NON-INTERVENTIONAL STUDY (NIS) PROTOCOL

Post-Authorisation Safety Study (PASS) Information

Title	Assessment of the effectiveness of additional Risk Minimisation Measures (aRMMs) among pharmacists for provision of desogestrel 75 microgram tablets in a community pharmacy setting
Protocol version identifier	CIG030921
Date of last version of protocol	Friday, 03 September 2021
EU Post Authorisation Study register number	Study not yet registered. Registration will be performed upon Medicines and Healthcare Products Regulatory Agency (MHRA) approval of this protocol
Active Substance	Desogestrel
Medicinal Product	Lovima 75 microgram film-coated tablets Hana 75 microgram film-coated tablets
Product Reference	ATC G03AC09
Procedure Number	PL 42807/0002 PL 17836/0015
Marketing Authorisation Holders	Maxwellia Ltd Laboratoire HRA Pharma
Joint PASS	Yes
Research questions and objectives	To evaluate the effectiveness of desogestrel 75 microgram tablets aRMMs by: • demonstrating that the training is effective in enabling pharmacists to make appropriate decisions to supply based on contraindications and special warnings; this includes awareness and mitigation of safety concerns; • identifying whether there are particular contraindications or warnings for which pharmacists consistently make the wrong supply decision; • establishing ease of access to and ease of use of the aRMMs.
Country of Study	UK
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2. List of Abbreviations

AE	Adverse Event
aRMMs	additional Risk Minimisation Measures
CI	Confidence Intervals
CIG	Communications International Group
DIA	Drug Information Association
DSG	Desogestrel
GDPR	General Data Protection Regulation
GP	General Practitioner
GSL	General Sales List medicine
hCG	human Chorionic Gonadotrophin
HCP	Healthcare Professional
KPI	Key Performance Indicator
KRMs	Key Risk Messages
MAH	Marketing Authorisation Holder
MHRA	Medicines and Healthcare Products Regulation Agency
MRP	Mutual Recognition Procedure
NIS	Non-Interventional Study
OC	Oral Contraception
OTC	Over The Counter
P	Pharmacy medicine
PASS	Post-Authorisation Safety Study
PGD	Patient Group Directions
POM	Prescription Only Medicine
POP	Progestin-only Pill
RM	Risk Management
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics
URL	Uniform Resource Locator

3. Responsible Parties

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Shared responsibility statement

This is a joint PASS submission and there is a shared responsibility between Laboratoire HRA Pharma and Maxwellia Ltd for the management and reporting of Adverse Events.

4. Abstract

This abstract provides a summary of study objectives and methodology. Detailed descriptions are included in corresponding sections in the main body of the protocol.

Rationale and Background

Desogestrel 75 microgram tablets was first authorised in Sweden in 1997 under the trade name Cerazette (Organon Pharmaceuticals) for oral contraception (OC) in women. It was then authorised in 1998 in other European countries, including the United Kingdom (UK), in the subsequent Mutual Recognition Procedure (MRP procedure number SE/H/0147/001, UK licence number PL 00025/0562).

Desogestrel 75 microgram tablets was reclassified to a pharmacy only (P) medicine in the UK separately by Maxwellia Ltd and HRA Pharma in July 2021. To support the safe supply of the products via pharmacy, both companies have independently developed a Pharmacy Training Guide and an optional Pharmacy Checklist as additional Risk Minimisation Measures (aRMMs). The training materials and consultation checklists together constitute important aRMMs for the non-prescription supply of the products, so that an appropriate decision is made by pharmacists to supply patients and correct advice is given. The content of the materials is aligned and has been agreed with the MHRA.

This post-authorisation safety study (PASS) will assess the effectiveness of the agreed aRMMs for desogestrel 75 microgram tablets.

Research Questions and Objectives

The overall objective is to evaluate the effectiveness of the aRMMs in mitigating the risks of incorrect supply of desogestrel 75 microgram tablets to patients in a community pharmacy. Specifically, the goals of the study are to:

- demonstrate that the training provided by each company is effective in enabling pharmacists to make appropriate decisions to supply desogestrel 75 microgram tablets based on contraindications and special warnings; this includes awareness and mitigation of safety concerns;
- identify whether there are particular contraindications or warnings for which pharmacists consistently make the wrong supply decision;
- establish ease of access to and ease of use of the aRMMs.

Study Design

The study will be a cross sectional, non-interventional web-based survey at six months post the first product launch following MHRA approval of the reclassification.

The survey will be distributed across the UK to a representative mix of independent and multiple ownership pharmacies with the aim of achieving a relevant sample size of pharmacists who have read the aRMM materials and conducted at least one consultation during the previous six months.

For this study, it will be important to ensure a representative mix of independent and multiple ownership pharmacies, including those in urban and small town settings.

The questionnaire has been designed such that all biases in question wording, scale responses and order effect are mitigated. This includes the use of:

- Balanced scales
- Randomisation of response options
- Non-leading question phraseology
- Survey flow, routing and question logic designed to maximise the respondent's efficient and considered response.

Prior to finalisation of the study questionnaire, the proposed questions will be peer reviewed and the functionality of the online survey will be user tested with 5 pharmacists in the UK to identify any ambiguity and estimate survey completion time.

A pilot study will run additionally with 30 pharmacists in order to evaluate the quality of the data produced by the respondents and ensure that it will lead to meaningful results.

Study Structure

The pharmacist survey will comprise two main sections, intended to:

1. Understand how the aRMMs are being used in practice. Pharmacists' feedback will be collected and analysed to determine whether changes to the aRMMs are required in order to support pharmacists more effectively when they are supplying desogestrel 75 microgram tablets;
2. Establish whether pharmacists can answer case study questions correctly and offer the correct advice to patients requesting desogestrel 75 microgram tablets for oral contraception from a pharmacy. Eight (8) case study scenarios are involved.

Pharmacists will be screened to ensure they have received and read at least one of the aRMMs and conducted a consultation on desogestrel 75 microgram tablets without a prescription in the last six months. The scenario section of the questionnaire is designed to mirror real life situations, in which pharmacists may choose to refer to information sources during consultations.

The pharmacist survey will take approximately 25 minutes to complete and will have to be completed in one sitting. However, the survey timer will be set for 60 minutes to allow respondents to take a break if required. During this time, the survey will remain open: respondents will not be able to save it and return to it later. Respondents will be informed about the length of the survey and allocated time to complete.

Data Sources

A structured, self-administered questionnaire comprised of closed and open ended questions or statements with multiple response choices (i.e. questions or statements asking the pharmacists to choose from a defined list of responses) will be used to collect the survey data. The questionnaire will collect data on pharmacist characteristics in addition to their responses pertaining to the effectiveness of the aRMMs.

Study Size

The survey will be distributed across the UK to a representative mix of pharmacists working in independent and multiple ownership community pharmacy businesses in city, urban, small town and rural settings, with the aim of achieving a sample size of 200 pharmacists who have all read at least one company's aRMMs and conducted at least one consultation during the previous six months.

The sample size chosen for this study is dependent on statistical and feasibility considerations. The 200 responses will generate a combined response to 1600 case study scenarios, which will be taken together to measure the proposed success criteria.

Data Analysis

Previous analysis of comparable PASS studies has shown that receipt and use rates for risk management (RM) materials among healthcare professionals (HCPs) rarely exceed 80% (preliminary results of a cumulative systematic review and meta-analysis of risk minimisation survey studies presented at EMA/DIA Information Day, 2017),[3] whereas percentages of correct knowledge of key safety messages mostly lie between 70% and 90%. On this basis, a threshold of 80% has been set as an average across the eight case study scenarios, rather than on each one individually.

Data segmentation will be generated for key variables e.g. splitting the sample by gender and age, outlet type and job title.

Success Criteria

The aRMMs will be deemed effective if the following criteria are met:

- An average of at least 80% of pharmacists correctly advise whether to supply or not supply for each of the eight case study scenarios. The Key Performance Indicator (KPI) will be deemed achieved at 73.2% plus to allow 6.9% statistical precision (see table 2);
- The total number of correct answers across the scenarios exceeds 80%. The KPI will be deemed achieved at 77.6% plus to allow 2.5% statistical precision (see table 2). This means that 1242 correct answers out of the 1600 answers will be achieved.

Quality Control

The study will be conducted in accordance with all applicable regulatory and privacy requirements.

Documentation of all data management activities will allow step-by-step retrospective assessment of data quality and performance. Management of data will be performed in accordance with applicable standards and data cleaning procedures to ensure its integrity (e.g. removing errors and inconsistencies in the data).

Where the percentage of pharmacists answering a scenario question correctly is below the level defined to represent success, the training materials relating to that particular scenario will be reviewed and improved as appropriate in both sets.

5. Amendments and Updates

None

6. Milestones

Milestone	Timelines
DSG reclassification approval	8th July 2021
Launch of product in pharmacy	July 2021
Roll out of aRMMs	July 2021
MHRA protocol approval	2nd September 2021
User testing	w/c 20th September 2021
Registration in the EU PAS Register®	30th September 2021
Pilot study launch	w/c 11th October 2021
Pilot study data collection and results reporting	w/c 1st November 2021
(If required) Submission of changes made to the protocol and questionnaire to MHRA	w/c 29th November 2021
(If required) MHRA updated protocol approval	w/c 3rd January 2022
Main study launch	w/c 10th January 2022
End of data collection	w/c 7th February 2022
Publication of final study report	w/c 18th April 2022

7. Rationale and Background

Desogestrel 75 microgram tablets was first authorised in Sweden in 1997 under the trade name Cerazette (Organon Pharmaceuticals) for oral contraception (OC) in women. It was then authorised in 1998 in other European countries, including the United Kingdom (UK), in the subsequent Mutual Recognition Procedure (MRP procedure number SE/H/0147/001, UK licence number PL 00025/0562).

Desogestrel 75 mcg film-coated tablets (DSG) was reclassified to a pharmacy only (P) medicine in the UK separately by Maxwellia Ltd and Laboratoire HRA Pharma. Both applications for non-prescription (over the counter) 75 microgram desogestrel (to be marketed as Lovima 75 microgram film-coated tablets and Hana 75 microgram film-coated tablets retrospectively) were approved in July 2021.

To support the safe supply of the products via pharmacy, both companies have independently developed a Pharmacy Training Guide and an optional Pharmacy Checklist as additional Risk Minimisation Measures (aRMMs). The training materials and consultation checklists together constitute important aRMMs for the non-prescription supply of DSG, so that an appropriate decision is made by pharmacists to supply patients and correct advice is given. The content of the materials is aligned and has been agreed with the MHRA.

The MHRA has asked Maxwellia Ltd and Laboratoire HRA Pharma to confirm that the aRMMs for their desogestrel 75 microgram tablet products operate effectively in the community pharmacy setting by conducting a joint post-authorisation safety study (PASS).

Product information

Hana 75 microgram film-coated tablets[1]
Each film-coated tablet contains 75 microgram desogestrel
Licence holder: Laboratoire HRA Pharma

Lovima 75 microgram film-coated tablets[2]
Each film-coated tablet contains 75 microgram desogestrel
Licence holder: Maxwellia Ltd

Hana and Lovima tablets are oral contraceptives used for the prevention of pregnancy in women of childbearing age. Hana and Lovima tablets contain desogestrel (DSG), a progestogen-only oral contraceptive (also known as a POP or mini-pill).

The contraceptive effect of DSG is achieved primarily by inhibition of ovulation. Other effects include increased viscosity of cervical mucus.

One tablet must be taken every day at the same time so that the interval between two tablets is always 24 hours. The first tablet should be taken on the first day of menstrual bleeding. Thereafter, one tablet each day is to be taken continuously without taking any notice of possible bleeding. When a pack of pills is finished, a new pack should be started the next day, maintaining the same 24 hour interval between pills.

Like other POPs, Hana and Lovima can be used during breast-feeding and by women who cannot or do not want to use oestrogen.

Further product information can be found in the Summary of Product Characteristics (SmPCs) for Hana[1] and Lovima[2].

Laboratoire HRA Pharma and Maxwellia Ltd believe the launch of Hana and Lovima in the UK, and their availability as Pharmacy (P) medicines, will increase access for women of childbearing age to oral contraception.

Pharmacist role and training

Pharmacists have been identified as having an important role in facilitating and counselling patients to determine suitability of use of DSG, and in directing women for whom it is unsuitable to their doctors.

Pharmacists have experience in counselling patients on the supply and use of emergency hormonal contraception, which has been available in the UK as a Pharmacy (P) medicine since 2001. Some pharmacists also supply contraception via Patient Group Directions (PGDs) and/or online clinic services.

The companies have produced pharmacy training materials consisting of a Pharmacy Training Guide and a Pharmacy Supply Aid Checklist. The checklist can be completed by women prior to their consultation, and acts as an aide memoire for the pharmacist in determining if the medicine is suitable for supply. The woman will have the patient information leaflet and packaging to refer to: these contain the key safety messages for the products. As part of the consultation in the pharmacy, women will be informed of and signposted to information on all methods of contraception available, so that they can make an informed choice regarding the method most suitable for them.

The training is being offered in a variety of formats to ensure the widest opportunity for accessing learning. This includes online resources and printed materials.

Key Risk Messages for Pharmacists

The Pharmacy Training Guides and Pharmacy Supply Aid Checklists include risk messages for pharmacists to consider when determining the suitability of a patient for supply of Hana or Lovima and other important messages for pharmacists to consider during consultations.

The aRMMs have been generated to manage the following potential risks, which are detailed in the risk management plans (RMPs) for both companies' products:

- Venous thromboembolism
- Arterial thromboembolism
- Disturbances of liver function
- Breast cancer
- Benign and malignant liver tumours
- Drug interactions.

It is important that pharmacists consider the potential risks when identifying women suitable for supply of DSG. The pharmacy training materials address each of these risks and provide advice to pharmacists on how to manage these risks appropriately.

The pharmacy training materials also provide additional information for pharmacists to consider when ensuring safe supply of DSG. These include, but are not limited to:

- Alternative contraception options to ensure women can make informed choices
- Safeguarding and consent, particularly when supplying DSG to women under 16 years of age
- Information on how to take and how to start taking DSG
- Counselling advice on potential side effects of DSG
- Quick starting and managing potential off-label use
- Managing a missed or forgotten pill.

Study protocol objective

The objective of this protocol is to describe in detail the methods that will be employed to evaluate the effectiveness of the aRMMs in the UK and to outline the estimated timeline for the major study milestones (Section 6: Milestones). This non-interventional study is designated as a Post-Authorisation Safety Study (PASS) and is a commitment to the MHRA.

8. Research Questions and Objectives

The overall objective of this study is to evaluate the effectiveness of the aRMMs. Specifically, the primary objectives are to:

- Demonstrate that the training is effective in enabling pharmacists to make appropriate decisions to supply based on contraindications and special warnings; this includes awareness and mitigation of safety concerns;
- Identify whether there are particular contraindications or warnings for which pharmacists consistently make wrong supply decisions;
- Establish ease of access to and ease of use of the aRMMs.

9. Research Methods

This section presents the methods that will be employed to evaluate the effectiveness of the aRMMs in the UK.

9.1 Study Design

The study will be a cross sectional, non-interventional web-based survey that will be conducted in the UK at six months post the first product launch for at least one of the two brands following MHRA approval of the reclassification. The study will be conducted anonymously among pharmacists who have read the aRMMs for at least one of the brands and have conducted at least one consultation regarding the supply of desogestrel 75 microgram tablets during the previous six months.

For this study, it will be important to ensure a representative mix of independent and multiple ownership pharmacies, including those in urban and small-town settings.

The questionnaire has been designed such that all biases in question wording, scale responses and order effect are mitigated. This includes the use of:

- Balanced scales
- Randomisation of response options
- Non-leading question phraseology
- Survey flow, routing and question logic designed to maximise the respondents' efficient and considered responses.

Prior to finalisation, the study will be subjected to user testing and a pilot study. Further details of these can be found in section 9.4.4.

9.1.1 Study Structure

The pharmacist survey will comprise two main sections, intended to:

1. Understand how the aRMMs are being used in practice. Pharmacists' feedback will be collected and analysed to determine whether changes to the aRMMs are required in order to support pharmacists more effectively when they are supplying the products. These questions are based on simple scales, single or multiple choices, and include two open ended questions. They cover the following areas:
    - aRMMs received and read prior to the study
    - Frequency of consultations
    - The setting within the pharmacy used for the consultation
    - aRMMs used during the consultation
    - Ease of access to the aRMMs
    - Level of pharmacist confidence in advising on the use of desogestrel 75 microgram tablets and correctly supplying.

2. Establish whether the pharmacists can answer questions correctly and offer the correct advice to customers requesting desogestrel 75 microgram tablets for oral contraception from a community pharmacy. Eight (8) case study scenarios are involved.

Pharmacists will be screened to ensure they have received and read the aRMMs from at least one of the brands and conducted a consultation on desogestrel 75 microgram tablets without a prescription in the last six months. The scenario section of the questionnaire is designed to mirror the real life situations, in which pharmacists may choose to refer to information sources during consultations. As the pharmacist may be completing the survey away from their usual place of

consultation and may not have access to the materials they would usually use, information on how to access the aRMMs will be provided after the screening process and before the scenario section of the questionnaire.

It will be possible to complete the survey on a desktop, tablet or mobile device. However, pharmacists will be advised to complete the survey on a desktop device for a better user experience.

The pharmacist survey will take approximately 25 minutes to complete and will have to be completed in one sitting. However, a survey timer will be set for 60 minutes to allow respondents to take a break if required. During this time, the survey will remain open: respondents will not be able to save it and return to it later. Respondents will be informed about the length of the survey and that it must be completed within one hour.

Pharmacists invited to participate in the study will agree to abide by the Adverse Events (AE) reporting requirements of both Maxwellia Ltd and Laboratoire HRA Pharma by submitting to Maxwellia Ltd or Laboratoire HRA Pharma an incident report, either anonymously or with their personal contact details. Participants will also agree to take part in the research voluntarily, supplying their information for the purposes of the study and within the CIG Research privacy rules.

The survey will be conducted online using proprietary market research questionnaire software. The survey has been designed with reference to both companies and scripted for completion by community pharmacists. The questionnaire will be accessed by means of a secure URL link, which will be sent in an email invitation to CIG Research's opt-in panel of pharmacists. The sample of 200 respondents to the survey will be quota controlled to be nationally representative of community pharmacists in the UK.

Both Maxwellia Ltd and Laboratoire HRA Pharma have provided aRMM tools to all UK pharmacies, so participants in the survey will have had access to and will recall reading the material provided by at least one of the two companies during the six months prior to the study. All participants will have conducted at least one consultation with a female customer for the supply of desogestrel 75 microgram tablets in the six months prior to the survey being conducted.

9.1.2 Success Criteria

The aRMMs will be deemed effective if the following criteria are met:

- An average of at least 80% of pharmacists correctly advise whether to supply or not supply DSG for each of the eight case study scenarios. In order to allow for ±<6.9% statistical precision (see table 2), the KPI will be deemed achieved at 73.2% plus;
- The total number of correct answers across all scenarios should exceed 80% . In order to allow for ±<2.5% statistical precision (see table 2), the KPI will be deemed achieved at 77.6% plus. This means that 1242 correct answers out of the 1600 answers will be achieved.

Table 1. Example of success criteria analysis

	Answered correctly	Answered incorrectly
Scenario 1	170 (85%)	30 (15%)
Scenario 2	190 (95%)	10 (5%)
Scenario 3	150 (75%)	50 (25%)
Scenario 4	180 (90%)	20 (10%)
Scenario 5	160 (80%)	40 (20%)
Scenario 6	200 (100%)	0 (0%)
Scenario 7	140 (70%)	60 (30%)
Scenario 8	190 (95%)	10 (5%)
TOTAL	1380	220
Average	86.25%	13.75%

The above example shows that aRMMs are effective because, on average, 86.25% of the pharmacists provided correct answers across all scenarios, equivalent to 1380 out of 1600 correct answers. While the average correct answer rate is above the 80% (±<2.5%) threshold across the eight scenarios, there is one (scenario7) which is below the threshold. In this instance, detailed analysis of which segment of pharmacists underperformed will be conducted, including e.g.:

- How many consultations these respondents estimate that they have conducted
- How they differ (if at all) from the main sample in terms of their demography, location, length of service and outlet type. Given that this may be based on small sub-samples (in the above example, at scenario 7, it is 60 respondents), this will be a qualitative analysis
- Level of confidence about advising patients and about supplying desogestrel 75 microgram tablets relative to the sample average
- Self-rated knowledge of the product
- Usefulness rating of the materials.

Should any scenario fall below the 80% (>-6.9%) answering correctly threshold, appropriate changes will be made to the aRMM tools. In the above example, scenario 7 did not pass the threshold, so the information relating to this scenario in the training materials would be amended. Any changes will take account of which wrong answer is selected by those giving incorrect answers in each scenario where the threshold is not met. Scenario 3 met the criteria as 75% is within the 6.9% statistical error for 80% threshold on 200 sample (73.2% plus).

9.2 Setting

Desogestrel 75 microgram tablets received its product licence in the UK in 1998 and has been available as a prescription only (POM) medicine since then. Since July 2021, it has been available as a pharmacy (P) medicine for women to purchase from pharmacies under the brand names Hana and Lovima. As a P medicine, desogestrel 75 microgram tablets can only be supplied through registered pharmacies under the personal supervision of a pharmacist. It is the pharmacist's role to help women assess whether desogestrel 75 microgram tablets is a suitable contraception option for them. Pharmacists are required to check that there are no contraindications to supply and to know when to refer women to their doctor for further advice.

9.2.1. Method of Pharmacist Recruitment for Participation

The study objectives will be accomplished by means of a cross-sectional survey of all targeted pharmacists that received and read the aRMM materials supplied for Hana and Lovima in the UK.

Invitations will be sent by email to pharmacists from CIG Research's opt-in panel of 12,500 UK community pharmacists. Response rates of 2-3% are typical in studies of this type and length.

Information on this panel is held on CIG's cloud-based servers and updated continuously to ensure all unsubscribes are removed and new participants wishing to join the panel are classified according to their job title, location and outlet type. When invitations are sent to participate in this survey, the panel stratification classification may be used to boost responses from under-represented segments in collected responses, by encouraging pharmacists in those segments to take part.

The respondents' understanding of the appropriate use and risks of desogestrel 75 microgram tablets will be evaluated using an online survey. Each invitation will include information on how to access the survey online.

CIG Research will compensate pharmacists for their time spent completing the survey in the form of reward points, which can be redeemed for vouchers. This remuneration programme is independent of Maxwellia Ltd and Laboratoire HRA Pharma, and is governed by UK laws and regulations.

9.2.2. Inclusion Criteria

All respondents invited to participate will be qualified pharmacists working in community pharmacies in the UK, will have read at least one of the aRMM materials and held at least one consultation with a female customer regarding the supply of desogestrel 75 microgram tablets in the previous six months. The sample will aim to be representative of community pharmacists by age, gender, outlet size, and by region within the UK, including Northern Ireland.

Respondents will be invited to participate on the basis that they meet and confirm their acceptance of the inclusion criteria:

- Their information will only be used for research purposes and will not be passed to any other organisation without their permission;
- They have the right to refuse to answer questions or withdraw at any time. They consent to CIG Research collecting and using the information that they voluntarily provide for the purposes of research;
- They understand that if they become aware of any AEs during the course of the study, they will report these to CIG Research, who will pass their comments to the client about whose products they relate. They may choose to have these passed on anonymously or with their contact details, which will be collected at the end of the survey.

9.2.3. Exclusion Criteria

Pharmacists will not be included in the study if they:

- Have not received and read the aRMM materials supplied for the products in the UK, or do not recall having received or read them;
- Have participated in the user testing of the draft questions for the survey (described in Section 9.4.4: User and pilot testing of the survey questions);
- Are employed in full-time research, GP practices or hospitals (i.e. not community-based pharmacists);
- Work only as online pharmacists and do not provide consultations;
- Are in the employment of or are contracted to the MHRA, Maxwellia Ltd, Laboratoire HRA Pharma, Communications International Group or Consensio LLP.

9.3 Variables

The variables for analyses will be derived from the study data to address the objectives outlined in Section 8: Research Questions and Objectives, as follows:

- Assessment of pharmacists' knowledge/understanding of how to supply desogestrel 75 microgram tablets to patients
- Utilisation of the aRMM materials during consultations
- Accessibility of each of the aRMMs to the pharmacist
- Confidence about advising customers on the use of desogestrel 75 microgram tablets
- Usefulness of the aRMMs.

9.4 Data Sources

A structured, self-administered questionnaire comprised of closed and open ended questions or statements with multiple response choices (i.e. questions or statements asking the pharmacists to choose from a defined list of responses) will be used to collect the survey data. Questions will be asked in an order which provides a 'funnel' from general introductory topics towards the scenario-based questions, which constitute risk knowledge responses, on which KPIs have been set. Open ended questions will be included to collect qualitative responses showing reasoning for previously provided answers.

The questionnaire will collect data on pharmacist characteristics (i.e. job title, outlet type, region), and their responses to the scenario-based risk knowledge questions. The data collected from the survey will be used to inform the evaluation of the effectiveness of the aRMMs.

The questionnaire will begin with screening questions to confirm eligibility. Depending on the answers to the screening questions, survey participation will either be terminated or continued. If ineligible, the respondent will be immediately notified with a 'thank you' message that survey participation has ended. If eligible, the respondent will be allowed to continue survey participation.

The full questionnaire can be found in **Annex 3**.

9.4.1 Screening questions for pharmacists

The following question types will be used to screen out respondents:

- Consent to participate
- Consent to report AEs
- Job title – to include pharmacists and exclude other roles within community pharmacy
- Whether the pharmacist has had at least one consultation with a female customer about the supply of desogestrel 75 microgram tablets as oral contraception during the six month period preceding the study
- Whether the pharmacist recalls reading one or both sets of aRMMs in the six months prior to the survey
- Whether they are employed by or contracted to the MHRA, Laboratoire HRA Pharma, Maxwellia Ltd, Communications International Group or Consensio LLP.

Pharmacists who have taken part in testing the aRMMs or in user testing of the survey questionnaire will be screened out of the invitation to participate.

9.4.2 Data on pharmacist demographic characteristics

The following question types will be used to collect demographic characteristics data:

- Outlet type
- Brand of multiple outlet
- Location of pharmacy
- Job title within the pharmacist cohort – supervisor/manager/proprietor/locum/pharmacist
- Length of time practising as a community pharmacist
- Age of respondent
- Gender of respondent.

9.4.3 Data pertaining to evaluation of the effectiveness of the aRMMs

The questionnaire includes eight case study scenarios in the form of short representations of typical situations in which a patient requests desogestrel 75 microgram tablets and is either supplied or not supplied, based on their presentation. In each case, the option to "supply" or "do not supply" will be chosen by the respondents and will be correct or incorrect. The number of correct responses to each scenario will assess the knowledge of the pharmacists. The knowledge level analysed using descriptive statistics and confidence intervals will be used to determine the effectiveness of the aRMMs. In the case of incorrect responses to the case study questions, respondents will be provided with the correct response for their information. In the case of correct responses, they will be informed that their response was correct.

Additional evaluation measures will include:

- Reading and utilising of each of the aRMMs among participants
- Ease of access to the aRMMs in the pharmacy during consultations
- Use of consulting facilities in the pharmacy
- Level of confidence in advising patients on the use of desogestrel 75 microgram tablets and correct supplying
- Self-rated knowledge/comprehension of the use of desogestrel 75 microgram tablets and correct supplying.

9.4.4 User and pilot testing of the survey questions

The proposed questions for the survey will be user tested with 5 pharmacists in the UK to establish that questions are clearly understood and that the completion time of the survey is within the range of 22-25 minutes. These respondents will be excluded from the main survey. This user testing will include an open ended question about the flow and ease of use of the questionnaire, and specifically the case study scenarios. Following the user testing, amendments to the questionnaire to improve flow or clarify issues with the scenarios will be made and then assessed in a full pilot study.

The pilot study will run with 30 pharmacists in order to evaluate the quality of data produced by respondents to ensure that it will lead to meaningful results. This will include evaluating each of the case study scenarios in terms of the answers given and whether they differentiate clearly between correct and incorrect answers. Given the pilot sample size of 30 responses, the statistical validity of correct answer rates on the scenarios will be limited, and will only indicate approximate levels of success or failure in each case. The pilot will also assess whether the process runs successfully and that all biases in question wording, scale responses and order effect are mitigated - i.e. all questions are answered and not skipped, open ended questions are filled in correctly, and the survey flow, routing and question logic ensure efficient and considered responses.

Participants in this this pilot study will be recruited from a random sample of approximately 1000 pharmacists from the CIG Research panel in order to establish response rates based on the inclusion criteria above. The sample of 30 responses is based on the expected response rate of 3% on 1000 targets, assuming a large proportion of pharmacists have read the aRMMs and are eligible to participate. The pilot will be used to predict response rates for the full survey. 30 responses allow effective assessment of the value and meaningfulness of responses to the survey. Within a sample of 30 responses, a variety of job titles, genders, ages, and multiple and independent outlet pharmacists would be expected.

The quality of the data collected will be analysed and any issues or shortcomings in the questionnaire design will be reported. Fieldwork and data analysis of the pilot will take four weeks from the pilot study launch. A report with results of the pilot study will then be provided to Maxwellia and HRA. Depending on the outcome, changes may be required in the questionnaire and in the protocol. If the quality of pilot data meets the criteria described above and meaningful results are achieved, no changes to the protocol or questionnaire will be required. In this case, the pilot sample data will be combined with the main study data to produce the final report. It is acceptable to do this as the pilot study will be conducted using the same software, questionnaire and recruitment methods as the main study, with the same high quality data being collected. The only difference is that the pilot will be conducted 3 months before the main study, but this is not deemed to be a major limitation. If the quality of pilot data does not meet the criteria described above, an updated protocol will be provided to the MHRA within four weeks and the pilot sample of 30 respondents will not be counted in the main study.

9.4.5 Data collection process

CIG Research will send invitations by email to its opt-in members of its pharmacist panel with a unique URL link to the online survey for each panel member, which will be hosted in the electronic surveying system QuestionPro. Responses may be completed on desktop, tablet or mobile devices, with the survey limited to one response per participant.

The email invitation (example in **Annex 1**) will include an overview of the rationale for the study and a URL link to the survey. Survey data collection will be open for a maximum of 30 days. The survey study date will begin six months after the first product launch.

All questions will be validated (compulsory to complete) within the surveying system. This means that respondents will not be able to complete the survey unless they have answered all questions. The survey will have to be completed in one sitting. However, the survey timer will be set for 60 minutes to allow respondents to take a break. The vast majority of surveys are completed ‘at one sitting’, but given that this questionnaire will be approximately 25 minutes long, it is possible that the break will be required. In this case, the survey will have to remain open as it will not be possible to close the survey and return to it later. All invitees will be notified about the length of the survey in the invitation.

Questions will be programmed to ensure that they are asked in the appropriate sequence. Skip patterns will be clearly indicated. Respondents cannot go back to a question once the question has been answered and they cannot skip ahead. Response options will be presented in randomised lists to minimise positional bias. Programming will be reviewed by Quality Control and simulated users (user testers) prior to implementation.

The first invitation will be sent to all panel members whose job title is within the pharmacist cohort. During the fieldwork, it is anticipated that the majority of responses will come in within the first

week, and reminders will be sent to pharmacists who have not started the survey after 3-7 days (see section 9.4.6).

Responses will be collated automatically within the survey software and will be monitored throughout the fieldwork process. The CIG Research team will check the flow of responses, any aberrant responses, and the number of minutes each respondent takes to complete the questionnaire. Once the sample has been achieved, with 200 respondents having completed the survey, it will be closed to further respondents.

In the case of potential AE reporting during fieldwork, a survey email address will be provided for respondents wishing to contact CIG Research. This will be checked at least twice daily for AE comments, which will be reported to the client(s) within 24 hours.

9.4.6 Follow-up reminder process

It is expected that two reminders will be required to achieve the sample defined above (2-3% response rate), with those who have already responded having been removed from the reminder process. The intervals between reminders will be approximately 3-7 days.

Further reminders to boost sampling will be issued should there be a shortfall in numbers within any segments, where specific sub-samples are under-represented in the collected responses (e.g. certain age groups, regions or outlet types). CIG Research will monitor the responses, and should any segment not achieve a sufficient number of responses, reminder invitations will be sent to specifically targeted panel members who have not yet started the survey. Filters will be used to target only profiles that match under-represented criteria (e.g. those who are 'female' or 'age 50+'). In order to attract these non-respondents to start and complete the survey, the incentive will be increased by 50%. This is expected to achieve the full sample successfully. If any sample group is still under-represented, CIG Research will explore the remaining of its panel further, in order to get desired results.

9.4.7 Respondent remuneration

CIG Research's panel of opt-in pharmacists are compensated for their time participating in surveys throughout the year. CIG Research funds this programme from its commercial research, and there is no link to individual clients in the process. CIG Research's pharmacist panel receive points for surveys completed. When they have accumulated 500 points, they may redeem these against Amazon vouchers. The number of points issued for a survey is usually proportionate to the length of the questionnaire and difficulty in obtaining the sample.

9.5 Study size

This section presents sample size and precision of the estimate calculations for various survey sample sizes. The precision of the estimate calculations are based on the following assumptions:

- The confidence intervals (CIs) around the estimate are two-sided
- The probability of type-I error (alpha) is 5%
- The table below provides precision of the estimate (width of 95% CI around the estimate) for a range of sample sizes at or around the 50% mark, which is the least accurate point in the standard deviation curve.

Table 2. Sample size obtained for various precisions

Sample size	Statistical precision (%)
100	± 9.8
150	± 8.0
200	± 6.9
250	± 6.2
300	±5.7
1600 (total case studies)	± 2.5

The sample size chosen for this study is dependent on statistical and feasibility considerations. On the basis of the maximum feasible sample size achievable within the scope of this study, and the relative precision of this dataset, a sample of 200 pharmacists has been chosen. It may be necessary to over-sample up to 250 in order to achieve the 200, based on 80% having read aRMMs and conducted at least one consultation with a patient on desogestrel 75 microgram tablets in the six months prior to the survey. This represents a response rate of approximately 2% of the CIG Research panel and is typical of the response rates achieved for questionnaires of 20-25 minutes' length.

Each respondent will be shown eight case study examples of consultations, and will answer corresponding questions. The 200 responses will generate a combined response to 1600 case studies, which will be taken together to measure the proposed success criteria, with a variance of ± 2.5% on 1600 responses.

9.6 Data management

All data collected during the study will be held confidentially by CIG Research using an electronic data collection system called QuestionPro. This system encrypts all identifiable information, and respondent identifiers are stored separately from survey responses.

To minimise data entry errors, skip logic for certain questions as well as the ability to mark only one response or multiple responses, as appropriate, form part of the survey programming. There will be no follow-up queries to respondents for this project. Detailed management of data is described in section 9.8 Quality control.

9.7 Data analysis

The threshold of 80% correct answers to supply or not supply desogestrel 75 microgram tablets in the eight case studies has been set as a KPI on the basis that previous analysis of comparable PASS studies has shown that receipt and use rates for RM tools among HCPs rarely exceed 80%[3], whereas percentages of correct knowledge of key safety messages mostly lie between 70% and 90%. On this basis, a threshold of 80% has been set as an average across the eight case studies, rather than on each case study.

On completion of the fieldwork, all data will be checked and validated to ensure that any erroneous or duplicated responses are excluded. Data extraction for the total sample and for each segment within the sample will be carried out and CIG Research will compile a series of tables and charts for the final report, combining and comparing segments as appropriate. Detailed commentary will be provided for each table and each chart, explaining the data, interpreting it and drawing appropriate conclusions.

Data segmentation will also be generated for key variables, each of which have a minimum sample size of 30 responses (e.g. splitting the sample by gender and age, outlet type and job title). In addition, key segments can be generated against specific answers.

Detailed methodology for summary and statistical analyses of data collected in this study will be included in the report on the survey.

Data collected from the survey will be reported as descriptive statistics. Frequency distributions with 95% CIs will be calculated for pharmacist responses to all questions that address the survey objectives.

CIG Research will apply all appropriate statistical validation to the recommended sampling approach, to the quota setting and recruitment processes. 100% of responses will be validated to ensure quality of completion, non-replication (i.e. ballot-stuffing) and response to all questions by all respondents.

Open ended questions will be analysed using the standard market research process of generating code frames. In this case, each open ended answer will be broken down into the individual statements it makes, and each statement will be given a code, such that all respondents making the same or very similar comments will be allocated that code. One respondent may make many statements within their answer and may therefore generate several codes, so the total number of coded answers usually exceeds 100% of the sample size. Once all respondents' answers are coded, there will be a residue of disparate 'other answers', which usually constitutes less than 5% of the total. In excess of 95% of the total will have been coded with (typically) between 10 and 20 codes in the code frame. The full study analysis will include the following statistics, including metrics for survey administration:

- The number and percentage of target respondents within the CIG Research opt-in panel who are invited to participate; number of invitations sent in total;
- The number and percentage of invitees who open the invitation but do not proceed to participate in the survey; open and click through rates;
- Reasons for ineligibility – i.e. the number opening the survey and commencing responses but who are ruled ineligible on the grounds of not recalling receiving and reading the aRMMs, job title, outlet type or agreement to have their data included;
- The number and percentage commencing the survey but failing to complete other than through eligibility – drop-outs;
- Final number of survey completions;
- The number and percentage of pharmacists by job title and outlet type who completed the survey;
- The comparative profile of pharmacists who gave correct or incorrect responses to the eight case study scenarios in terms of their demography;
- The demographic characteristics of those participating – e.g. age, gender, years since qualifying;
- Pharmacist responses to questions pertaining to the survey objectives:
    - Pharmacists' knowledge/understanding of the risks associated with the supply of desogestrel 75 microgram tablets
    - The number and percentage of pharmacists who correctly responded to each scenario about the risks of supplying desogestrel 75 microgram tablets
    - Recall of reading and utilising the aRMMs
    - Utilisation of the aRMMs during consultations

- Number of consultations in the last six months
- Location of consultations within the pharmacy.

Detailed analysis will be carried out for each scenario. Where the percentage of pharmacists answering a scenario question correctly is below the level defined to represent success, the training materials relating to that scenario will be reviewed and improved as appropriate. **Annex 4** includes risks and contraindications that are covered in the scenarios and four corresponding answer options. All scenario answers will be analysed and the percentage proportion of correct versus incorrect answers will be shown. If less than 80% correct answers are provided, the aRMMs have not passed the success criteria and the relevant training materials will be amended. There are three possible incorrect answers for each scenario question. If one incorrect answer is overperforming, related section in training materials will be updated, but if all three incorrect answers over-index to a statistically significant level at the 95% confidence limit applied to all analysis of this data (see table 2), changes will be made in all of them.

Given that the aRMMs from both brands are closely aligned, and that pharmacists may forget or be mistaken as to which set they have used, both sets of materials will be amended as appropriate if an issue is identified.

The report will include a detailed executive summary, together with conclusions and recommendations in line with the information required for the EMA PASS template for the final study report.

9.8 Quality control

The study will be conducted in accordance with all applicable regulatory requirements. The testing will also be conducted in accordance with all applicable subject privacy requirements (including European GDPR), and the guiding principles of the current version of the Declaration of Helsinki.

Documentation of all data management activities will allow step-by-step retrospective assessment of data quality and performance. Management of data will be performed in accordance with applicable standards (including MHRA *'GXP' Data Integrity Guidance and Definitions*[4]) and data cleaning procedures to ensure the integrity of the data (e.g. removing errors and inconsistencies in the data).

The survey data will be collected using a secure online data entry system. The proposed system has been validated and is secure for receiving and storing survey data. A cloud-based data repository will be used to warehouse survey data and other relevant programme information. This platform ensures compliance with Annex 11 *EudraLex The Rules Governing Medicinal Products in the European Union*[5] for the entry, storage, manipulation, analysis and transmission of electronic information.

The system is integrated with dashboard reporting services to enable real time access to data collected online. All data entered will be single data entered by the respondent. Data will be checked in real time against the programmed edit specifications as they are entered to ensure that data are being entered according to acceptable parameters and requirements. Data exported into Excel for the purposes of generating presentation charts for reporting will be aggregated and not manipulated in any way that alters the results of the survey, and will match the data held within the secure online data entry system. All versions generated will be dated, kept with accompanying documentation and

archived. This archived data will be available for independent audit throughout the study and retrospectively.

9.9 Limitations of the research methods

It is a limitation that the participating pharmacists will be self-selected since respondents will voluntarily respond to the invitation to participate. However, the survey recruitment strategies are intended to recruit a representative sample. All data from the survey are self-reported and therefore susceptible to possible reporting bias. There could be discrepancies between what pharmacists report about their practices and their actual behaviours. In this case, it would be difficult to validate whether pharmacists' responses to practice-related questions completely concur with their actual behaviours since this is a self-reported survey.

A secondary limitation inherent in survey research is the reliance on the respondent's recall of whether or not the aRMM materials were read and utilised. If respondents say they did not read and utilise the aRMMs, they will be screened out. It is possible that pharmacists may simply not recall the tools that were received and read. It is possible that removing those who do not recall reading the aRMMs will reduce the overall sample size, depending on the proportion of all pharmacists eligible to participate in the survey.

Given that this study is being conducted jointly on behalf of two companies whose products and support information are provided to pharmacies in the UK, it is likely that a small proportion of respondents may be confused as to which company's product is which and which company has supplied which support materials. In this case, it is not envisaged that the two companies will receive different analyses based on their brands, although the survey questionnaire does include awareness questions for both brands, which will allow for segmentation by brand. An option for 'brand unknown' is included in the survey questions, so respondents can select that if they are not sure which brand's materials they have used.

The objective of this PASS is to measure the effectiveness of the pharmacy training materials. This study will look at two process indicators: a) reaching the target population and b) assessing clinical knowledge. These process indicators are intended to provide insight into to what extent the dissemination of pharmacy materials has been executed as planned and whether the intended measures impact on behaviour.

For the switch of desogestrel from POM to P, where it is not feasible for the two applicants to obtain data on outcome indicators for reductions in adverse events, effectiveness evaluation of this PASS is exclusively based on the careful interpretation of data on process indicators. Situations like these are acknowledged in the *Guideline on good pharmacovigilance practices Module XVI*[6], where measurement of effectiveness may need to rely on process indicators instead of outcome indicators.

10. Protection of human subjects

All parties will ensure protection of pharmacists' personal data and will not include names on any client forms, reports, publications, or in any other disclosures, except where required by laws. In the case of data transfer, parties will maintain high standards of confidentiality and protection of pharmacist data. In the specific case of AE reporting, respondents are required to give their permission for information to be passed to the appropriate company (see Section 11, below).

Due to the nature of the study, informed consent is not required. Participants need to go to the survey website in order to complete the survey. Consent is implied by these actions. Additionally, at the beginning of the survey, the respondent will be asked if they agree to take part in the survey. If yes, the respondent continues with the survey questions. If no, the survey is terminated.

11. Management and reporting of adverse events/adverse reactions

This study does not involve data collection on clinical endpoints on individual patients. However, safety information may be identified during the course of data collection (e.g. through an email note to CIG Research). Any safety information for an individual patient that is volunteered by a study participant during the course of this research will be reported as described below.

The following safety events must be reported on the NIS AE monitoring report form: serious and non-serious adverse events associated with the use of the Maxwellia or Laboratoire HRA Pharma products, and scenarios involving exposure during pregnancy, exposure during breast feeding, medication error, overdose, abuse, misuse, lack of efficacy and occupational exposure (all reportable, regardless of whether associated with an AE), when associated with the use of a Maxwellia or Laboratoire HRA Pharma product. These AEs will be reported to the appropriate client as outlined above (Section 9.4.5).

In the case of AE reporting, it is envisaged that wherever possible, each company will receive information pertaining to their own brand and will not receive information pertaining to their competitor's brand. Where it is not possible to identify which brand an AE refers to, both companies will receive the AE information.

12. Plans for disseminating and communicating study results

A final report describing the survey objectives, detailed methods, results, discussion and conclusions will be developed at the end of the survey for submission to the MHRA within the timeframe specified in 'Section 6: Milestones.' In addition, the study results will be posted on the EU PAS register.

13. References

1. Hana Summary of Product Characteristics (SmPC) https://www.medicines.org.uk/emc/product/12735/smpc
2. Lovima Summary of Product Characteristics (SmPC) https://www.medicines.org.uk/emc/product/12736/smpc
3. EMA/DIA Information Day, 2017: Preliminary results of a cumulative systematic review and meta-analysis of risk minimisation survey studies Minutes of the PRAC meeting 6-9 March 2017 (europa.eu)
4. MHRA *'GXP' Data Integrity Guidance and Definitions* letter (publishing.service.gov.uk)
5. EudraLex: The Rules Governing Medicinal Products in the European Union, Volume 4 *Good Manufacturing Practice Medicinal Products for Human and Veterinary Use*, Annex 11: Computerised Systems *Annex 11 Final 0910 (europa.eu)*
6. Guideline on good pharmacovigilance practices (GVP) – Module XVI – Risk minimisation measures: selection of tools and effectiveness indicators (Rev 2) (europa.eu)

Annex 1. Example invitation to participate in the survey

Dear Pharmacist,

CIG Research has been commissioned to conduct a survey among pharmacists to understand your attitudes and behaviour in relation to the recent switch of desogestrel 75 microgram tablets from POM to Pharmacy (P) and the information and training you may have received about the product to enable you to correctly advise patients and mitigate risk. This survey should take approximately 25 minutes to complete and it will have to be completed in one sitting within 60 minutes. Please do not close the survey until you have completed it as you will not be allowed to re-open it. It is possible to complete the survey on a desktop, laptop, tablet or mobile device, but we recommend completing it on your desktop for the best experience.
When the survey fieldwork ends, you will receive **Reward Points** in appreciation of your time and cooperation, which can be redeemed against Amazon vouchers.

Start survey

Many thanks for your ongoing support. We will have one or two more surveys launching in the next month, and you can add to your points total by participating. Please look out for your invitations to these.

Please make sure to complete the survey, fill in your details and opt in to receive your Reward Points. To check your accumulated Reward Points, please email rewardpoints@1530.com

Your help is greatly appreciated.
Yours faithfully,

Adrian Wistreich
Research Director

Annex 2. ENCePP checklist for study protocols

Study title:
Assessment of the effectiveness of additional Risk Minimisation Measures (aRMMs) among pharmacists for provision of desogestrel 75 microgram tablets in a community pharmacy setting

EU PAS Register® number:
Study reference number (if applicable):

Section 1: Milestones	**Yes**	**No**	**N/A**	**Section Number**
1.1 Does the protocol specify timelines for				6
1.1.1 Start of data collection[1]	☒	☐	☐	
1.1.2 End of data collection[2]	☒	☐	☐	
1.1.3 Progress report(s)	☐	☐	☒	
1.1.4 Interim report(s)	☐	☐	☒	
1.1.5 Registration in the EU PAS Register®	☒	☐	☐	
1.1.6 Final report of study results	☒	☐	☐	

Comments:

Section 2: Research questions	**Yes**	**No**	**N/A**	**Section Number**
2.1 Does the formulation of the research questions and objectives clearly explain:	☒	☐	☐	
2.1.1 Why the study is being conducted? (e.g. to address an important public health concern, a risk identified in the risk management plan, an emerging safety issue)	☒	☐	☐	7
2.1.2 The objective(s) of the study?	☒	☐	☐	8
2.1.3 The target population? (i.e. population or subgroup about whom the study results are intended to be generalised)	☒	☐	☐	9
2.1.4 Which hypothesis(es) is(are) to be tested?	☐	☐	☒	
2.1.5 If applicable, that there is no *a priori* hypothesis?	☐	☐	☒	

Comments:

[1] Date from which information is first recorded in the study dataset or, in the case of secondary use of data, the date from which data extraction starts.
[2] Date from which the analytical dataset is completely available.

Section 3: Study design	**Yes**	**No**	**N/A**	**Section Number**
3.1 Is the study design described? (e.g. cohort, case-control, cross-sectional, other design)	☒	☐	☐	9
3.2 Does the protocol specify whether the study is based on primary, secondary or combined data collection?	☒	☐	☐	
3.3 Does the protocol specify measures of occurrence? (e.g. rate, risk, prevalence)	☐	☐	☒	
3.4 Does the protocol specify measure(s) of association? (e.g. risk, odds ratio, excess risk, rate ratio, hazard ratio, risk/rate difference, number needed to harm (NNH))	☐	☐	☒	
3.5 Does the protocol describe the approach for the collection and reporting of adverse events/ adverse reactions? (e.g. adverse events that will not be collected in the case of primary data collection)	☒	☐	☐	11

Comments:

Section 4: Source and study populations	**Yes**	**No**	**N/A**	**Section Number**
4.1 Is the source population described?	☒	☐	☐	9
4.2 Is the planned study population defined in terms of:				9
4.2.1 Study time period	☒	☐	☐	
4.2.2 Age and sex	☐	☐	☒	
4.2.3 Country of origin	☒	☐	☐	
4.2.4 Disease/indication	☐	☐	☒	
4.2.5 Duration of follow-up	☒	☐	☐	
4.3 Does the protocol define how the study population will be sampled from the source population? (e.g. event or inclusion/exclusion criteria)	☒	☐	☐	9

Comments:

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
5.1 Does the protocol describe how the study exposure is defined and measured? (e.g. operational details for defining and categorising exposure, measurement of dose and duration of drug exposure)	☐	☐	☒	
5.2 Does the protocol address the validity of the exposure measurement? (e.g. precision, accuracy, use of validation sub-study)	☐	☐	☒	
5.3 Is exposure categorised according to time windows?	☐	☐	☒	

Section 5: Exposure definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
5.4 Is intensity of exposure addressed? (e.g. dose, duration)	☐	☐	☒	
5.5 Is exposure categorised based on biological mechanism of action and taking into account the pharmacokinetics and pharmacodynamics of the drug?	☐	☐	☒	
5.6 Is (are) (an) appropriate comparator(s) identified?	☐	☐	☒	

Comments:

Section 6: Outcome definition and measurement	**Yes**	**No**	**N/A**	**Section Number**
6.1 Does the protocol specify the primary and secondary (if applicable) outcome(s) to be investigated?	☒	☐	☐	8
6.2 Does the protocol describe how the outcomes are defined and measured?	☒	☐	☐	9.7
6.3 Does the protocol address the validity of outcome measurement? (e.g. precision, accuracy, sensitivity, specificity, positive predictive value, use of validation sub-study)	☒	☐	☐	9
6.4 Does the protocol describe specific outcomes relevant for Health Technology Assessment? (e.g. HRQoL, QALYs, DALYs, healthcare services utilisation, burden of disease or treatment, compliance, disease management)	☐	☐	☒	

Comments:

Section 7: Bias	**Yes**	**No**	**N/A**	**Section Number**
7.1 Does the protocol address ways to measure confounding? (e.g. confounding by indication)	☐	☐	☒	
7.2 Does the protocol address selection bias? (e.g. healthy user/adherer bias)	☒	☐	☐	9.9
7.3 Does the protocol address information bias? (e.g. misclassification of exposure and outcomes, time-related bias)	☐	☐	☒	

Comments:

Section 8: Effect measure modification	**Yes**	**No**	**N/A**	**Section Number**
8.1 Does the protocol address effect modifiers? (e.g. collection of data on known effect modifiers, sub-group analyses, anticipated direction of effect)	☐	☐	☒	

Comments:

Section 9: Data sources	**Yes**	**No**	**N/A**	**Section Number**
9.1 Does the protocol describe the data source(s) used in the study for the ascertainment of:				
9.1.1 Exposure? (e.g. pharmacy dispensing, general practice prescribing, claims data, self-report, face-to-face interview)	☒	☐	☐	9
9.1.2 Outcomes? (e.g. clinical records, laboratory markers or values, claims data, self-report, patient interview, including scales and questionnaires, vital statistics)	☒	☐	☐	9
9.1.3 Covariates and other characteristics?	☐	☐	☒	
9.2 Does the protocol describe the information available from the data source(s) on:				
9.2.1 Exposure? (e.g. date of dispensing, drug quantity, dose, number of days of supply prescription, daily dosage, prescriber)	☐	☐	☒	
9.2.2 Outcomes? (e.g. date of occurrence, multiple event, severity measures related to event)	☐	☐	☒	
9.2.3 Covariates and other characteristics? (e.g. age, sex, clinical and drug use history, co-morbidity, co-medications, lifestyle)	☐	☐	☒	
9.3 Is a coding system described for:				
9.3.1 Exposure? (e.g. WHO Drug Dictionary, Anatomical Therapeutic Chemical (ATC) Classification System)	☐	☐	☒	
9.3.2 Outcomes? (e.g. International Classification of Diseases (ICD), Medical Dictionary for Regulatory Activities (MedDRA))	☐	☐	☒	
9.3.3 Covariates and other characteristics?	☐	☐	☒	
9.4 Is a linkage method between data sources described? (e.g. based on a unique identifier or other)	☐	☐	☒	

Comments:

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.1 Are the statistical methods and the reason for their choice described?	☒	☐	☐	9.5

Section 10: Analysis plan	**Yes**	**No**	**N/A**	**Section Number**
10.2 Is study size and/or statistical precision estimated?	☒	☐	☐	9.5
10.3 Are descriptive analyses included?	☒	☐	☐	8.3
10.4 Are stratified analyses included?	☐	☐	☒	
10.5 Does the plan describe methods for analytic control of confounding?	☐	☐	☒	
10.6 Does the plan describe methods for analytic control of outcome misclassification?	☐	☐	☒	
10.7 Does the plan describe methods for handling missing data?	☒	☐	☐	9.8
10.8 Are relevant sensitivity analyses described?	☒	☐	☐	9.8

Comments:

Section 11: Data management and quality control	**Yes**	**No**	**N/A**	**Section Number**
11.1 Does the protocol provide information on data storage? (e.g. software and IT environment, database maintenance and anti-fraud protection, archiving)	☒	☐	☐	9.6
11.2 Are methods of quality assurance described?	☒	☐	☐	9.8
11.3 Is there a system in place for independent review of study results?	☒	☐	☐	9.8

Comments:

Section 12: Limitations	**Yes**	**No**	**N/A**	**Section Number**
12.1 Does the protocol discuss the impact on the study results of:				
12.1.1 Selection bias?	☒	☐	☐	9.9
12.1.2 Information bias?	☒	☐	☐	9.9
12.1.3 Residual/unmeasured confounding? (e.g. anticipated direction and magnitude of such biases, validation sub-study, use of validation and external data, analytical methods)	☐	☐	☒	
12.2 Does the protocol discuss study feasibility? (e.g. study size, anticipated exposure uptake, duration of follow-up in a cohort study, patient recruitment, precision of the estimates)	☒	☐	☐	9

Comments:

Section 13: Ethical/data protection issues	**Yes**	**No**	**N/A**	**Section Number**
13.1 Have the requirements of the Ethics Committee/ Institutional Review Board been described?	☐	☒	☐	
13.2 Has any outcome of an ethical review procedure been addressed?	☐	☒	☐	
13.3 Have data protection requirements been described?	☒	☐	☐	10

Comments:

Section 14: Amendments and deviations	**Yes**	**No**	**N/A**	**Section Number**
14.1 Does the protocol include a section to document amendments and deviations?	☒	☐	☐	5

Comments:

Section 15: Plans for communication of study results	**Yes**	**No**	**N/A**	**Section Number**
15.1 Are plans described for communicating study results? (e.g. to regulatory authorities)	☒	☐	☐	12
15.2 Are plans described for disseminating study results externally, including publication?	☐	☐	☒	

Comments:

Name of the main author of the protocol: _____

Date: dd/Month/year

Signature: _____

Annex 3. Questionnaire design

SURVEY LEGEND

Instructions to the programmer who is tasked with scripting the survey into the survey software.

MULTI CODE is inserted for questions in which respondents may choose more than one option from the pre-defined list of answers.

SINGLE CODE is inserted for questions where only one answer is permitted from the pre-defined list of answers.

Close on codes (x-y) requires that those who choose any of the specified answers denoted by those codes will be redirected to terminate the survey because they are not eligible to continue. These respondents will receive a notification that they are not eligible to continue with the questionnaire.

OPEN ENDED An open ended question is a comment box in which respondents may write as much as they wish in answer to the question. Analysis of open ended questions follows the standard market research guidelines of generating code frames.

IF QA code (x or y) denotes that the following question will be filtered (i.e. visible) only to those who answered QA with a pre-defined answer which is attributed with the code (i.e. x or y).

SLIDER less than one to x describes the format for answering a question using a scale with x points, where a score of 0 is entitled 'less than one' and a score of x or more is entitled 'x plus'. A slider is a graphic response option within the survey software allowing respondents to drag their cursor to a specific point on this scale.

[Show image] describes the facility for a respondent to click on a link to a new window in their browser in which a single image is shown. When they have looked at the image, respondents may close the new window and continue with the survey.

RANDOMISE Randomising is an option within survey software to ensure that each respondent sees the list of answers or names in a different (random) order, thus removing Order Effect from the survey. The software automatically re-combines the responses for each answer prior to presenting them for analysis.

QB PIPE FROM QA refers to the process of branching, whereby those who select options in QA are shown options pertaining to QA in QB.

REPEAT FOR X SCENARIOS repeat the same instruction for each of the x scenarios which appear in the survey.

SLIDER SUM 100% This is a feature within the survey software whereby respondents may attribute percentages to each of two or more answers, and the software will require their answers to add up to 100%. This feature uses the same slider visual described above.

SINGLE CODE GRID A single code grid is a matrix of scale questions where a respondent may answer only once per row in the matrix, and is required to do so.

INTRODUCTION

Dear pharmacist,

The purpose of this research is to understand your attitudes and behaviour in relation to the recent switch of desogestrel 75 microgram tablets from POM to P and the information and training you may have received about the products to enable you to correctly advise patients and mitigate risk. This survey should take **approximately 25 minutes** to complete and it will have to be completed in one sitting within 60 minutes. Please do not close the survey until you have completed it as you will not be allowed to re-open it. It is possible to complete the survey on a desktop, laptop, tablet or mobile device, but we recommend completing it on your desktop for the best experience.

Upon completion of the questionnaire, you will receive Reward Points in appreciation of your time and cooperation.

Any information you provide will be treated as confidential. It will be combined with feedback from others like yourself. You will remain anonymous unless you give permission to be identified.

Your information will only be used for research purposes, with the requirement that reports on aggregated results will be shared with health authorities, and will not be passed to any other organisation without your permission.

You have the right to refuse to answer questions or withdraw at any time. For more information about your rights, please see our privacy notice, available here: Privacy Policy

By proceeding to the next screen:

· I consent to CIG Research collecting and using the information about me that I voluntarily provide for the purposes of research.
· I have read, understand and agree to the terms described above.

a. YES, I am happy to proceed with the research survey on this basis
b. NO, I am not happy to proceed with the research survey on this basis and I do not wish to continue

This survey has been commissioned by healthcare manufacturers upon request from the MHRA. When working on their projects, we are required to report if any participant mentions an adverse event in relation to one of their products.
Should this happen, it would be necessary for us to complete a report and pass your comments to our clients so that they can investigate. We can submit a report anonymously or with your personal details. Please confirm whether you are happy to proceed:

a. Yes, I am happy to proceed, but please submit my report anonymously as I do not want the company to contact me
b. Yes, I am happy to proceed. Please submit the report with my personal details (name and e-mail address). I understand that the company may contact me for further information about the adverse event
c. No, I am not happy to proceed. I understand that this means I will not be able to continue with this survey – CLOSE

Which, if any, of these organisations have you worked for or been contracted to in the last year?
MULTI CODE Close on codes a-e

a. Maxwellia Ltd
b. Laboratoire HRA Pharma
c. Communications International Group
d. Consensio LLP
e. MHRA
f. None of these

DEMOGRAPHIC QUESTIONS

QA What is your job title?
SINGLE CODE Close on codes e-m

a. Pharmacist Proprietor
b. Pharmacist Manager / Supervisor
c. Pharmacist
d. Locum Pharmacist
e. Non-pharmacist Manager/Supervisor
f. Non-pharmacist Proprietor
g. Accuracy Checking Technician
h. Pharmacy Technician
i. Dispensing Assistant
j. Medicines Counter Assistant / Pharmacy Assistant / Beauty Counter Assistant
k. Healthy Living Advisor / Champion
l. Healthcare Advisor / Consultant
m. Other

QB. What type of outlet do you work in?
SINGLE CODE Close on codes g-j

a. One shop independent
b. Group branch shop (2 to 5 outlets)
c. Group branch shop (6 to 9 outlets)
d. Group branch shop (10 to 49 outlets)
e. Group branch shop (50 plus outlets)
f. Multiple head office
g. Hospital
h. GP practice pharmacy
i. Exclusively online pharmacy (no consultations)
j. Other

QC. IF QB code e or f Which multiple do you work in?
SINGLE CODE

a. Boots
b. LloydsPharmacy
c. Superdrug
d. Rowlands Pharmacy
e. Well Pharmacy
f. Day Lewis
g. Supermarket pharmacy
h. Other

QD. In what type of location is your pharmacy based?

SINGLE CODE

a. City centre
b. Town centre
c. Suburb
d. Village
e. Rural

QE. Where is your pharmacy?

SINGLE CODE

a. Scotland
b. Northern Ireland
c. Wales
d. North East
e. North West
f. Yorkshire and the Humber
g. West Midlands
h. East Midlands
i. South East
j. South West
k. East of England
l. Greater London

QF. What is your gender?

SINGLE CODE

a. Male
b. Female
c. Other
d. Prefer not to say

QG. What is your age?

SINGLE CODE

a. Under 25
b. 25-29
c. 30-34
d. 35-39
e. 40-44
f. 45-49
g. 50-54
h. 55-59
i. 60-64
j. 65 plus
k. Prefer not to say

QH. For how many years have you been qualified as a pharmacist?

SLIDER less than one to 30 plus

STUDY QUESTIONS

Q1. In the last six months, have you held any consultations regarding the supply of desogestrel 75 microgram tablets (DSG) in the pharmacy without a prescription?
SINGLE CODE Close on code b

a. Yes
b. No

Q2. In the last six months have you received and read training materials or consultation checklists regarding the supply of desogestrel 75 microgram tablets without a prescription to help minimise risk when having consultations? [show image]
SINGLE CODE Close on b and c

a. Yes, received and read
b. Yes, received but not read
c. No

Q3. Which, if any, of these materials have you read to help minimise risk when having consultations regarding the supply of desogestrel 75 microgram tablets without a prescription? **MULTI CODE**
[Show image] **Close if Pharmacy training guide or Checklist not selected**

RANDOMISE MULTI CODE	Hana	Lovima	Brand unknown
Pharmacy training guide	o	o	o
Consultation/ supply aid checklist	o	o	o
SmPC	o	o	o
Pack copy	o	o	o

Q4. How many consultations do you estimate that you have had with patients about non-prescription desogestrel 75 microgram tablets in the pharmacy in the last six months?
SLIDER from 1 to 500 plus (increments of 20)

Q5. When these consultations did not result in the supply of desogestrel 75 microgram tablets, what were the main reasons for this? *Please write in short descriptions and try to be very specific* **OPEN ENDED**

Q6. Where in the pharmacy are these consultations conducted?
SLIDER SUM 100%

a. In a private consultation area
b. At the pharmacy counter
c. Elsewhere

Q7. How confident do you feel about advising patients on the use of desogestrel 75 microgram tablets?
SINGLE CODE

a. Completely
b. Very
c. Fairly

d. Not very
e. Not at all

Q8. And how confident are you about correctly supplying desogestrel 75 microgram tablets without a prescription?
SINGLE CODE

a. Completely
b. Very
c. Fairly
d. Not very
e. Not at all

Q9. How would you rate your own level of knowledge about desogestrel 75 microgram tablets?
SINGLE CODE GRID

RANDOMISE	Excellent	Good	Fair	Poor	Very Poor	None at all
Its mode of action	o	o	o	o	o	o
Its side effects	o	o	o	o	o	o
Recommended dosage, frequency	o	o	o	o	o	o
Its use with concomitant medication	o	o	o	o	o	o
Exclusion of pregnancy	o	o	o	o	o	o

Q10. **PIPE FROM Q3**Which, if any, of these materials have you used in conjunction with consultations regarding the supply of desogestrel 75 microgram tablets without a prescription?
[Show image]

RANDOMISE MULTI CODE	Hana	Lovima	Brand unknown
Pharmacy training guide	o	o	o
Consultation/ supply aid checklist	o	o	o
SmPC	o	o	o
Pack copy	o	o	o
Other	o	o	o

Q11a. After using the materials for consultations regarding the supply of desogestrel 75 microgram tablets without a prescription, how useful did you find them?
SINGLE CODE

a. Extremely useful
b. Very useful
c. Somewhat useful
d. Not useful
e. No opinion

Q11b **IF Q11a is d**: Why were the materials not useful to you? *Please write a short description and try to be very specific* **OPEN ENDED**

Q12. **PIPE FROM Q3** Were the materials easily accessible to you when giving consultations?
SINGLE CODE

RANDOMISE MULTI CODE	Yes	No
a. Pharmacy training guide – Hana	o	o
b. Consultation/ supply aid checklist – Hana	o	o
c. SmPC – Hana	o	o
d. Pack copy – Hana	o	o
e. Pharmacy training guide – Lovima	o	o
f. Consultation/ supply aid checklist – Lovima	o	o
g. SmPC – Lovima	o	o
h. Pack copy - Lovima	o	o
i. Other	o	o

Q13. **DESOGESTREL 75 microgram tablets SCENARIOS**

We would like you to take time reading the following scenarios of typical situations in which a patient requests desogestrel 75 microgram tablets. Please select one of the four “supply” / “do not supply” options that you believe to be correct. While considering your answer, you can access any of the support materials you would typically use during this type of consultation, including the training materials for Lovima and Hana.

Scenario 1

A woman in her early 20s asks if she can buy the contraceptive pill without having to see a GP. She has recently moved to the area to start a new job after having a gap year travelling and hasn't yet registered with a GP practice in the area. She has a regular boyfriend and they always use condoms and haven't had sex since her last period, which started about 10 days ago. She doesn't have any medical conditions and is not taking any other medicines. Her periods are regular. However, she says that she has started to experience occasional bleeding after sex. She contracted hepatitis A couple of months ago while traveling and felt quite poorly for a couple of weeks.

Select the correct course of action from the following for supplying desogestrel:

a. Supply desogestrel and advise her to start taking it on day 1 of her next menstrual period
b. Do not supply desogestrel as she is experiencing unexplained vaginal bleeding
c. Do not supply desogestrel as she has a recent history of liver disease
d. Do not supply desogestrel as she is experiencing unexplained vaginal bleeding and has a recent history of liver disease

Correct course of action: d. Do not supply desogestrel as she is experiencing unexplained vaginal bleeding and has a recent history of liver disease

Desogestrel should not be supplied for 2 reasons: the customer has been experiencing unexplained vaginal bleeding, and she has a history of liver disease; you may not know if her liver function has returned to normal. She should be advised to register with a GP for further investigation.

Scenario 2

A woman in her 30s asks to speak to you as she has heard she can buy a contraceptive pill from the pharmacy. She has previously had a progestogen-only contraceptive pill prescribed by her GP, but stopped taking it about a year ago as she had split up with her partner. Her periods are regular and her last period was about 2 weeks ago; she has not had sex since her last period. She is taking sertraline for depression and has no other medical conditions.

Select the correct course of action from the following:

a. Do not supply desogestrel as it interacts with sertraline
b. Do not supply desogestrel as depression is a contraindication
c. Supply desogestrel and advise her to start taking it on day 1 of her next period
d. Supply desogestrel and advise that she can start taking it straight away

Correct course of action: c. Supply desogestrel and advise her to start taking it on day 1 of her next period

Desogestrel can be supplied as depression and sertraline are not contraindications for its use, although some women using hormonal contraceptives including desogestrel have reported experiencing depression. The woman should be advised to read the patient information leaflet and speak to her GP if she notices changes in her mood or depressive symptoms. She should be advised to start taking desogestrel on day 1 of her next period.

Scenario 3

A woman in her 20s comes into the pharmacy and asks if she can buy the contraceptive pill. She has just started a new relationship; she and her boyfriend have not yet had sex, but have discussed it and she would like to start taking a reliable form of contraception before they do. She says that she split up with her previous boyfriend about 6 months ago and has not had sex with anyone since. She has regular periods with no bleeding in between, and has not experienced bleeding after sex in the past. On further questioning, she says that she is taking carbamazepine for epilepsy and says that her epilepsy is well controlled.

Select the correct course of action from the following:

a. Supply desogestrel as it is reasonable to assume she isn't pregnant as she hasn't had sex for 6 months
b. Supply desogestrel as there are no contraindications
c. Do not supply desogestrel as it may affect her epilepsy and increase her risk of seizures
d. Do not supply desogestrel as carbamazepine is a hepatic enzyme-inducing drug which may reduce the efficacy of desogestrel

Correct course of action: d. Do not supply desogestrel as carbamazepine is a hepatic enzyme-inducing drug which may reduce the efficacy of desogestrel

Women taking carbamazepine long-term should be referred to their GP for further advice on contraception options.

Scenario 4

A woman in her 30s comes into the pharmacy with a young baby. She asks if she can have a word in private as she would like to start taking desogestrel and has heard that she can buy it from the pharmacy. She gave birth just over 4 months ago and since then she and her husband have been using condoms and spermicide when having sex, but she would prefer to take a contraceptive pill as that is what she has used in the past. She confirms that she is fully breastfeeding, hasn't had a period since giving birth and confirms that she is not pregnant. She is taking enalapril to manage hypertension, which is well controlled, and has no other medical conditions.

Select the correct course of action from the following:

a. Do not supply desogestrel as she may be pregnant
b. Do not supply desogestrel as she has hypertension
c. Supply desogestrel and advise her that she can start taking it straight away but should use additional contraceptive measures (abstinence or barrier) for the first 7 days
d. Do not supply desogestrel as she is breastfeeding

Correct course of action: c. Supply desogestrel and advise her that she can start taking it straight away but should use additional contraceptive measures (abstinence or barrier methods) for the first 7 days

Desogestrel can be supplied as pregnancy can be ruled out with reasonable certainty as this woman meets one or more of the criteria for exclusion of pregnancy. It is reasonable to exclude pregnancy if a woman has used a reliable method of contraception correctly and consistently, is fully breastfeeding, not having periods and is less than 6 months after giving birth.

Scenario 5

A woman in her 30s asks to have a chat to find out if desogestrel would be a suitable contraceptive for her. She has been with her partner for over 10 years and previously had a contraceptive implant, but had it removed a couple of months ago. She and her partner have been using condoms since she had her implant removed. She says her periods are regular and she has no bleeding between her periods or after sex. She has type 2 diabetes, which is well controlled; she is taking metformin. She had a deep vein thrombosis about 5 years ago, but has not had a recurrence. She has a BMI of >30.

Select the correct course of action from the following:

a. Do not supply desogestrel as her BMI indicates that she is obese
b. Supply desogestrel as her diabetes is well controlled
c. Do not supply desogestrel and refer her to her doctor as she has a history of thrombosis
d. Do not supply desogestrel and refer her to her doctor as she has type 2 diabetes

Correct course of action: d. Do not supply desogestrel and refer her to her doctor as she has type 2 diabetes

Although this customer's diabetes is well controlled, women with diabetes should be carefully observed during the first few months of taking desogestrel and should be referred to their GP or nurse before taking it. Obesity and past history of venous thromboembolism (VTE) are not contraindications for desogestrel. Only active VTE represents a contraindication, but women who have had a previous VTE should be made aware of the possibility of recurrence.

Scenario 6

A teenager asks for a further supply of desogestrel. She has been taking desogestrel for 3 months. She says that she has been experiencing some spotting and her periods haven't been as regular as they used to be, but this isn't bothering her. She has been taking desogestrel as directed every day and hasn't missed a dose. She has no medical conditions and is not taking any other medicines.

Select the correct course of action from the following:

a. Do not supply desogestrel as she is experiencing side-effects
b. Do not supply as the woman could be under 16
c. Supply desogestrel and advise her to consult her GP if the spotting is after sex or the irregular periods become bothersome
d. Do not supply desogestrel as she may be pregnant

Correct course of action: c. Supply desogestrel and advise her to consult her GP if the spotting is after sex or the irregular periods become bothersome

Women can continue to take desogestrel if they experience changes to their bleeding pattern, but should consult their GP if their bleeding is after sex or becomes bothersome. Desogestrel is indicated for women of childbearing age. Pharmacists should refer to relevant guidance on safeguarding and consent in women under the age of 16.

Scenario 7

A woman in her 40s asks if she can buy desogestrel. She and her husband have been using condoms and spermicide for contraception since she had breast cancer nearly 10 years ago, but he doesn't really like using condoms. She asks if desogestrel would be suitable for her as she gets occasional migraines. Apart from this, she has no other medical conditions and isn't taking any prescription medicines. Her periods are regular and she hasn't experienced any bleeding between her periods or after sex.

Select the correct course of action from the following:

a. Do not supply desogestrel as she has a history of breast cancer
b. Do not supply desogestrel as she gets occasional migraines
c. Supply desogestrel and advise her to see her GP if her migraines get worse or become more frequent
d. Supply desogestrel as she had breast cancer more than 5 years ago

Correct course of action: a. Do not supply desogestrel as she has a history of breast cancer

Women who have or have a history of sex steroid-sensitive malignancies such as breast, uterine or ovarian cancer should be referred to their GP to discuss the use of hormonal contraceptives before starting treatment.

Scenario 8

A woman in her 30s asks to speak to you in private. She explains that she had unprotected sex a couple of days ago and would like to buy emergency contraception. She has taken ulipristal acetate in the past and would like to take the same tablet again as she didn't experience any side-effects. You determine that she is suitable for ulipristal acetate and provide her with a pack. She says that she has just started a new relationship and would also like to start taking regular contraception. You discuss contraceptive options with her, including long-acting reversible contraceptives (LARCs), and explain that only barrier methods such as condoms will protect her from STIs. She decides she would like to start taking desogestrel. She isn't taking any other medication, has no medical conditions and her periods are regular. She mentions that she smokes.

Select the correct course of action from the following:

a. Supply desogestrel and advise her to start taking it straight away
b. Do not supply desogestrel as she may be pregnant
c. Supply desogestrel and advise her to start taking it on day 1 of her next menstrual period and to use additional contraceptive measures (abstinence or barrier methods) until then
d. Do not supply desogestrel as she is a smoker

Correct course of action: c. Supply desogestrel and advise her to start taking it on day 1 of her next menstrual period and to use additional contraceptive measures (abstinence or barrier methods) until then

If a woman wishes to start taking desogestrel after using emergency contraception, it is advisable to start taking it on day 1 of her next menstrual period. If the first day of her next menstrual period is within 5 days of taking ulipristal acetate for emergency contraception, she should wait 5 days after taking ulipristal acetate before starting desogestrel. She should use additional contraceptive measures (abstinence or barrier methods) during these 5 days and for an additional 7 days after starting desogestrel. Ulipristal acetate and desogestrel both bind to the progesterone receptor. Concomitant use may result in reduced efficacy of both and is therefore not recommended. Smoking is not a contraindication for desogestrel.
The woman should be reminded that if her period does not come, she will need to take a pregnancy test and/or speak to her GP. This is because emergency contraception is not always effective and there is still a risk of pregnancy.

Annex 4: Risks assessed in case study scenarios

Number	Answer	Risk/contraindication
Scenario 1	a. Incorrect	Contraindicated if there is a recent history of liver disease and unexplained vaginal bleeding
	b. Incorrect	Contraindicated if there is unexplained vaginal bleeding
	c. Incorrect	Contraindicated if there is a recent history of liver disease
	d. Correct	Correct understanding of recent history of liver disease and unexplained vaginal bleeding
Scenario 2	a. Incorrect	Not contraindicated when taking an SSRI
	b. Incorrect	Depression is not a contraindication
	c. Correct	Correct understanding of using desogestrel in depression and taking an SSRI
	d. Incorrect	Quick starting, which is outside of the Pharmacy (P) product licence
Scenario 3	a. Incorrect	Contraindicated if taking a hepatic enzyme-inducing drug
	b. Incorrect	Contraindicated if taking a hepatic enzyme-inducing drug
	c. Incorrect	Contraindicated if taking a hepatic enzyme-inducing drug
	d. Correct	Correct understanding of the effect hepatic enzyme-inducing drugs on desogestrel
Scenario 4	a. Incorrect	Not contraindicated if pregnancy can be excluded
	b. Incorrect	Hypertension is not a contraindication
	c. Correct	Correct understanding of using desogestrel during pregnancy, hypertension and breastfeeding
	d. Incorrect	Breastfeeding is not a contraindication
Scenario 5	a. Incorrect	Diabetes is a contraindication Obesity is not a contraindication
	b. Incorrect	Diabetes is a contraindication
	c. Incorrect	Diabetes is a contraindication History of thrombosis is not a contraindication
	d. Correct	Correct understanding of using desogestrel in diabetes, obesity and a history of thrombosis
Scenario 6	a. Incorrect	Not contraindicated unless bleeding is after sex or becomes bothersome

	b. Incorrect	Not contraindicated if relevant guidance on safeguarding and consent in women under the age of 16 is followed
	c. Correct	Correct understanding of periods, side-effects, age and pregnancy
	d. Incorrect	Not contraindicated if pregnancy can be excluded
Scenario 7	a. Correct	Correct understanding of using desogestrel in breast cancer (sex steroid-sensitive malignancies) and migraine
	b. Incorrect	A history of sex steroid-sensitive malignancies is a contraindication Migraine is not a contraindication
	c. Incorrect	A history of sex steroid-sensitive malignancies is a contraindication
	d. Incorrect	A history of sex steroid-sensitive malignancies is a contraindication
Scenario 8	a. Incorrect	Desogestrel should not be started immediately after taking ulipristal acetate
	b. Incorrect	Not contraindicated if pregnancy can be excluded
	c. Correct	Correct understanding of emergency contraception and excluding pregnancy
	d. Incorrect	Smoking is not a contraindication