Summary of Safety and Clinical Performance for the L112 product range

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This summary of safety and clinical performance is designed to enable public access to the key aspects of safety and clinical performance of the L112 product range. The information listed below is intended for patients or laypersons. A more detailed summary for expert groups can be found in the first part of this document.

The summary is not intended as a consultation document for the treatment of diseases and complaints. Please consult your doctor with any questions relating to the treatment of your diseases and complaints, or please consult your doctor or pharmacist with any questions relating to the use of the L112 product range. This summary also does not replace the instructions for use, which can be found in every carton.

1. Product identification and general information

Device Trade name
Variants of the L112 product range can be marketed under the following trade names: formoline, formoline EXTRA, formoline L112, formoline L112 EXTRA, Sterolsan, Liporeform protect

Name and address of the manufacturer
Certmedica International GmbH, Magnolienweg 17, 63741 Aschaffenburg, Germany

Basic UDI-DI
426010333L112T4

Year in which the first certificate (CE) was issued for the device
2001

2. Intended use of the device

Intended purpose

Devices in the L112 product range are lipid binders for weight reduction, for weight management with LDL cholesterol-lowering accompanying effect.

The devices in the L112 product range reduce the digestibility of lipids through physical binding, thus leading to reduced calorie uptake. As a result, they support weight reduction, maintenance of weight loss and lowering of LDL cholesterol.

Indication and target group

For treatment of excess weight and obesity

Devices in the L112 product range are intended for adults with a body mass index (BMI) above 25 in conjunction with a calorie-reduced diet.

Recommended dosage
Twice daily 2 tablets.

Swallow the tablets whole together with plenty of low-calorie fluid (at least 250 ml) to ensure that the tablets make their way into the stomach. Since the L112 product range is a preparation rich in fibre, make sure that you consume enough fluids (at least 2 litres per day).

For weight management, the dosage can be reduced to 2 tablets daily.

Contraindications
Devices in the L112 product range should not be taken by people who:

- have a known allergy to crustaceans or to any of the ingredients;
- are underweight (BMI < 18.5 kg/m²)
- are pregnant or breastfeeding;
- suffer from chronic constipation, intestinal obstruction etc.; or
- are on long-term medication that reduces intestinal activity.

3. Device description

Product description
The L112 product range comprises round, biconvex tablets with a weight of 500 mg or 750 mg. The percent proportion of ingredients is identical in both sizes. Consequently, the 750 mg tablet contains 50% more active dietary fibre. We recommend the larger variant for people above 75 kg.

Composition:
Active dietary fibre polyglucosamine L112 (73%): L112 specification of ß-1,4-polymer from D-glucosamine and N-acetyl-D-glucosamine from crustacean shells

Excipients: Ascorbic acid, tartaric acid, tableting excipients (magnesium stearate plant-based, cellulose plant-based, sodium sulphate, silicon dioxide)

These tablets are packaged in blisters. The blisters are contained inside a carton together with the instructions for use.

Mode of action
The main ingredient of devices in the L112 product range is the indigestible active dietary fibre polyglucosamine L112. This ingredient is of natural origin. On account of its high fat binding capacity, it is capable of binding large amounts of lipids (fats, fatty acids and cholesterol) in the digestive tract. The uptake of fats, which normally takes place very efficiently through the intestinal wall of the small intestine, is significantly reduced under the presence of polyglucosamine L112. L112 is capable in particular of

influencing excess weight caused by high-fat diets such as fatty meat, sausage, butter, cheese, crisps, nuts, cakes or ice cream. Other food components such as sugar, carbohydrates, protein or alcohol are not bound; this type of calorie intake should be reduced, as it will otherwise be fully available to the body.

4. Risks and warnings

Risks and undesirable effects

Consult your doctor or pharmacist if you think you are noticing side effects linked to the use of medical devices in the L112 product range, or if you are concerned about potential risks. This report does not – and is not intended to – replace a consultation with your doctor or pharmacist.

Side effects:
In order to register the frequency of side effects, all reports of side effects from patients or health professionals are recorded and compared with the number of packs sold in the same period. Side effects are reported as “very rare” if a maximum of one report is received for every 10,000 packs sold.

Taking products from the L112 product range can lead to temporary changes in stool consistency. In very rare cases, digestion problems (constipation, flatulence, bloatedness) have been reported, in particular if fluid intake is too low. The incidence is less than 1:10,000 per package sold.

Allergic reactions to one of the ingredients or in cases of an existing allergy to dust mites are possible in very rare cases (symptoms may include: skin rash, swelling, itching, nausea, vomiting, diarrhoea). The incidence is less than 1:10,000 per package sold.

If any side effects or interactions occur, we recommend discontinuing devices from the L112 product range and consulting a doctor or pharmacist if necessary. If you notice a severe deterioration in your health in connection with the use of devices from the L112 product range, please report this to the manufacturer Certmedica International GmbH, Magnolienweg 17, 63741 Aschaffenburg, Germany, as well as to the competent authority.

Interactions:
Due to the fat-binding capacity of devices in the L112 product range, it is also possible that fat-soluble active pharmaceutical ingredients (such as anti-epileptic drugs, blood thinners, hormone preparations, contraceptive pill) or fat-soluble vitamins (A, D, E, K) may also be bound as well as dietary fats. The availability of fat-soluble (lipophilic) active substances may be reduced. In this case, it is recommended to leave a gap of at least four hours before taking L112 products.

It is not recommended that devices from the L112 range are taken with high-vitamin meals (salad, vegetables) with high-quality oils or with omega-3 fatty acids (salmon etc.) as the fat-soluble vitamins and essential fatty acids may be partially bound.

Warnings and precautions

Warnings:
Consult a doctor before taking devices from the L112 range of products in the following cases:

- Long-term medication use
- Serious gastrointestinal diseases, or after surgery on the gastrointestinal tract
- Very elderly people (older than 80 years)

Keep out of the reach of children.

Includes dietary fibre of animal origin.

Precautions:
Swallow the tablets whole together with plenty of low-calorie fluid (at least 250 ml) to ensure that the tablets make their way into the stomach. Since the L112 product range is a preparation rich in fibre, make sure that you consume enough fluids (at least 2 litres per day).

To ensure that the requirement for essential fatty acids and fat-soluble vitamins (A, D, E and K) is met, we recommend only taking products in the L112 product range with 2 out of 3 main meals. You should consume at least one meal per day containing high-quality oils that supply the body with fat-soluble vitamins and essential fatty acids.

Further relevant safety aspects

To date there has been one instance of an FSCA (Field Safety Corrective Action):
Date: 07-AUG-2008
BfArM case no.: 2977/08; NCA Report Number: DE-BfArM-2008-09-22-119
Recall due to limit-exceeding microbial contamination
The affected batches were recalled in full from the market and destroyed, and a root cause analysis was performed. Expanded and additional measures for ensuring microbiological safety were implemented throughout the entire manufacturing process. Additional checks were implemented in the manufacturing process.

5. Clinical data in support of safety and performance

Clinical studies with the L112 product range

The efficacy of the tablets in the L112 product range has been investigated in several clinical studies. The studies were controlled, which means that there was a comparator group whose participants were given the same treatment apart from the product under investigation. In addition, they were also double-blind, which means that neither the participants nor the investigators know who receives the medical device and who is given a comparator device. In most cases, the comparator device is a dummy medical device with no active ingredients (placebo). The assignment to these groups was also randomised, i.e. it was performed randomly.

Long-term study over 12 months

In a long-term study over 12 months, 50 participants were given L112 (2 x 2 tablets every day) and 50 participants were given a placebo. All 100 participants were asked to reduce their calorie consumption and to move more. They were asked about these behavioural changes every 3 months. 49 participants from the L112 group completed the study, as well as 48 from the placebo group; three participants (1 from the L112 group and 2 from the placebo group) stopped the study early. Within the space of one year, the patients with L112 lost over 12 kg (12.7%) on average. In the placebo group this was just 8 kg (8.4%). Waist circumference was reduced by approx. 13 cm with L112; in the placebo group this was 10.2 cm. These differences were statistically significant. In the results, the strongest change was achieved during the first 6 months in both groups. In addition, certain blood values that are regarded as risk factors for cardiovascular diseases showed changes that were significantly better with L112 than in the control group. In this study, LDL cholesterol dropped by 12.9% with L112 and by 5.3% in the placebo group.

This high-quality, long-term clinical study proves that the use of the L112 product range leads to a statistically significant and clinically relevant weight reduction if it is used as described in the instructions for use. The requirements for clinical benefit were met: The proportion of test subjects who achieved a 5% weight reduction was significantly higher in the group with L112 than in the placebo group; more test subjects achieved this target sooner. The goal of 5% weight reduction was reached earlier with L112 by more participants than with the placebo: After 3 months, 55% of participants on L112 and 17% of participants on the placebo had achieved 5% weight reduction. After six months, almost everyone on L112 had reached the 5% mark (98%), in the placebo group just 67%. Use of the L112 product range led to significantly higher weight loss in the L112 group at the end of the study.

This paper was published: Cornelli et al.: Long-term treatment of overweight and obesity with polyglucosamine (PG L112): Randomized Study compared with placebo in subjects after caloric restriction. Current developments in nutrition (2017) 1: e000919. DOI: 10.3945/cdn.117.000919

Long-term study over 25 weeks

107 participants were investigated for this study. All participants were expected to consume a low-calorie diet and move more. The participants in the L112 group lost 1.8 kg more weight than those in the comparator group, which was significant. The weight reduction was 5.8 ± 4.09 kg in the L112 group, and it was 4.0 ± 2.94 kg in the placebo group. After 25 weeks, more participants in the L112 group were able to reduce their body weight by 5% (64.1%) than in the placebo group (42.6%).
This high-quality clinical study with a duration of 25 weeks proves that the use of the L112 product range leads to a statistically significant and clinically relevant weight reduction if it is used as described in the instructions for use. The additional benefit achieved with the use of the L112 product range leads to a clearly detectable superiority in terms of reaching a 5% weight reduction. This demonstrates the clinical benefit of the use of the L112 product range in addition to the basic therapy.

This paper was published: Pokhis et al.: Efficacy of polyglucosamine for weight loss—confirmed in a randomized, double-blind, placebo-controlled clinical investigation. BMC Obesity (2015) 2:25. DOI 10.1186/s40608-015-0053-5.

Comparison with Orlistat (60 mg)

Orlistat is a drug for the treatment of obesity. It reduces Intake of fat, and therefore energy uptake from the intestine, by inhibiting enzymes that break down fats.

In this study, the 64 participants were given either L112 (2 x 2 tablets) or, in the control group, the over-the-counter medicine Orlistat at a dosage of 60 mg. The participants were treated for 12 weeks. In this clinical study as well, all participants were expected to reduce their calorie intake and move more. 64 participants were investigated in two different study centres in Germany and Italy. The difference in terms of weight reduction was statistically significant: In the L112 group the participants lost 6.7 ± 3.14 kg; in the Orlistat group this was 4.8 ± 3.14 kg. The number of participants who were able to reduce their weight by 5% was slightly higher in the L112 group (70%) than in the Orlistat group (55%). However, this difference was not statistically significant.

This paper was published: Stoll et al.: Randomised, double-blind, clinical investigation to compare orlistat 60 milligram and a customised polyglucosamine, two treatment methods for the management of overweight and obesity. BMC Obesity (2017) 4:4. DOI 10.1186/s40608-016-0130-4.

L112 together with a formula diet

120 overweight or obese participants took part in this study. The study lasted for 12 weeks. As a fundamental dietary change, all patients took a meal replacement (protein-rich formula diet) once a day. In addition, the participants took either 1 x 2 L112 tablets or a placebo. Both groups achieved a noticeable weight loss. In the L112 group, the weight loss was 5.5 ± 3.8 kg; in the placebo group, the weight loss was 4.7 ± 3.9 kg. In the L112 group the weight loss was 0.74 kg more than in the placebo group. However, this difference was not statistically significant. The additional administration of L112 was more effective in terms of reducing blood sugar levels and blood fats than the formula diet alone: HbA1c (a value that records the average glucose level over a longer period of time), total cholesterol, LDL cholesterol and blood fats (TAG) were reduced significantly more in the L112 group.

This paper was published: Willers et al.: The combination of a high-protein formula diet and polyglucosamine decreases body weight and parameters of glucose and lipid metabolism in overweight and obese men and women. European journal of food research and review (2012) 2(1): 29-45

Comparison of L112 tablets with different tabletting excipients

45 overweight subjects, 34 men and 11 women, took part in this study. In an initial period of 4 weeks, all subjects followed a lifestyle change programme with a reduction in dietary calorie and salt intake as well as increased physical exercise (standard management).
Immediately after this first period, a second period of 4 weeks followed in which subjects continued standard management and received either the existing product (PGA) or the product with the new excipient formula (PGB) on a random basis. The tablets were administered in the same dosage of 4 tablets of 750 mg (2 x 2) before the main meals.

In both groups, the body weight decreased by about 1.6 kg in just the first 4 weeks. In the subsequent four-week treatment phase, both groups showed a further, statistically significant loss of 3.5 kg (PGA) to 3.7 kg (PGB). Other measurements such as waist circumference, fat mass and certain blood values, which are viewed as risks for cardiovascular disease, also decreased comparably and significantly in both groups. No side effects or stool changes were reported, apart from very few cases of temporary bloating, which were not clinically significant.

This investigation shows that the two formulas can be considered equivalent. However, to draw general conclusions about efficacy, among other things the investigation period of 4 weeks was too short, and the test persons only partially corresponded to typical users.

Three-month study with new tablet excipients

150 patients with overweight or obesity participated in this study at an Italian study centre. All participants received individual advice on nutrition and a change in lifestyle. The patients received either 2 x 2 of 750 mg tablets from the L112 product range with new tablet excipients or 2 x 2 placebo tablets for a period of 90 days. Of the 150 subjects, 119 (58 in the L112 group, 61 in the placebo group) completed the study. Patients who showed COVID-19 infection were excluded from the study.

Despite these restrictions, the patients on L112 achieved a significantly higher weight reduction than those in the placebo group: Patients who had taken L112 for 3 months lost an average of 3.71 kg, patients on placebo only 1.12 kg. Tolerability of both treatments was similar, with no side effects in the placebo group and one case of faecal stones in the L112 group. No changes were found in the fat-soluble vitamins (A, E, D3 and K1) after taking L112.

Overall, patients lost at least three times as much weight with comparable lifestyle changes with L112 as patients with the placebo. For the rather short duration of treatment, this is a noticeable improvement.

This paper was published: Rondanelli et al.: A Randomized Double-Blind Placebo-Controlled Clinical Study to Evaluate the Effect on the Weight of a Medical Device with Polyglucosamine L112 in a Group of Overweight and Obese Subjects. Nutrients 2023, 15, 3516. DOI 10.3390/nu15163516

Results of the user survey 2020-2023

In order to actively determine the safety of and conditions under which the L112 product range is taken under everyday conditions, feedback from users was collected via an online questionnaire. For this purpose, inserts with QR codes had been placed in the cartons of various pack sizes. The QR codes provide access to an online questionnaire, which is used to collect, among other things, data about the users, safety and conditions of use in an anonymous manner.

The data from the patient survey has been available since the end of 2023. Even if this is only data from a user survey, the results on performance are within the range of values determined in clinical investigations. It can therefore be assumed that the results achieved in clinical trials can also be achieved under everyday conditions. The frequency of reported side effects shows that the benefit-risk balance remains favourable.

Ongoing observations after placing on the market

In order to actively determine the safety of and conditions under which the L112 product range is taken under everyday conditions, feedback from users is again being collected via an online survey. In the first half of 2024, as in the 2020–23 user survey, inserts with QR codes were placed in folding cartons of various package sizes containing the 2020 formulation. The QR codes again provide access to an online questionnaire, which is used for anonymised collection of, among other things, data about the users, safety, and the conditions of use. The survey will be evaluated once it can be assumed that no significant further responses are expected.

Reports on side effects and safety are regularly evaluated to enable appropriate action.

Overall summary of clinical performance and safety

The intended purpose claimed by the L112 product range:

Lipid binder
- for weight reduction
- for weight management

with accompanying LDL cholesterol-lowering effect

for the target group
Adults with a body mass index (BMI) of 25 or higher

for the indication
For treatment of excess weight and obesity

is clearly evidenced by the identified and evaluated clinical data. In this patient group, use of the L112 products leads to a clearly demonstrable, clinically relevant benefit for weight reduction. The clinical benefits achieved are in the order of magnitude of effects that are achieved with non-prescription medicinal products. This is the consequence of a purely physical mode of action of polyglucosamine L112. This effect is independent of the tabletting excipients used, so that the 2020 formulation can also claim this intended purpose and indication.

In addition, the risks associated with use of the L112 products fade almost entirely into the background and are limited to potential, mild, temporary impairments of the gastrointestinal tract, which can be compared to those of a high-fibre diet.

As a result of this favourable risk/benefit profile, use of the L112 products can even be used during basic therapy of excess weight and obesity.

6. Therapeutic alternatives

Please discuss alternative treatment methods with a doctor or pharmacist who can take your personal situation into account.
Treatment for weight management comprises two main phases: A phase of weight loss and a phase of long-term stabilisation of body weight. Both are important for long-term therapy success.

In the process, there are two fundamental groups of treatment for therapy for excess weight and obesity:

- conservative therapies and
- invasive therapies.

Invasive therapies (endoscopic procedures such as gastric balloons or surgery for the treatment of excess weight) are only recommended in the Guidelines of the German Association for the Study of Obesity (Deutsche Adipositas Gesellschaft) for people whose obesity is in class III (BMI ≥ 40 kg/m^2) or class II (BMI 35.0 - 39.9 kg/m^2) and who also suffer from key diseases triggered by the obesity.

Conservative therapy for excess weight and obesity

The basic therapy for every treatment of excess weight and obesity consists of changes to diet, exercise and behaviour. How much weight can be lost through basic therapy very much depends on exactly what measures are taken. The guideline sees a health benefit with a weight loss above 5% of the starting weight in persons with a BMI up to 35 kg/m².

Nutritional advice results in an average weight reduction of 6% in 12 months. This was shown by a study that evaluated various, very diverse studies (meta-analysis).

The use of formula diets can limit the amount of calories consumed to a much greater extent. Formula diets usually consist of ready-made drinks or food powders to be mixed with liquids. They fully or partially replace individual meals. By using formula diets under medical supervision, 77% of the participants achieved weight reduction of more than 5% within a year, and just under half of the participants achieved weight reduction of more than 10%. In another study, very severe restriction of calorie intake through formula diets led to a 16.1% reduction in weight, and severe restriction to a 9.7% reduction. How much weight can be lost with basic therapy depends strongly on how great the restrictions are that the participants have to accept.

Here, investigations that summarise various studies have shown that a reduction in fat intake alone – i.e. without additional measures – leads to slightly lower weight, BMI, waist circumference and percentage body fat. This underlines the importance of reducing the amount of fat provided to the body from food in the treatment of excess weight and obesity. The concept of the L112 product range tackles precisely this point.

Supportive therapy options

This basic therapy can be accompanied by various other conservative therapies, such as special nutrition therapies, ready-made products, food supplements, medical devices or medicinal products. A basic therapy is recommended as a matter of principle for the prevention of obesity. It should be noted that, as a general rule, therapies should only be used if their efficacy and safety has been demonstrated in clinical studies. For the use of food supplements and medical devices, no general recommendations are available from the professional societies (e.g. DAG, the German Association for the Study of Obesity/Deutsche Adipositas Gesellschaft) on account of the limited clinical data available. If, for medical devices, data on the efficacy and safety of the relevant medical device is available, use of that medical device for weight reduction in overweight or obese patients may be meaningful according to the opinions of the professional societies.

Supportive therapy with drugs

The DAG Guidelines only consider a treatment with drugs as an addition to dietary measures and physical activities for obese patients (BMI ≥ 30 kg/m²) or for overweight people (BMI ≥ 25 kg/m²) displaying key accompanying illnesses.

Among the conservative approaches, the approach involving the use of drugs is the one with the potentially highest risks on account of the pharmacological action and the side effects associated with this. For this reason, according to the consensus opinion of the professional societies, this approach for overweight subjects without diseases caused by obesity is not meaningful (DAG Guideline 2014). This recommendation is only cast aside in cases where the safety profile of a medicinal therapy is demonstrably very low. In this way, the status of the active ingredient Orlistat as a prescription drug was changed across Europe to non-prescription status in 2009 due to its favourable safety profile, and it is now available to overweight and obese patients as an adjuvant therapy even during basic therapy.

As the L112 product range has no pharmacological effects on account of its purely physical mode of action, and as the interactions with the body of the patient are limited solely to the gastrointestinal tract, the disadvantages of a supportive drug therapy associated with the pharmacological mode of action are avoided.

7. Proposed profile and training of users

L112 products are used by the end user in their home environment or as part of their day-to-day life. L112 products are freely available over the counter. Use takes place without involvement of medical expert staff and does not take place in a clinical environment. The instructions for use include all the important information for the user.