The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

GSK Medicine: Orlistat

Study Number: 204675

Title: Evaluating the effectiveness of the revised alli® pack information in helping pharmacy staff within the EU supply alli® appropriately

Rationale: To assess the effectiveness of the updated alli® pack label in enabling pharmacy staff to supply alli® appropriately.

Phase: Phase 4

Study Period: 24-Dec-16 to 26-Jun-17

Study Design: This was an observational study testing pharmacy staff knowledge and behaviour using virtual customers to provide evidence of the effectiveness of the revised label. It was run in the relevant European Union (EU) markets and where the alli® supplies were re-introduced (UK and Spain).

Pharmacy staff were recruited from online communities and via direct contact. Recruitment was targeted to capture a range of geographical locations across each country, and a mixture of different types of pharmacies (large chains, small chains, independents). All pharmacy staff in the UK or Spain (countries where alli® had been resupplied) who might be involved in either providing point of contact advice, or in supplying alli® to customers were involved in the study. These included: practicing community pharmacist or pharmacy assistant, counter assistants, pharmacy technicians and pre-registration pharmacists in the United Kingdom (UK) and Spain. All participating pharmacy staff were provided with updated on-pack information for alli® approximately one-two weeks before completing the survey. This time interval between receiving the updated on-pack information and completion of the survey ensured that pharmacy staff have had an opportunity to see the updated information but it did not bias the results of the survey. The survey was therefore more likely to reflect true levels of knowledge of the updated pack information. Pharmacy staff was not restricted from accessing their on-shelf or supplied updated on-pack information to check details whilst completing the survey because this is what they would probably do in practice. Participants were not engaged in any training or study other than from the materials provided. Conferring or seeking advice from others in order to complete the task was also prohibited as the study design was to simulate real life scenarios.

Pharmacy staff completed an online questionnaire in their native language in which they were presented with a series of 33 virtual customers (developed in conjunction with clinical experts [endocrinologists, general practitioners and consultant physicians]) in random order and asked to decide whether each customer was suitable for alli®. If a customer was deemed unsuitable, eliciting the rationale for this enabled further detailed assessment of pharmacy staff knowledge and understanding of the indication, contraindications and warnings for use of alli®. The reasons for not supplying alli® to a virtual customer were captured via a free-text field within the online questionnaire for each 'no' response. The text entered was then coded according to the keywords used by the pharmacy staff in their reasoning. The virtual customers were developed in conjunction with clinical experts. The virtual customers represent the spectrum of customers who could present to a pharmacy requesting alli® and were based on the indications and contraindications and selected warnings specified in the pack text, as well as clinical experience of factors that drive customers to seek alli®. They included a photograph of the customer to enable participants to make an estimation of Body Mass Index (BMI). Additional BMI values were provided to pharmacy staff if they requested.

Centre: This study setting was online (pharmacists from UK and Spain took part in an online survey)

Indication: Weight Loss

Treatment: Not applicable (As this study was an online survey conducted on pharmacists, no interventions were dispensed in this study)

Objectives:

1. To evaluate whether revisions to the on-pack label for alli® are effective in enabling pharmacy staff to make an appropriate decision to supply or not supply alli® to customers based upon the following criteria:

    - BMI (≥28 kilograms per meter square [kg/m^2]
    - Age (≥18 years old)
    - Contraindications to use of alli® (taking ciclosporin, chronic malabsorption syndrome, cholestasis, pregnancy or breastfeeding, taking warfarin or other oral anticoagulant)
    - Special warnings to use of alli® (kidney disease, taking medicinal products for diabetes, hypertension,

hypercholesterolemia, taking antiepileptics, anti-retrovirals, benzodiazepines, antidepressants, antipsychotics, levothyroxine or amiodarone).

2. To identify whether there are specific indications, contraindications or warnings for the use of alli® which pharmacy staff do not recognise.

Primary Endpoint:

Proportion of overall correct answers provided by the pharmacy staff to:

- Supply alli® when the virtual customer is suitable for the product and
- Not supply alli® when the virtual customer is not suitable for the product

Suitability was defined by the clinical expert and based on the summary of product characteristics (SmPC). Correct answers in 80% of virtual customers was considered good agreement, signifying that the revised label was effective in enabling pharmacy staff to supply alli® appropriately. The primary endpoint was the % number of correct answer to the 33 vignettes.

Secondary Endpoints:

1. **Proportion of correct responses for each sub-score (indications, contraindications and warnings):** 80% correct answers were considered to signify that the revised label is effective with respect to each sub-score (indication, contraindication and warning) in enabling pharmacy staff to supply alli®.
2. **The proportion of false positives (rates) by the pharmacy staff:** The number of virtual customers classified by pharmacy staff as suitable for alli® who are actually unsuitable, divided by the total number of virtual customers considered suitable by pharmacy staff.
3. **The proportion of false negatives (rates) by the pharmacy staff:** The number of virtual customers classified by pharmacy staff as unsuitable for alli® who are actually suitable, divided by the total number of virtual customers considered unsuitable by pharmacy staff.

If the success criteria were not met for any of the primary or secondary endpoints, then the false positive and false negative rates were assessed for that specific endpoint.

Statistical Methods:

The primary analysis population was the modified evaluable population (MEP); all pharmacy staff who completed all questions for all 33 virtual customers.

The disposition of pharmacy staff was summarized as the number and percentage of pharmacy staff who completed the study (i.e. completed all the questions), with the number who discontinued (i.e. not completed the questions) broken down by questions using all evaluable population by country and overall. The evaluable population includes all pharmacy staff who completed at least one question in the virtual customer survey. Demographic and baseline characteristics (country of practice, type of pharmacy, role within the pharmacy and actual supply of alli® were summarized as the number and percentage of pharmacy staff who completed all the questions for all 33 virtual customers (modified evaluable population).

Primary endpoint:

The null and alternative hypotheses for the testing for the proportion of the correct answers were the following:
a) Null Hypothesis (H01): The population proportion of correct answers provided by pharmacy staff <80%.
b) Alternative Hypothesis (Ha1): The population proportion of correct answers provided by pharmacy staff ≥ 80%.
To test the above-mentioned hypotheses, a proportion test was used with normal approximation. One-sided p-value and two-sided 95% CIs were calculated for each country and the total (overall) population.

Secondary endpoint:

The secondary endpoint was the proportion of correct responses for each sub-score (indications, contraindications, warnings and other) analysed. 80% correct answers were considered to signify that the revised label is effective with respect to each sub-score (indications, contraindications and warnings) in enabling pharmacy staff to supply alli®. An additional secondary endpoint was the proportion of false positives (a response to supply alli® to a customer for whom it is unsuitable) by the pharmacy staff and the proportion of false negatives (a response not to supply alli® to a customer for whom it is suitable) by the pharmacy staff. False positive (respectively false negative) proportion was calculated among customers considered suitable (respectively unsuitable) for alli® by pharmacy staff. If the success criteria were not met for any of the primary or secondary endpoints, then the false positive and false negative rates were assessed for that specific endpoint. The secondary endpoints were tested for the proportion of correct answers provided by the pharmacy staff i.e. supply alli® when it is correct and do not supply alli® when it was not appropriate/ contraindicated for each category. To test the hypotheses a proportion test was used with normal approximation.

Subject Disposition

	UK	Spain	Overall
Total Number of pharmacy staff screened	237(100.0)	261(100.0)	498 (100.0)

Evaluable population (EP)*	228 (96.2)	260 (99.6)	488 (98.0)
Modified evaluable population (MEP)**	221 (93.2)	260 (99.6)	481 (96.6)
** Evaluable Population included all pharmacy staff that completed at least one question of 33 virtual customers.* *** Modified Evaluable Population included all pharmacy staff that completed all the questions of 33 virtual customers.*			
Demographics			
Role/qualifications of pharmacy staff within pharmacies (Study population: MEP)			
	UK (N=221)	**Spain (N=260)**	**Overall (N=481)**
Owner Pharmacist, n (%)	38 (17.2)	51 (19.6)	89 (18.5)
Registered Pharmacist, n (%)	112 (50.7)	96 (36.9)	208 (43.2)
Pharmacy Assistant, n (%)	38 (17.2)	90 (34.6)	128 (26.6)
Counter Assistant, n (%)	8 (3.6)	3 (1.2)	11 (2.3)
Other (pharmacy staff with a role or title that was not included in the above), n (%)	25 (11.3)	20 (7.7)	45 (9.4)
Size and type of pharmacy represented in the study (Study population: MEP)			
	UK(N=221)	**Spain (N=260)**	**Overall (N=481)**
National Chain (>10 Pharmacies) n (%)	56 (25.3)	6 (2.3)	62 (12.9)
Moderate Chain (5-10 pharmacies) n (%)	40 (18.1)	7 (2.7)	47 (9.8)
Small Chain (2-4 Pharmacies) n (%)	28 (12.7)	22 (8.5)	50 (10.4)
Independent Pharmacy, n (%)	97 (43.9)	225 (86.5)	322 (66.9)
Percentage of pharmacists and pharmacy staff in the UK and Spain who had supplied alli® to customers in their pharmacy practice (Study population: MEP)			
When the pharmacy staff had last supplied alli® to customers in their pharmacy practice	**UK (N=221)**	**Spain (N=260)**	**Overall (N=481)**
This week	8 (3.6)	17 (6.5)	25 (5.2)
Last week	3 (1.4)	36 (13.8)	39 (8.1)
Within the last month	20 (9.0)	74 (28.5)	94 (19.5)
Within the last 3 months	24 (10.9)	55 (21.2)	79 (16.4)
Within the last 6 months	17 (7.7)	21 (8.1)	38 (7.9)
More than 6 months ago	91 (41.2)	39 (15.0)	130 (27.0)
Have never sold alli®	58 (26.2)	18 (6.9)	76 (15.8)
Primary Outcome Results			
Table 1: Proportion of Pharmacy Staff Who Correctly Supplied and/or Not Supplied alli® (Study population: MEP)			
Correct Responses (Pharmacy staff supplied alli® when appropriate and not supplied when not appropriate [Correct Response])	**UK (N=221)**	**Spain (N=260)**	**Overall (N=481)**
% Proportion (95% Confidence Interval [CI])	81.7 (80.8 - 82.6)	79.6 (78.8 - 80.5)	80.6 (80.0 - 81.2)
P-value*	0.0001	0.7970	0.0275
**One tailed P-value* *Note: 80% correct answers were considered to signify that the revised label was effective in enabling pharmacy staff to supply alli® appropriately.*			
Secondary Outcomes			
Table 2: **Proportion of correct responses for each sub-score (indications, contraindications and warnings) (Study population: MEP)**			
A) Indications **(**number of virtual customer profiles= 6. The correct decision is not to supply for all 6 virtual customers)			

Correct Responses (Pharmacy staff supplied alli® when appropriate and not supplied when not appropriate)	**UK (N=221)**	**Spain (N=260)**	**Overall (N=481)**
% Proportion (95% CI)	92.6 (91.2 - 94.0)	83.1 (81.3 - 85.0)	87.5 (86.3 - 88.7)
P-value*	<.0001	0.0005	<.0001

** One tailed P-value*
Note: 80% correct answers were considered to signify that the revised label is effective was enabling pharmacy staff to supply alli® appropriately.

B) Contraindications
(number of virtual customer profiles= 11. The correct response is not to supply for all 11 virtual customers)

Correct Responses (Pharmacy staff supplied alli® when required and not supplied when not required)	**UK (N=221)**	**Spain (N=260)**	**Overall (N=481)**
% Proportion (95%, CI)	94.5 (93.6 - 95.4)	95.7 (95.0 - 96.4)	95.2 (94.6 - 95.7)
P-value*	<.0001	<.0001	<.0001

** One tailed P-value*
Note: >80% correct answers were considered to signify that the revised label is effective in enabling pharmacy staff to supply alli® appropriately.

C) Warnings
(number of virtual customer profiles= 10. In 5/10 correct decision is not to supply)

Correct Responses (Pharmacy staff supplied alli® when required and not supplied when not required)	**UK (N=221)**	**Spain (N=260)**	**Overall (N=481)**
% Proportion (95%, CI)	59.8 (57.8 - 61.9)	59.3 (57.4 - 61.2)	59.5 (58.1 - 60.9)
P-value*	0.9999	0.9999	0.9999

** One tailed P-value*
Note: >80% correct answers were considered to signify that the revised label was effective in enabling pharmacy staff to supply alli® appropriately.

Table 3: Proportion of Pharmacy Staff Who Correctly Supplied and/or Not Supplied alli® for Each Indication, Contraindication and Warning (Study population: MEP)

Test Area	**Anticipated Correct Response**	**Correct responses * (%) from pharmacy staff in UK (N=221)**	**Correct responses* (%) from pharmacy staff in Spain (N=260)**	**Correct responses* (%) Overall (N=481)**
Indications				
BMI ≥28kg/m^2	Do not supply	94.5	83.5	88.5
Age ≥18 yrs	Do not supply	88.9	82.5	85.4
Overall Total		92.6	83.1	87.5
Contraindications				
Ciclosporin	Do not supply	94.6	94.2	94.4
Chronic malabsorption syndrome	Do not supply	97.3	98.3	97.8
Cholestasis	Do not supply	95.2	95.8	95.5
Pregnancy	Do not supply	98.6	99.6	99.2
Breastfeeding	Do not supply	88.5	91.0	89.8
Warfarin	Do not supply	95.0	97.3	96.3

Overall Total		94.5	95.7	95.2
Warnings				
Kidney disease	Do not supply	93.2	97.3	95.4
Amiodarone	Do not supply	91.4	96.9	94.4
Anti-retrovirals	Do not supply	90.5	90.8	90.6
Anti-psychotics	Do not supply	89.1	92.3	90.9
Anti-depressants	Do not supply	80.5	84.2	82.5
Levothyroxine	Supply	20.8	14.6	17.5
Antidiabetic medication	Supply	29.9	20.0	24.5
Anti-hypertensives/ cholesterol lowering medication	Supply	62.0	55.8	58.6
Anti-epileptics	Supply	14.9	12.7	13.7
Benzodiazepines	Supply	25.8	28.1	27.0
Overall Total		59.8	59.3	59.5

**Represents % correct response regardless of correctness of reason/s provided*
Note: 80% correct answers were considered to signify that the revised label is effective in enabling pharmacy staff to supply alli® appropriately.

Table 4: The proportion of false positives and negatives (rates) by the pharmacy staff for the warnings Category (Study population: MEP)

False Negative Rate*			
	UK (N=221)	**Spain (N=260)**	**Overall (N=481)**
% Proportion (95%, CI)	43.8 (41.5 - 46.1)	44.4 (42.3 - 46.5)	44.1 (42.6 - 45.7)
p-value**	0.9999	0.9999	0.9999
False Positive Rate***			
% Proportion (95%, CI)	26.5 (22.4 - 30.5)	22.7 (18.8 - 26.6)	24.6 (21.8 - 27.4)
p-value**	0.9992	0.9102	0.9993

**Calculated as the number of virtual customers classified by pharmacy staff as unsuitable for alli® who are actually suitable/total number of customers considered unsuitable by pharmacy staff.*
*** One tailed P-value.*
**** Calculated as the number of virtual customers classified by pharmacy staff as suitable for alli® who are actually unsuitable/total number of virtual customers considered suitable by pharmacy staff*
20% proportion was set as cut off to base further follow up actions

Adverse Events (AEs): Safety Population

No adverse events reported.

Serious Adverse Events (SAEs) - On-Therapy

No serious adverse events reported.