesterone (M6P and M6NP). For PUV: - Patients under 15 - multiple pregnancies
Use in combination with other devices and software	N/A
Limitations of use	EPC is designed for clinical decision support and is not intended for diagnostic purposes. It must not be used as a stand-alone basis for clinical decisions

Operating instructions
Minimum System Requirements

Supported Browsers and System Requirements

Our medical device is accessed through a web application (the platform) that is compatible with a range of modern browsers on both desktop and mobile devices. This web application can also be installed on a personal device for a native-app-like experience. To ensure proper functionality, security, and the best user experience, it is essential to use a supported browser with the minimum required version. The platform will check to ensure it only works on supported devices.

Supported Browsers

The following browsers are supported for use with our medical device. Older versions of these browsers are not supported, and you must update to the specified version or higher.

- **Chrome (Desktop & Mobile)**: Version 82 or higher.
- **Edge (Desktop & Mobile)**: Version 82 or higher.
- **Firefox (Desktop & Mobile)**: Version 77 or higher.
- **Safari (Desktop & Mobile)**: Version 12 or higher.
- **Chromium-based browsers**: Any browser built on the Chromium engine (e.g., Brave, Opera) that is based on Chromium version 82 or higher should be supported, though official testing is limited to Chrome and Edge.

Browsers that have reached their "end-of-life" and are no longer receiving security updates, such as Internet Explorer, are not supported.

Hardware Requirements

The performance of the application is dependent on the hardware of your device. The following are general minimum system requirements to run the supported browsers and our application correctly on a desktop/laptop or a mobile phone.

Desktop/Laptop:

- **Processor:** A processor with support for SSE3 instructions (e.g., Intel Pentium 4 or newer) is a general requirement for modern browsers.
- **RAM:** 2GB for 64-bit browsers is the minimum, but 4GB or more is recommended for optimal performance.
- **Operating System:** An actively supported operating system such as Windows 10 or higher, macOS 12 (Monterey) or higher, or a recent version of a Linux distribution.
- **Screen Resolution:** A minimum resolution of 1024 x 768 is required.

Mobile Devices:

- **Operating System:** A modern mobile operating system that supports the latest versions of the browsers listed above (e.g., Android 10 or later, iOS 12 or later).
- **RAM:** 3GB RAM is recommended for optimal performance.

Installation

The application can be installed on a mobile device as a PWA (progressive web app) for quick access from the home screen, similar to a native app. The installation process varies slightly between operating systems.

On iPhone (iOS) using Safari:

1. Open the web application in the Safari browser.
2. Tap the **Share** button (a square with an arrow pointing upwards) at the bottom of the screen.
3. Scroll down and select **Add to Home Screen**.
4. You will be prompted to customize the name of the application. Tap **Add** in the top right corner to confirm.
5. The application icon will now appear on your home screen.

On Android using Chrome:

1. Open the web application in the Chrome browser.
2. An "Install app" prompt may appear automatically. If it does, follow the on-screen instructions.
3. If no prompt appears, tap the **three-dot menu** in the top-right corner of the browser.
4. Select **Add to Home screen** from the menu.
5. A pop-up will appear where you can customize the app's name. Tap **Add** to confirm.
6. The application icon will now be on your home screen and in your app drawer.

Performance characteristics

Clinical Benefits

EPC Clinical Benefit	Clinical Outcome Parameter
The M6/PUL model provides clinical decision support by informing EPC-trained specialist healthcare professional about women who may require closer monitoring for a potential EP within the established clinical pathways.	Net Benefit for threshold probabilities of EP between 3% and 10% showed superior clinical utility of M6/PUL compared to the default strategies (treat all (closely monitor all women) and treat none (closely monitor no-one))
The use of the PUV scoring system is limited to patient counseling purposes and does not imply a clinical benefit.	NA

Clinical Performance

EPC Clinical Performance	Performance endpoint/measure
The M6/PUL model is able to give probabilities to differentiate between pregnancies at high and low risk of ectopic pregnancy.	For the M6/PUL model with progesterone (M6P), the AUC to differentiate between pregnancies at high and low risk of ectopic pregnancy is 0.89 for internal-external cross-validation and 0.84–0.88 for temporal external validation. For the model without progesterone (M6NP), the AUCs are 0.85 and 0.82-0.86 respectively. Calibration performance is good overall, but with heterogeneity between centers.
The PUV scoring system is able to give probabilities for first trimester (11-14 weeks) viability.	The AUC for first trimester viability is 0.901 (95% CI 0.881–0.920) in the training set and 0.924 (0.900–0.947) in the test set.

Variable Influence – How the Output is Generated

The M6/PUL component of EPC uses a published multivariable statistical prediction model based on multinomial logistic regression (Kyriacou et al., 2024). The model combines biochemical variables that are known to be associated with the outcome of a Pregnancy of Unknown Location (PUL). The core variables are: (1) the initial serum β-hCG concentration (measured at first assessment); (2) the β-hCG ratio, defined as the serum β-hCG measured 48 hours after the initial sample divided by the initial value — this reflects how hCG is changing over time and (3) when available and clinically suitable, the initial serum progesterone concentration. When progesterone levels are not available or clinically suitable (for example, in women using progesterone supplements), the model without progesterone (M6NP) is used, relying solely on the two β-hCG measurements. Each variable contributes to the probability estimate. The model output is a probability estimate for each of three possible outcomes: ectopic/persistent PUL (high risk), intrauterine pregnancy (low risk), or failed PUL (low risk). The versions implemented in EPC are the updated M6P and M6NP models published by Kyriacou et al. Ultrasound Obstet Gynecol. 2024 doi: 10.1002/uog.27515, developed and validated using multicentre prospective clinical data from specialist early pregnancy units.

The PUV component of EPC is a scoring system based on the published multivariable logistic regression model developed by Bottomley et al. (2013) to predict the likelihood of a viable ongoing intrauterine pregnancy at the end of the first trimester (11–14 weeks of gestation). This system was developed and validated using prospectively collected clinical and ultrasound data and incorporates five variables that are independently associated with pregnancy outcome. The five variables are: (1) maternal age; (2) vaginal bleeding severity, quantified using a pictorial bleeding assessment chart (PBAC score, from 0 for no bleeding to 4 for clots or flooding); (3) mean gestational sac diameter (MSD), measured in three planes on transvaginal ultrasound; (4) presence or absence of a visible fetal heartbeat; and (5) mean yolk sac diameter. Each variable contributes to the overall probability estimate with a specific mathematical weight. The output of the scoring system is a probability representing the estimated likelihood of an ongoing viable pregnancy at 11–14 weeks. This probability is intended solely for patient counselling and does not constitute a diagnosis.

Performance Metrics and Clinical Validation

The M6/PUL model implemented in EPC was developed and validated using prospectively collected clinical data from specialist early pregnancy units in a large multicentre study (Kyriacou

et al. Ultrasound Obstet Gynecol. 2024 doi: 10.1002/uog.27515,). The updated model was developed on data from 2,894 pregnant women (age ≥16 years and with initial β-hCG > 25 IU/L) across eight clinical centres and subsequently validated in two independent centres on more recent data from 1,870 additional patients. Discrimination and calibration performance are summarised in the Clinical Performance table above. The software implementation used in EPC was independently verified using predefined clinical test cases and reference datasets to confirm that the device accurately reproduces the published model calculations. Clinical performance may vary between healthcare settings and patient populations, and model outputs should always be interpreted together with ultrasound findings, laboratory results, clinical assessment, and local clinical protocols.

The PUV scoring system implemented in EPC was developed and validated using prospectively collected clinical and ultrasound data from a specialist early pregnancy assessment unit in London, United Kingdom (Bottomley et al., Hum Reprod. 2013 doi: 10.1093/humrep/des352). The derivation dataset included 1,435 consecutive women (age ≥15 years) undergoing transvaginal ultrasound at a gestational age <84 days; the final outcome was a viable pregnancy in 61.7% and early pregnancy loss in 38.3%. Discrimination performance is summarised in the Clinical Performance table above. The software implementation used in EPC was independently verified to confirm that it accurately reproduces the published model calculations. The PUV probability output should always be interpreted in conjunction with the full clinical assessment, ultrasound findings, and local clinical protocols. It is not intended for, and must not be used as, a standalone basis for clinical decision-making, and must not be used as a basis for diagnosing miscarriage.

Maintenance

No maintenance is required.

For both security and technical performance reasons (including speed, user experience, and accurate risk visualization) it is strongly recommended to use the latest available version of the operating system and browser on the device running the EPC application.

Warning and precautions

WARNING – Intended Use and Clinical Decision-Making	EPC provides probabilistic risk estimates intended to support clinical assessment of possible ectopic pregnancy. The output is informative in nature and must be interpreted in the context of the full clinical picture, established guidelines, and clinician expertise. EPC does not recommend, determine, or automate clinical management actions, and does not replace clinical judgment. Clinical decisions remain the responsibility of the healthcare professional.
WARNING – Use Only Within Intended Population	Use outside the intended population may result in outputs that are not clinically reliable within the intended use.
WARNING – Use by Trained Users Only	EPC is intended for use only by EPC-trained specialist healthcare professionals who have completed appropriate training and hold a valid “Early Pregnancy training and certification” certificate. Access to the application is restricted by login and will not be granted to non-certified users. Incorrect interpretation by untrained or insufficiently trained users may result in misunderstanding of the model output and its clinical relevance .
CAUTION – Correct Data Entry Required	Incorrect, incomplete, or inconsistent data entry may result in inaccurate risk estimates, which may affect

	how the output is interpreted within the broader clinical assessment
CAUTION – Input Validity and Applicability	Users must not bypass or ignore system checks or warnings. Doing so may reduce the reliability of the output and its appropriate use within the clinical assessment.
CAUTION – Use in Case of System Unavailability	If EPC is unavailable due to technical issues, patient management must not be delayed. An alternative clinically accepted assessment approach should be used. Expert evaluation (or repeated ultrasound examination every 48 hours) could be considered to determine further management in case of PUL.
CAUTION – Calibration and Generalizability	Predicted risks may not fully reflect all local patient populations and should be interpreted in the context of local clinical practice and the full clinical picture.
NOTICE – Low progesterone concentrations	Low progesterone concentrations (e.g. ≤ 2 nmol/L [0.63 ng/mL]) may be associated with a lower likelihood of ectopic pregnancy As part of the two-step PUL triage protocol, patients with an initial progesterone 2 nmol/L (0.63 ng/mL) or less can be stratified in the low risk group for EP. In these patients, running the M6/PUL model is optional.
NOTICE – Instructions for Use Availability	Instructions for Use are provided electronically (eIFU). Paper copies are available upon request and are considered uncontrolled documents. Users are responsible for ensuring they consult the most current version before use. Failure to consult the Instructions for Use may increase the risk of incorrect interpretation or use.

Residual Risks - Information for Safety

Despite implementation of risk control measures in accordance with ISO 14971, residual risks remain due to the inherent statistical nature of predictive models. These residual risks cannot be eliminated without adversely affecting the benefit–risk profile of the device:

1.Overestimation of probabilities

EPC may overestimate the probability of a potential ectopic pregnancy or non-viable pregnancy outcomes.

Potential impact

If given disproportionate weight within the clinical assessment, this may contribute to unnecessary procedures and patient emotional stress.

Mitigation/Safe use:

- Interpret outputs within the full clinical context.
- Apply specialist clinical judgment and follow applicable clinical guidelines

2.Underestimation of probabilities

EPC may underestimate the probability of an ectopic pregnancy or non-viable pregnancy outcomes.

Potential impact

If given disproportionate weight, this may contribute to delayed intervention.

Mitigation / Safe use

- Do not rely on EPC as a stand-alone assessment
- Maintain appropriate follow-up and surveillance; following applicable clinical guidelines

3.Misinterpretation of probabilistic output

Probability outputs may be misunderstood.

Potential impact

Incorrect weighting within clinical decision-making

Mitigation/ Safe Use:

- Ensure appropriate training (EPC certification)
- Interpret absolute vs relative risk correctly
- Use EPC outputs as one component of the overall clinical assessment and ensure that all input parameters are correctly understood and entered.

4.Population variability

Model performance may vary across clinical settings.

Potential impact

Predicted risks may not fully reflect local populations

Mitigation/ Safe Use:

- Interpret results in context of local prevalence
- Combine with clinical expertise

Data Security – User Responsibilities

Area	Physician Responsibility (Duty of Care)
Active Use & Logout	NEVER leave the application logged in and unattended. After every consultation or period of use, you must securely log out (or rely on the system's *immediate* automatic log-off feature).
Screen Privacy (Public View)	ENSURE Visual Privacy while using the application. Position your screen (PC, smartphone, tablet) so that it cannot be viewed by unauthorized persons**.**
Device Security	Your device must be secured with a strong PIN, password, or biometrics (fingerprint/face ID). Ensure the device's operating system and the application are updated **t**o the latest security versions.
Data Transmission	Only use the application over trusted, encrypted networks (e.g., your clinic's secured Wi-Fi or a trusted VPN).
Personal Data Export	Do not download or take screenshots of Protected Health Information (PHI) to your personal device's local storage unless absolutely necessary and immediately secure or delete the file after use**.**

DISCLAIMER

The manufacturer is not responsible for security breaches, data loss, or system compromise resulting from the user's failure to adhere to the security and data protection responsibilities outlined in this IFU, including but not limited to, the use of weak passwords, the use of unapproved operating environments, or failure to apply recommended software updates.

Manufacturer

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Incidents and Support

For technical support or questions contact Gynaia support team via **support@gynaia.com**.

Serious incidents should be reported immediately to Gynaia and to the competent authority of the Member State in which the user/patient is established or the incident took place.

Document Version

Version	Issue date	Description of modification
1.0	15 January 2026	New document
2.0	15 June 2026	Separate warning/Precautions from residual risk section with further clarification Added explanatory section on "*Variable Influence – How the Output is Generated*" and "*Performance Metrics and clinical validation*"

3.0	02 July 2026	Improved sections (clarifications): Intended Purpose, Patient target group, Contra indications and Variable Influence