

Is Orlistat (Xenical) an effective weight loss tool despite its unpleasant side effects?

Tricia Robinson, May 2010

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Introduction

Throughout my nutrition studies I have been taught that essential fats are vital for health and must be obtained through the diet. For example, fats build cell membranes and perform key functions in the brain, eyes and lungs. The brain is composed of 60% fat with fats being essential for brain function, learning abilities, memory retention and moods. Fats are especially important for pregnant women, since they are essential to foetal brain development. Essential fatty acids help cells to stay moveable and flexible, thus allowing nutrients into the cells and allowing waste to be excreted. Fats are used to produce energy and keep the heart beating in a regular rhythm. Fats compose the material that insulates and protects the nerves. The lungs require a high concentration of fats to function and prevent them from collapsing. Apart from providing energy, fats in a meal slow down the digestive process allowing the body to absorb more nutrients and enjoy sustained energy. Eating fats allows fat soluble vitamins A, D E and K to be absorbed. Some fats are inflammatory and some are anti-inflammatory and a balance between the two is required for optimum health. ¹

My interest in the drug Orlistat was initially sparked by chatting with a couple of friends over dinner. I have known this couple for more than twenty years and they have battled with weight problems ever since I have known them. They described how they had been prescribed Orlistat in an attempt to lose weight and recalled that the side effects were “horrendous”, and that there had been no weight loss as they simply could not tolerate sustained use due to the unpleasant side-effects. On looking further into this I found the following statement in the British Medical Association’s Concise Guide to Medicines & Drugs:

“Because of the way Orlistat works, the faeces become oily and this can cause flatulence. Part of the drug’s effect may be due to people reducing their fat intake in order to avoid the unpleasantness of these side effects”.

The most common side effects are headache, upper and lower respiratory infection, abdominal pain and discomfort, oily spotting from the rectum, flatus with discharge, fatty oily stools, flatulence, liquid stools, oily evacuation, rectal pain/discomfort, faecal incontinence, tooth disorder and gingival disorder. It is not uncommon to experience urinary tract infection, hypoglycaemia, flu, fatigue, menstrual irregularity and anxiety. ²

“Orlistat is a potent, specific and long-acting inhibitor of gastrointestinal lipases. It exerts its therapeutic activity in the lumen of the stomach and small intestine by forming a covalent bond with the active serine site of the gastric and pancreatic lipases. The inactivated enzyme is thus unavailable to hydrolyse dietary fat, in the form of triglycerides, into absorbable free fatty acids and monoglycerides.”²

In other words, because lipase, the enzyme that breaks down fats, is inactivated, fats are excreted undigested.

Orlistat does not discriminate between “good” and “bad” fats – it treats saturated and unsaturated fats in the same way. Furthermore, if there is no fat present, vitamins A, D, E & K cannot be absorbed. It is for this reason that it is recommended that users of Orlistat should be advised to take a daily multivitamin. The vitamin supplement should be taken at least two hours either before or after taking Orlistat.²

Orlistat (also known as Xenical) is available on prescription. Each tablet contains 120 mg, the recommended dose being 3 tablets per day i.e. 360mg.² Alli is an over-the-counter drug containing Orlistat, given in 60mg capsules. The recommended dose being 3 capsules per day i.e. 180mg. The pharmacist should check that the Body Mass Index is 28 or more on purchase. At the time of researching, Alli cost £49.95 for 84 capsules (approximately one month’s supply) from my local chemist. It is possible to buy Alli on-line where prices seem to be lower than at the chemists. The manufacturer claims that for every 2lb you lose through healthy eating, Alli can help you to lose 1lb more.³

The drug manufacturer recommends that users are advised to be on a nutritionally balanced, mildly hypo-caloric diet that contains approximately 30% of calories from fat. It is recommended that the diet should be rich in fruit and vegetables. The daily intake of fat, carbohydrate and protein should be distributed over three main meals.²

The manufacturers of Orlistat, Roche, carried out a 2 year study and a 4-year study where a hypo-caloric diet was used in conjunction with treatment with an Orlistat treated group and a placebo treated group.²

Data from the 2-year study showed that after one year 20% of patients treated with 120mg of Orlistat three times a day lost more than 10% of body weight as opposed to 8% of the placebo takers.²

In the 4-year clinical trial, after 4 years of treatment, 21% of those treated with Orlistat as opposed to 10% of the placebo takers lost more than 10% of body weight.²

Since Orlistat was approved in July 1998, there has been much research done on health concerns associated with taking Orlistat.

In July 2000, the British Medical Journal published a paper by Matty Persson, and Sigurd Vitols; “Orlistat associated with hypertension”. A previously healthy 40-year old woman prescribed Orlistat experienced dizziness, peripheral oedema, and pulsating headache and stopped the treatment. On medical examination her blood pressure was 190/100 mm Hg on three different occasions. Her heart rate was regular, at 60 beats/min. She was advised to stop taking orlistat, and a few days later her blood pressure had decreased to 160/90 mm Hg and the oedema had regressed. The research

into this case concluded that Orlistat was causal to hypertension in a patient and that 13 other cases of hypertension had been reported to the drug manufacturer.

In July 2006, the Public Citizen issued a petition to the Food & Drug Administration (FDA) in the United States asking for a ban on the use of Orlistat (Xenical) based on a Brazilian study where cases of aberrant crypt foci in the colon of rats had been found, being a pre-cursor for colon cancer. Crypts are folds found in the lining of the intestine that lead into the tissue of the gastrointestinal tract. Aberrant crypt foci are either single crypts or groups of crypts that show errors such as increased size, unusual openings or thick linings.⁴ Although some medical experts believe that aberrant crypt foci are precancerous, others do not believe that the association between aberrant crypt foci and cancer has yet been fully proven.⁵

The Public Citizen petition stated that Orlistat “should not remain on the market for the long term treatment of a non-lethal condition when it combines with so little efficacy coupled with a still unresolved potential to cause breast and colon cancer”. Elizabeth Barbehenn, Ph.D. *Research Analyst*, Sidney Wolfe, M.D. *Director Public Citizen’s Health Research Group* Theresa P. Pretlow, Ph.D. *Professor of Pathology Case Western Reserve University School of Medicine**Thomas G. Pretlow, M.D. *Professor of Pathology, Urology, Oncology, and Environmental Health Sciences Case Western Reserve University School of Medicine**

The FDA agreed to continue to review the drug but did not impose a ban. Instead, they went on to approve and allow the manufacture and release of the over-the-counter version of the drug, Alli.⁶

In contrast a study published in 2005 provided evidence of Orlistat having potential for treating breast cancer.⁷

According to an article in the Cancer Letter (Vol 32, No 21, June 2, 2006) the FDA was made aware of the animal studies linking Orlistat to aberrant crypt foci as early as 1997. The article claims that the agency failed to share this information with its advisory panel when it met to consider over-the-counter sales of Orlistat. Four of the researchers have since protested about the withholding of this information, including Neal Benowitz, professor of medicine and biopharmaceutical sciences at the University of California, San Francisco.⁶

In January 2010 a report was produced by Faheem Asem Ahmad and Sajid Mahmud of Hairmyres Hospital, East Kilbride on “Acute Pancreatitis Following Orlistat Therapy: Report on Two Cases”. Their report concluded that two patients had presented with acute pancreatitis soon after commencement of Orlistat. The report suggested that the drug was a contributing factor and that this potentially adverse event was of clinical importance. They recommended that for any user to commence with the new onset of severe abdominal pain, the diagnosis of pancreatitis should be considered. They claim that whilst the drug is generally safe, where pre-existing risk factors for pancreatitis are present, the drug should be introduced cautiously.⁷

Methodology

I decided to obtain research with the use of a questionnaire. In order to target users of Orlistat or Alli, with the help of my brother who builds websites for a living, I posted my questionnaire on www.weightlossresources.co.uk (WLR). In this way I was able to target people with a desire to lose weight. As my friends who had sparked my initial interest in Orlistat had tried all manner of slimming aids, I thought it was highly likely that subscribers to WLR would have tried other weight loss measures such as Orlistat or Alli.

As I not only wished to gather information from current users, but also from anyone who may have used the drug in the past, two questionnaires were posted on the site. The participants therefore had a choice between the questionnaire headed "currently taking" or "previously taken". (Appendices 1 & 2)

With the addition of a few users who were known to me, the total number of responses received amounted to 23. All the responses were in the form of emails. These were printed and the information entered on a spreadsheet.

Results

Of the 23 people surveyed, the average length of time using the drug ranged from 1 month to 12 months, the average time being 5.7 months, although this number included some who were continuing to use the drug at the time of the survey.

11 of the participants had their health monitored throughout the period of usage, with 7 not receiving any health monitoring. 5 participants did not answer the question.

Although the information leaflet accompanying the drug stresses that it is advisable to take a multivitamin supplement to guard against malabsorption of vitamins A, D, E and K, only 3 participants were advised to take a multivitamin supplement whilst on the drug, equating to 13%. These 3 participants had followed the advice and had taken/were taking the supplement.

Of the 23 participants, 21 were taking prescribed Orlistat, leaving 2 who were self-prescribed and taking Alli, bought from the chemist. One participant was taking Alli despite the fact that her Body Mass Index was a mere 22.7. She was however advised to take a multivitamin. She was using Orlistat as “an aid through a plateau period during her weight loss”. Her target weight was 49.5 kg and she had already reached 54.5 kg.

All 23 participants experienced at least one side effect with the average number of side effects per participant being 3. 7 separate side effects was the highest number experienced by any one participant.

The pie chart in Figure 1 shows the proportion of side effects experienced by those surveyed. “Other” side effects included abdominal pain, two incidences of constipation and one continuous bloating.

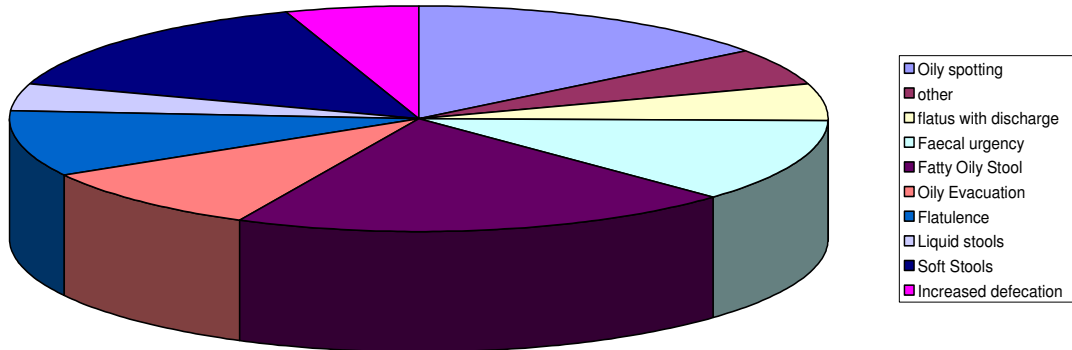


Figure 1 Pie chart showing the proportion of side-effects experienced by participants

The amount of weight lost by participants whilst using Orlistat as a weight loss aid varied from 0 kg to 54 kg.

Interestingly, those who experienced no weight loss were those participants who were not using any other weight loss methods at the time, such as exercise, calorie controlled diet etc, being totally reliant on the drug alone to achieve weight loss.

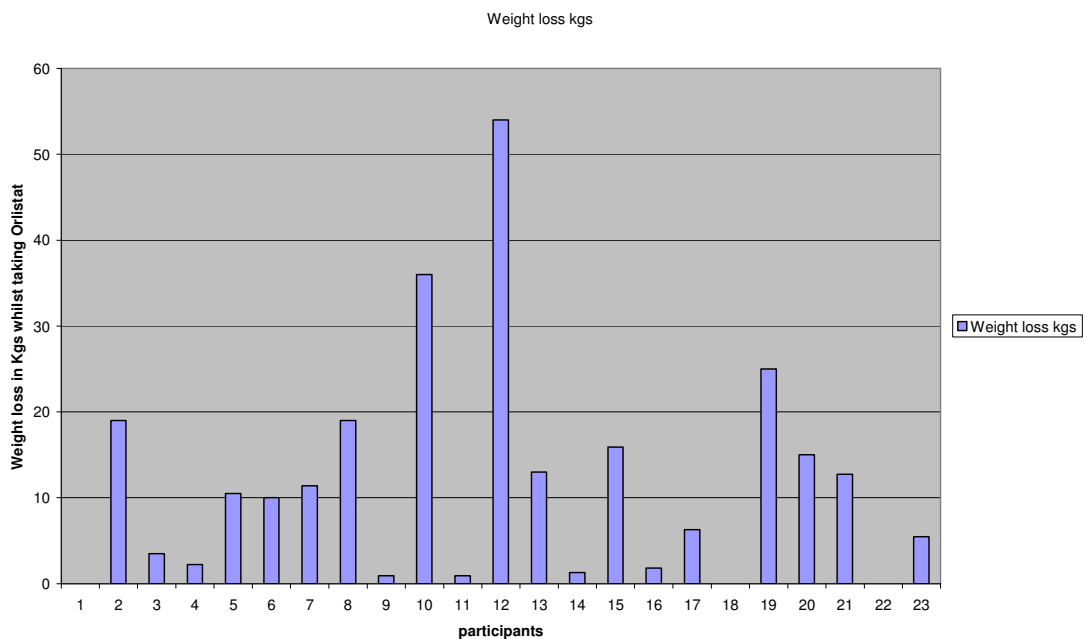


Figure 2 Amount of weight lost in kilograms by participants whilst using Orlistat as a weight loss aid.

Under the “other comments” section of the survey, participants made the following comments in relation to the side effects:

“I couldn’t afford to keep it up and also the constipation was not pleasant”

“I experienced some light-headedness at the start, but this has stopped now”.

“The idea of having an oily poo because I ate fatty food gave me incentive not to eat the fatty food. For about a year after I came off Xenical, I could not bear the taste of fatty or oily food and almost threw up when I had a bite of deep fried (batter) fish”

“It is a good drug to help you lose weight and makes you stick to healthy food because the side effects are so horrible but you still have to be in the right frame of mind to begin with”

“It’s easier and safer to lose weight other ways!”

“I would never take this medication again, or recommend it to anyone. The GPs seem quick to put their patients on it, if only they had experienced it for themselves (they would never recommend it). The fact that you seem to lose control of your bowels is totally humiliating”

“I found the drug very useful in helping kick-start my weight loss. I believe it acts as a very good motivational tool and I, no doubt, benefited from the psychological effects of taking it more than the physiological. I have very few side-effects and those I did have were only after I had knowingly gone over my fat allowance and knew what to expect. I no longer take the drug; however, I continue to lose weight through healthy eating and exercise – I believe Xenical helped me to adapt to this new way of living and I would recommend it”.

The following comments were offered in respect of how effective the individual participants found Orlistat to be as a weight-loss aid:

“Was a quick fix but put 2 of the 3 stones back on when I finished taking it”

“Didn’t lose much weight at all. Very disappointed”.

“Great drugs. Feel they helped give a kick start to weight loss”

“This is my third try on this drug, and I can honestly say my current weight loss is 75% due to the drug. Saying that, didn’t stay on it for this long the first two times”.

“Love it and find it a great help to speed up weight loss. Had no side effects or issues with the bowels etc”

“I have had no problems at all and it’s been a very positive experience.”

“Only my third week but have been disappointed so far”

“I do not believe that this form of treatment suited me and I would not consider taking it again.”

“The weight gain afterwards wasn’t down to the Xenical, it was down to me changing back to my old eating habits – Xenical couldn’t stop me eating pizza and Ben & Jerry’s every night ☺”

“I lost weight with the drug but I was still not able to change my habits. I realise that my reliance on food and drink for enjoyment is something that will need to be monitored through diet and exercise not drugs.”

“Lost the same amount of weight that I would have done simply by following a calorie controlled lifestyle change.”

Almost half of the participants who had previously taken Orlistat regained weight following cessation of the drug.

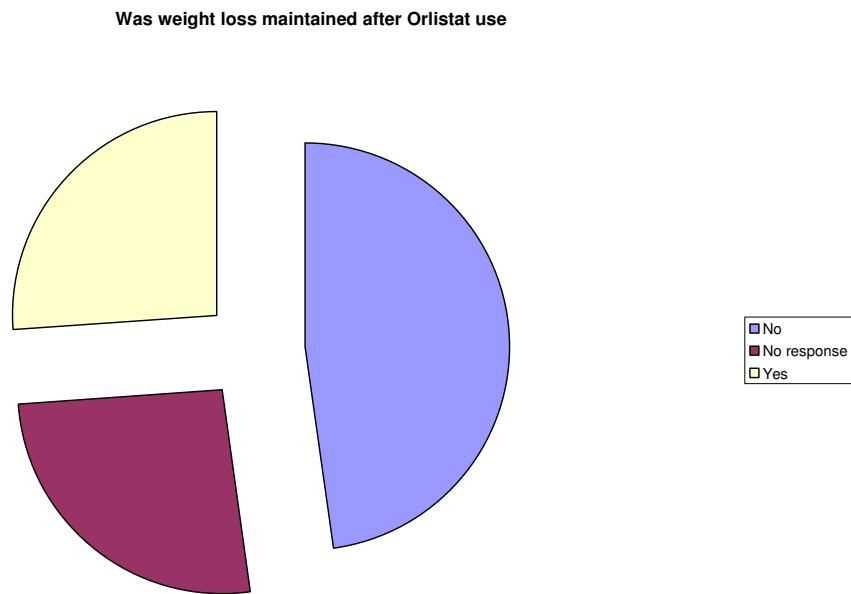


Figure 3 Maintenance of weight-loss following cessation of the use of Orlistat

Conclusion

Having gathered all the information we need to assimilate the data and see if it is possible to conclude that Orlistat is an effective weight loss aid despite the unpleasant side effects.

12 participants said that the drug had met their expectations, whereas 10 said it hadn't and 1 did not respond. This equates to 54% of the sample stating that their expectations had been met. However, this is a little misleading and it should be said that 5 of the 12 who said their expectations had been met did not maintain any weight loss following cessation of the drug. One could conclude from this that at outset they did not expect to maintain any weight loss following cessation of the drug. 2 participants who have maintained weight loss appear to believe that this is due to other weight loss measures rather than the drug itself and have declared that the drug did not measure up to their expectations.

For those participants in the sample who were using only the drug in the hope of losing weight, there was zero weight loss. Participants who were using the drug in conjunction with other weight loss measures, such as calorie counting, healthy eating, and sustained exercise programme etc all lost weight.

As all participants who successfully lost weight were engaged in some form of calorie reduction, healthy eating and/or exercise, it would appear that Orlistat or Alli may be useful as a psychological tool rather than merely a physiological aid to weight loss.

Most of those surveyed, persevered with the drug, despite the side-effects. 21% of those surveyed found the side-effects so unpleasant that they stopped taking it.

I do feel that we live in a culture where the vast majority of people want and expect a quick fix. When it comes to losing weight, the idea of a taking a pill appeals much more than adopting the mindset to make dietary changes and engage in exercise for a sustained period.

The market for this type of drug is ever increasing. In 2008 statistics published by the NHS showed that in the UK 24% of men and 25% of women were obese, with 66% and 57% respectively being overweight including obese.

My worry is that few people are aware at the start of treatment the difference between good and bad fats and the need for certain fats in the diet for optimum health to be achieved. Even though the manufacturers recommend taking a supplement containing vitamins, A, D, E & K, only 13% of those taking part in my survey had been told about this and had acted upon it.

From the evidence unfolding about links between Orlistat and pancreatitis, colon cancer, breast cancer and hypertension, I would prefer more resources

into educating people about natural weight loss methods without any side-effects other than positive ones.

To recap - is Orlistat (Xenical) an effective weight loss tool despite its unpleasant side effects? For 4 out of the 23 people surveyed (17%), Orlistat did work as an effective weight loss tool where the side-effects were not troublesome enough to worry the taker.

Overall, I do not believe the benefits of taking Orlistat or Alli outweigh the risks and I would advocate instead a slow and sustained weight loss programme through a healthy eating regime and a manageable exercise routine. However, leaving personal preferences aside, I must concede that Orlistat did work for some but not for the majority of my survey participants.

With more research required on its safety measured against the small percentage of people for whom the drug worked in my own survey, I conclude by echoing the sentiments of the petition letter written to the FDA in 2006 – that Orlistat should not be used for the long term treatment of a non-lethal condition when it combines with so little efficacy coupled with a still unresolved potential to cause breast cancer, colon cancer, hypertension and pancreatitis.

Appendix 1 Survey Questionnaire - "Previously taken"

Questionnaire for those who are not currently taking the medication but have done in the past.

Name

Email address

Age

Weight:

Height:

Please tick which of the following medicinal products you have taken:

Orlistat, also known as Xenical

Alli

Date medication started

Date medication stopped (approximate dates will suffice)

Did you experience any of the following side-effects as a result of taking this medication?

Yes/No/Tick???

Anxiety

Oily spotting

Flatus with discharge

Faecal urgency

Fatty oily stool

Oily evacuation

Flatulence

Soft stools

Abdominal pain

Faecal incontinence

Liquid stools

Increased defecation

Please describe any other side effects you may have experienced that are not mentioned above.

Did you take the medication in conjunction with any other weight loss measures e.g. diet plans?

Did you participate in any exercise whilst taking this medication?

How much exercise did you do each day whilst taking the medication?

What type of exercise did you do?

How much weight did you lose whilst on the medication?

Did you maintain the weight loss after stopping the medication?

Was your health monitored whilst on the medication: Please give brief details?

Did you receive any counselling?

Did you receive regular health checks whilst taking the medication?

Did your GP or chemist advise you to take a multivitamin whilst taking this medication?

Have you received any dietary advice from your GP or Chemist? If so please give brief details.

Did the drug meet your expectations?

Any other comments

Thank you for taking the time to complete this survey. As this research ongoing, would you be prepared to answer any further questions if required?

Appendix 2 – Survey Questionnaire “currently taking”.

Questionnaire for those currently taking the medication:

Name

Email address

Age

Weight:

Height:

Please tick which of the following medicinal products you are taking

Orlistat, also known as Xenical

Alli

Are you experiencing any of the following side-effects as a result of taking this medication:

Yes/No/Tick???

Anxiety

Oily spotting

Flatus with discharge

Faecal urgency

Fatty oily stool

Oily evacuation

Flatulence

Soft stools

Abdominal pain

Faecal incontinence

Liquid stools

Increased defecation

Please describe any other side effects you may have experienced that are not mentioned above.

How much weight have you lost so far and over what period of time?

Are you taking the medication in conjunction with any other weight loss measures e.g. diet plans?

Are you participating in any exercise? Yes/No.

How much exercise do you do each day?

What type of exercise do you do?

Have you maintained the weight loss?

Has your health been monitored whilst on the medication? Please give brief details.

Have you received any counselling whilst on this medication?

Have you received regular health checks whilst taking the medication?

Have you been advised to take a multivitamin whilst taking this medication?

Have you received any dietary advice from your GP or Chemist? If so please give brief details.

Is the drug meeting your expectations?

Any other comments

Thank you for taking the time to complete this survey. As this research ongoing, would you be prepared to answer any further questions if required?

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