

Summary of Safety and Clinical Performance for the L112 product range

1. Product identification and general information

1.1. Trade name of the device

Variants of the L112 product range can be marketed under the following trade names:
formoline L112, formoline L112 EXTRA, Sterolsan.

1.2. Name and address of the manufacturer

Certmedica International GmbH, Magnolienweg 17, 63741 Aschaffenburg, Germany

1.3. Manufacturer single registration number (SRN)

DE-MF-000006199

1.4. Basic UDI

426010333L112T4

1.5. Medical device nomenclature

CND code: G030699 Devices for Non-Surgical Therapy of Obesity – Others

1.6. Product class

Class III

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

2001

1.8. Authorised representative (if applicable), name and SRN

Not applicable

1.9. Name of notified body and identification number of the notified body

TÜV SÜD Product Service GmbH, 0123

2. Intended use of the device

2.1. 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.

2.2. Indications, target population and recommended dosage

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.

2.3. 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. Description of the medical device

3.1. Product description

The L112 range of products comprises 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 β -1,4-polymer from Dglucosamine and N-acetyl-D-glucosamine from crustacean shells

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

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

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.

It is not recommended that products 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.

3.2. Product history

The L112 product range medical device was first placed on the market in 2001 as a CE-labelled medical device by Biomedica Pharma-Produkte GmbH after conclusion of a conformity assessment process by the notified body mdc medical device certification GmbH (CE 0483). Since then, the qualitative and quantitative composition of the efficacy-relevant ingredients polyglucosamine L112, ascorbic acid and tartaric acid has remained unchanged.

In 2003 the device was reclassified and a conformity assessment process for the Class III device was concluded.

Since 2005, the manufacturer has been Certmedica International GmbH.

When the manufacturing process was switched to the direct compression method in 2012, the only change that was made was to omit granulating aids – the formula for the tablet remained unchanged.

In 2017, the product line was expanded to include a tablet with a total weight of 750 mg, which has the same relative composition as the biconvex 500 mg tablet.

The L112 product range is marketed in different variants (pack sizes, languages, trade names, active ingredient quantity). The focus of the sales and distribution activities of Certmedica GmbH is Germany and Austria. In addition, local distribution companies in 51 countries have been supplied over the past 19 years. For 30 countries that are outside the scope of validity of the CE certification, national approvals have been obtained in accordance with local approval regulations.

Since 2001, variants of the L112 product range have been sold in many millions, and they have proved themselves to be safe and effective.

3.3. Description of accessories intended to be used with the device

Medical devices in the L112 product range are used without additional accessories.

3.4. Description of other devices or products with which the device is to be used in combination

Medical devices in the L112 product range are not used in combination with other devices or appliances.

4. Risks and warnings

4.1. Risks and undesirable effects

Side effects:

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.

Side effects at the target site – the gastrointestinal tract – occur as mild, isolated cases. The frequency is below 1:10,000 per pack 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).

Side effects with symptoms of an allergic reaction occur as mild, isolated cases. The frequency is below 1:10,000 per pack sold.

For the L112 product range, no severe allergic reactions are known from the marketing history, and research carried out as part of risk management have revealed no indication of a link between anaphylactic shock and oral intake of chitosan.

However, such a reaction is conceivable in theory in people who react allergically to crustaceans. For this reason, the L112 product line is contraindicated for people who have a known hypersensitivity to or who have previously had allergic reactions to crustaceans or to any of the other ingredients in the product.

An evaluation of the data from reporting shows that no notifiable side effects have occurred since 2010. The most common side effects are gastrointestinal complaints of a mild and temporary nature, as well as intolerance reactions. The frequency of occurrence is in a very low range, which underlines the safety of application

In the studies performed with the L112 product range, the treatment of 529 people resulted in no severe side effects at all.

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.

There are no suggestions of interactions that have occurred between L112 devices and medicinal products. Two clinical studies with the L112 product range designed to assess this property for multiple active ingredients that are relevant for clinical practice revealed no suggestion of a relevant risk. In order to minimise the risk of such interactions, we do however recommend leaving a minimum gap of four hours between taking a product in the L112 product range and taking other medicinal products.

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 Palestinian MOH www.pharmacy.moh.ps.

4.2. 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. If required, a multivitamin preparation can also be taken as a supplement to ensure a sufficient supply of vitamins.

The risk that the L112 product range could potentially impair the absorption of fat-soluble vitamins (A, D, E and K) can be classed as low. Nonetheless, it can be recommended to patients that they can use a multivitamin preparation to ensure that an adequate supply of vitamins is guaranteed. This is also standard for comparator preparations that also affect lipid resorption.

4.3. Further relevant safety aspects, including a summary of all measures (FSCA including FSN)

FSCA:

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 throughout the entire manufacturing process were implemented. Additional checks were implemented in the manufacturing process.

FSN:

None

5. Summary of the clinical evaluation and the post-market clinical follow-up

5.1. Summary of clinical data for a comparable product, if applicable

Data for other products was not used to determine the performance of this product.

5.2. Summary of clinical data for the L112 product range

5.2.1. Study by Cornelli et al. 2017

Description of the study

Cornelli et al. describe a double-blind, randomised and placebo-controlled long-term study on 100 participants of both sexes with a body-mass-index (in kg/m²) in the range from >30 to <35 (Cornelli et al. 2017). A group of 50 participants was treated for 1 year with the medical device L112 product range, with a dosing regimen of 2 x 2 tablets per day prior to the 2 main meals. A comparison group was given a placebo with a comparable dosing regimen. The participants were instructed to reduce their calorie consumption by 10% and to increase their physical activity level by 9 metabolic equivalent of task hours per week. It was checked every 3 months with the aid of weekly questionnaires that the participants were sticking to the diet [Food Intake Assessment (FIA) on the basis of 25 different food portions]. Body weight (BW), waist circumference (WC), blood pressure (BP), glucose, lipids and high-sensitivity C-reactive protein (hs-CRP) were also monitored. The study was registered with clinicaltrials.gov under the reference number U111111292405 (WHO).

Results:

Ninety seven participants completed the study (49 in the L112 product range group, 48 in the PL group).

Reduction in BW in the L112 product range group was 12.1 kg (12.7%) in comparison to 8.0 kg (8.4%) in the PL group ($P < 0.05$). The BW change with the L112 product range was also faster ($P < 0.05$), as the weight loss in the first 6 months was 8.9 kg, compared with 5.6 kg in the placebo group. The reduction was less noticeable in both groups (3.2 kg for the L112 product range and 2.4 kg for placebo) in the second half of the experiment (6-12 months). The reduction in BW in the group with the L112 product range was, however, significant again ($P < 0.05$, Tukey's test). Only 17% (8 of 49) of the patients in the placebo group achieved a reduction of BW by 5% after 3 months, whereas 55% (27 of 49) in the L112 product range group achieved this reduction; this difference was significant ($\chi^2 = 16.04$, $P < 0.0001$). After 6 months the percentages were 67% and 98% ($\chi^2 = 16.43$, $P < 0.0001$). The reduction in BMI was similar to the reduction in BW and was significant for both treatments ($P < 0.05$). In the first 6 months, the reduction in BMI in the PG group was 3, followed by a slower rate of reduction, which reached 4.3 after 12 months.

The reduction in BMI was significantly lower in the PL group ($P < 0.05$) and was characterised by a flatter curve, which only achieved a reduction of 2.8 after 12 months. A change in WC of 13.3 cm was achieved in the L112 product range group and 10.2 cm in the placebo group ($P < 0.05$). In both cases the fastest reduction was recorded in the first 6 months.

It is noteworthy that the participants' detailed records of the food they consumed showed that the degree of calorific restriction in this study was low compared with other clinical trials that also investigated the L112 product range.

The variables total cholesterol (TC), low-density cholesterol (LDL-C), high-density cholesterol (HDL-C) and triglycerides (TG) were not defined as primary variables. As the efficacy of chitosan for the lowering of cholesterol concentration is known and well documented (the European Food Safety Authority EFSA permits the advertising of chitosans for cholesterol management provided the daily dose is $\geq 3g$, regardless of the type of chitosan in question), this does not restrict the value of the observed results. Although the dosage of polyglucosamine in this study was much lower than this EFSA recommendation and the uptake of cholesterol was probably simultaneously reduced by the diet imposed, significantly higher reductions of TC, LDL-C and TG were observed in the L112 product range group.

Authors' conclusions:

The L112 product range proved more effective than the placebo in terms of the reduction of BW, WC, glucose, BP, plasma-lipids and hs-CRP in moderately obese people who undertook a 10% calorie reduction and a slight increase in physical activity. Dietary supervision with the aid of an FIA was an effective instrument for supporting dietary compliance.

Source:

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

Summary:

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 active substance group than in the placebo group; more test subjects achieved this target sooner. Use of the L112 product range led to significantly higher weight loss in the active substance group at the end of the study. The capability of the L112 product range to reduce cholesterol uptake from food is also proven.

5.2.2. Study by Willers et al. 2012**Description of the study**

Willers (Willers et al. 2012) included 120 overweight and obese test subjects in this study. As a fundamental change in diet, the patients took a protein-rich formula diet once a day as a meal replacement. In addition, half of the participants (n=60) also took two tablets from the L112 product range (F+LA group) once a day, while the other half (n=60) were given two placebo tablets (F+P group). No further restriction or assessment of the calorie intake of the participants was intended and/or documented. Measurements were performed in Weeks 0, 6 and 12 in order to determine the reaction to the intervention.

Results:

Both groups achieved a highly significant weight loss ($P < 0.001$) (F+LA group: -5.5 ± 3.8 kg vs. F+P group: -4.7 ± 3.9 kg, Full Analysis Set (FAS) population). The weight decrease in the F+LA group was 0.74 kg higher than in the F+P group, even though the difference between the two groups was not statistically significant.

There was a significant lowering of HbA1c ($P < 0.01$), total cholesterol ($P < 0.001$), LDL cholesterol ($P = 0.002$) and triacylglycerol ($P = 0.001$) in the F+LA group, whereas the F+P group experienced no changes. The investigation showed that a formula diet alone or in combination with the L112 product range (2 tablets once a day) both contributed effectively to weight reduction. The additional administration of products from the L112 product range was more effective in terms of reducing glucose and lipid parameters than the formula diet alone.

Authors' conclusions:

The clinical investigation showed that moderate application of a meal replacement strategy led to a significant loss of clinically relevant body weight within twelve weeks. The additional administration of lipid-absorbing tablets with polyglucosamine from the L112 product range (2 tablets once per day) at one meal a day showed a further slight, but not significant, weight loss in comparison to the placebo. More important than the weight loss may be the fact that this treatment method had advantageous

effects on carbohydrate and lipid metabolism and led to a significant lowering of HbA1c, insulin, TC, LDL-C and TAG.

Source:

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

Summary:

Although the efficacy of the L112 product range in the treatment of excess weight could not be demonstrated in this clinical trial, this does not question the intended purpose of the medical device. This is because only half the amount of the L112 product range intended for the treatment of excess weight was administered to the patients. At the same time, a slightly – but not significantly greater – increased weight reduction was observed in the L112 product range group in comparison to the placebo group. This result shows that the claimed intended purpose of supporting weight management is supported with clinical data.

5.2.3. Study by Pokhis et al. 2015**Description of the study:**

Pokhis et al. used a randomised, double-blind, placebo-controlled design in two study centres (Pokhis et al. 2015). The study participants followed a standard treatment (ST), which consisted of a combination of a low-calorie diet, which was achieved with a daily calorie deficit (500 calories), and increased physical activity (7 MET hours/week). The patients were randomised to receive standard treatment plus placebo (ST + PL) or standard treatment plus L112 product range (ST + PG). The participants were instructed to take 2 x 2 tablets before the two meals with the highest fat content over a minimum period of 24 weeks. Body weight, BMI, waist circumference and the time required to achieve a 5% body weight reduction (5R) were used as the primary outcome measures.

Results

Of the 115 patients originally included in the study, six failed to satisfy the inclusion criteria in terms of BMI, and two only took part in the inclusion visits. These eight patients were excluded from the intention to treat (ITT) population. The average weight loss over a time period of 25 weeks in the ITT population (N=107) was 5.8 +/- 4.09 kg in the ST + PG group, compared to 4.0 +/- 2.94 kg in the ST + PL group (pU = 0.023; pt = 0.010). After 25 weeks, 34 participants achieved a 5% body weight reduction in the ST + PG group (64.1%), in comparison to only 23 participants in the ST + PL group (42.6%) (ITT) (p Fisher = 0.033). The weight reduction due to hypocaloric diets has proven to be effective. The additional effect of the PG in combination with the standard treatment is capable of achieving significantly better weight reduction than the placebo. The external validity of the reported data and findings is supported by the fact that the ST + PL group experienced a weight loss that is comparable to a stage-1 dietary intervention as described by experts from the relevant associations (German Association for the Study of Obesity/Deutsche Adipositas Gesellschaft 2019).

Authors' conclusions:

Participants who were treated with ST + PG displayed a significant weight loss of an additional 1.8 kg in comparison to the controls treated with ST + PL.

Source:

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.

Summary

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 the target criterion of 5% weight reduction. This demonstrates the clinical benefit of use of the L112 product range in addition to the basic therapy.

5.2.4. Study by Stoll et al. 2017**Description of the study:**

Sixty four overweight or obese test subjects were included in a double-blind study, which was carried out at two study centres (Stoll et al. 2017). One centre was in Germany [centre 1] and the other in Italy [centre 2]. It was recommended to the test subjects (26 in centre 1 and 38 in centre 2) that they should maintain a calorie deficit of around 2000 kJ per day and increase their physical activity to 3 metabolic equivalent of task hours (MET h) per day. In both centres, the test subjects were randomised and treated over a period of 12 weeks with L112 product range (2 tablets x 2 times a day) or Orlistat (1 capsule x 3 times a day). In order to ensure successful blinding of patients and doctors despite the fact that the active substance and placebo had different dosage forms, a double dummy design was used. Every participant was required to take two tablets and one capsule before each of the three main meals of the day (breakfast, lunch, evening dinner). To ensure compliance with the recommended dosages, the patients in the L112 product range group were given placebo tablets in the mornings, which led to a dosage of 2 x 2 active substance tablets. Weight loss was considered as a main variable together with the reduction of 5 percent (%) of body weight (5R). Body mass index (BMI) and waist circumference (WC) were used as secondary variables.

Results

A significant difference in weight loss was observed between the two groups: 6.7 +/- 3.14 kilograms (kg) in the L112 product range group, compared with 4.8 +/- 2.24 kg in the Orlistat group (t-test $p < 0.05$). BMI and WC reduction were also more consistent with treatment with the L112 product range than they were in the treatment with Orlistat (t-test $p < 0.05$). No significant difference was observed in terms of the number of test subjects who attained 5R (70% for the L112 product range and 55% for the Orlistat group; chi-squared $p > 0.05$). Administration of L112 product range after reduced energy intake and increased physical activity reduces body weight, BMI and WC more efficiently than Orlistat. Although both groups were instructed to follow a reduced-calorie diet together with increased physical activity, an additional weight loss of 1.6 kilograms (kg) was observed in both centres in the L112 product range group in comparison to the Orlistat group (6.2 +/- 3.46 versus 4.6 +/- 2.36 kg), despite the higher carbohydrate consumption in Italy (centre 2).

Authors' conclusions:

A typical Italian diet is generally carbohydrate rich, whereas Germans tend to consume meals with a higher fat content. This leads to the assumption that the L112 product range limits both fat and carbohydrate absorption, which would explain the comparatively effective weight reduction among the Italian participants.

Source:

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.

Summary:

This high-quality clinical study with a duration of 12 weeks shows that the administration of the L112 product range in accordance with the dosing regimen set out in the instructions for use reduces body weight, BMI and WC more efficiently than the approved medicinal product Orlistat. The weight reductions / weight loss successes (5R) achieved with the active substance control are in the range that is described as the expected effect for the medicinal product. The fundamental suitability of the study design for the determination of clinical effects is therefore proven. The study demonstrated a superior clinical benefit of the L112 product range with regard to weight reduction. Likewise, the effects achieved with the L112 product range for the parameter 5R also displayed a better tendency, but the difference was not statistically significant.

5.3. Clinical data from other sources**5.3.1. Study by Sanhueza et al. 2018****Description of the study:**

In this open-label, uncontrolled study with 25 obese patients (80% female sex, type-2 diabetics or prediabetics, metformin and non-pharmacological therapy), the L112 product range was administered for 12 weeks in combination with a nutrition plan and individualised and controlled physical activity. Patients were excluded who had: Neoplasms, cardiovascular diseases, gastrointestinal diseases, kidney diseases, allergies and psychiatric pathologies such as bulimia and/or anorexia. Anthropometric and nutritional parameters were monitored every two weeks. Laboratory values were recorded at the start and end of the treatment. The statistical analysis was performed by means of SPSS using mean values, standard deviations, median values and percentiles. The significance level was defined as $p < 0.05$.

Results

The test subjects achieved the following results during the course of the 12-week study: Weight reduction from 93 ± 18 to 90 ± 19 kg, body mass index from 35 ± 6 to 34 ± 6 kg/m², waist circumference from 109 ± 11 to 105 ± 11 cm, and systolic blood pressure from 125 ± 12 to 117 ± 11 mmHg ($p < 0.05$). Fasting blood glucose levels dropped from 100 ± 40 to 96 ± 33 mg/dl, HbA1c from 7.8 ± 1.1 to $7.2 \pm 0.9\%$, and triglycerides from 151 ± 68 to 126 ± 39 mg/dl ($p < 0.05$). LDL cholesterol changed from 109 ± 34 to 106 ± 30 mg/dL (NS).

Authors' conclusions:

Administration of the L112 product range is a safe and effective option for the treatment of obesity in diabetics and pre-diabetics for the 12-week treatment duration.

Source:

Sanhueza et al: Formoline L112® associated with non pharmacological therapy in the management of obesity in diabetic and prediabetic patients. Rev. Chil. Endo Diab. (2018) 11(3):91-96.

Summary:

This uncontrolled, open-label study only offers a low evidence level. As it is an Investigator Initiated Trial (IIT) and the study documentation is not available to the manufacturer, no information is available about the dietary guidance and about the monitoring of the nutrition of the test subjects. Nevertheless, a clinically relevant weight loss success was achieved with use of the L112 product range.

5.4. 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 LDL cholesterol lowering accompanying 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.

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.

5.5. Ongoing or planned clinical follow-up observations after placing on the market

The safety and performance of the L112 product range were demonstrated in clinical studies (5.2). 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 collected via an online questionnaire. For this purpose, inserts with QR codes have 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.

A mechanistic study is being carried out in order to further clarify the mode of action. The purpose of this prospective, placebo-controlled, randomised, double-blind crossover study is to investigate the influence of the L112 product range on cholesterol resorption from food.

6. Possible diagnostic or therapeutic alternatives

The following consensus opinions can be derived from the recommendations of the medical professional associations and professional societies in relation to the current treatment options for the treatment of excess weight and obesity: Therapy for weight management comprises two major phases: A phase of weight reduction and a phase of long-term stabilisation of body weight. Both are essential for long-term therapy success.

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

- conservative, non-invasive therapies, and
- invasive therapies.

Invasive therapies are only a treatment option in patients with class III or class II obesity with significant diseases due to the obesity (DAG Guideline 2014, NICE Guideline 2016).

DAG Guideline 2014: Berg A, et al. Interdisziplinäre Leitlinie der Qualität S3 zur „Prävention und Therapie der Adipositas“. Deutsche Adipositas-Gesellschaft. 2014

NICE Guideline 2016: Obesity in adults: prevention and lifestyle weight management programmes. National Institute for Health and Clinical Excellence. 2016

Conservative therapy for excess weight and obesity

Basic therapy

The basic therapy for every treatment of excess weight and obesity consists of modifications to diet, exercise and behaviour. Here, Cochrane meta analyses show that a reduction in fat intake alone – i.e. without further measures – already leads to slightly lower weight, BMI, waist circumference and percentage body fat, while the participants displayed no indication of impairment of the serum lipids, blood pressure or quality of life. This underlines the importance of a reduction of alimentary fat intake for the therapy of excess weight and obesity. The concept of the L112 product range tackles precisely this point (reduction of the uptake of lipids from food), which explains the general meaningfulness of the therapy option.

Cochrane meta analyses:

Hooper L, et al. Effects of total fat intake on body weight. Cochrane Database of Systematic Reviews. 2015; 8: CD011834

Hooper L, et al. Effects of total fat intake on body fatness in adults. Cochrane Database of Systematic Reviews. 2020; 6: CD013636

Adjuvant 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 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 (DAG Guideline 2014).

DAG Guideline 2014: Berg A, et al. Interdisziplinäre Leitlinie der Qualität S3 zur „Prävention und Therapie der Adipositas“. Deutsche Adipositas-Gesellschaft. 2014

Pharmacological adjuvant therapy vs. L112 product range

In the evaluation of the conservative approaches considered, the pharmacological options are only considered as a supplement to dietary measures and physical activity for obese or overweight patients with relevant comorbidities (DAG Guideline 2014). Among the conservative approaches, the pharmacological approach 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 nonprescription 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 inherent in the system of an adjuvant pharmacological therapy are avoided.

DAG Guideline 2014: Berg A, et al. Interdisziplinäre Leitlinie der Qualität S3 zur „Prävention und Therapie der Adipositas“. Deutsche Adipositas-Gesellschaft. 2014

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.

8. Reference to all applied harmonised standards and CS

The L112 product range is subject to the regulatory requirements from:

- Council Directive 93/42/EEC of 14 June 1993 concerning medical devices, most recently amended on 5 September 2007
- In combination with Directive 2007/47/EC of the European Parliament and of the Council of 5 September 2007 amending Council Directive 90/385/EEC on the approximation of the laws of the Member States relating to active implantable medical devices, Council Directive 93/42/EEC concerning medical devices and Directive 98/8/EC concerning the placing of biocidal products on the market
- REGULATION (EU) 2017/745 of 5 April 2017 on medical devices
- Commission Implementing Regulation (EU) 2017/2185 of 23 November 2017 on the list of codes and corresponding types of devices etc.
- Gesetz zur Durchführung unionsrechtlicher Vorschriften betreffend Medizinprodukte (Medizinprodukte-Durchführungsgesetz - MPDG) Ausfertigungsdatum: 28.04.2020
- Gesetz über Medizinprodukte (Medizinproduktegesetz - MPG) in der Fassung vom 07.08.2002, zuletzt geändert 19.06.2020
- Verordnung zur Regelung der Abgabe von Medizinprodukten Medizinprodukte-Abgabeverordnung – MPAV vom 25. Juli 2014, zuletzt geändert 15.01.2021
- Verordnung über klinische Prüfungen von Medizinprodukten – MPKPV vom 10. Mai 2010, zuletzt geändert 13.07.2020
- Verordnung über Medizinprodukte Medizinprodukte-Verordnung – MPV vom 20.12.2001, zuletzt geändert 27.09.2016
- Verordnung über das Errichten, Betreiben und Anwenden von Medizinprodukten Medizinprodukte-Betreiberverordnung – MPBetreibV vom 21.08.2002, zuletzt geändert 29.11.2018
- Verordnung über die Erfassung, Bewertung und Abwehr von Risiken bei Medizinprodukten Medizinprodukte-Sicherheitsplanverordnung – MPSV vom 24.06.2002, zuletzt geändert 28.04.2020
- Gebührenverordnung zum Medizinproduktegesetz und den zu seiner Ausführung ergangenen Rechtsverordnungen Medizinprodukte-Gebührenverordnung – BkostV-MPG vom 27.03.2002, zuletzt geändert am 19.05.2020
- DIN EN 1041:2013-12, Information supplied by the manufacturer of medical devices
- ISO 10993-1:2018-08, Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process

- DIN EN ISO 13485:2016-08, Medical devices - Quality management systems - Requirements for regulatory purposes
- DIN EN ISO 14155:2020-12, Clinical investigation of medical devices for human subjects - Good clinical practice
- DIN EN ISO 14971:2020-07, Medical devices - Application of risk management to medical devices
- DIN EN ISO 15223-1:2017-04, Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied
- DIN EN ISO 22442-1:2016-05, Medical devices utilizing animal tissues and their derivatives - Part 1: Application of risk management
- DIN EN ISO 22442-2:2016-05, Medical devices utilizing animal tissues and their derivatives - Part 2: Controls on sourcing, collection and handling
- DIN EN ISO 22442-3:2008-03, Medical devices utilizing animal tissues and their derivatives - Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents
- DIN EN ISO 10993-2:2006: Biological evaluation of medical devices - Part 2: Animal welfare requirements
- DIN EN ISO 10993-5-2009: Biological evaluation of medical devices - Part 5: Tests for in vitro cytotoxicity
- DIN EN ISO 10993-9:2009-08: Biological evaluation of medical devices - Part 9: Framework for identification and quantification of potential degradation products
- DIN EN ISO 10993-10:2010-12: Biological evaluation of medical devices - Part 10: Tests for irritation and skin sensitization
- DIN EN ISO 10993-17:2009-08: Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances
- DIN EN ISO 10993-18:2009-08: Biological evaluation of medical devices - Part 18: Chemical characterization of materials
- ISO/TR 10993-22:2017 (E): Biological evaluation of medical devices – Part 22: Guidance on nanomaterials
- Ph. Eur. 10.0/1774 Chitosan hydrochloride
- Ph. Eur. 10.0/0253 Ascorbic acid
- Ph. Eur. 10.0/0460 Tartaric acid
- Ph. Eur. 10.0/0434 Silicon dioxide, highly dispersed
- Ph. Eur. 10.0/0316 Microcrystalline cellulose
- Ph. Eur. 10.0/0472 Carmellose-sodium
- Ph. Eur. 10.0/0685 Povidone
- Ph. Eur. 10.0/0229 Magnesium stearate
- Ph. Eur. 10.0/2.02.24.00 2.2.24 IR spectroscopy
- Ph. Eur. 10.0/2.09.34.00 2.9.34 Bulk density and tapped density of powders

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- Ph. Eur. 10.0/2.09.12.00 2.9.12 Analytical sieving
- Ph. Eur. 10.0/2.09.38.00 2.9.38 Determination of particle size distribution through analytical sieving
- Ph. Eur. 10.0/2.02.32.00 2.2.32 Loss on drying
- USP Monograph Chitosan
- USP <61> MICROBIOLOGICAL EXAMINATION OF NONSTERILE PRODUCTS: MICROBIAL ENUMERATION TESTS
- USP <62> MICROBIOLOGICAL EXAMINATION OF NONSTERILE PRODUCTS_TESTS FOR SPECIFIED MICROORGANISMS
- USP <211> ARSENIC
- USP <281> RESIDUE ON IGNITION
- USP <616> BULK DENSITY AND TAPPED DENSITY OF POWDERS
- USP <731> LOSS ON DRYING
- USP <786> PARTICLE SIZE DISTRIBUTION ESTIMATION BY ANALYTICAL SIEVING
- USP <852> ATOMIC ABSORPTION SPECTROSCOPY
- USP <911> VISCOSITY – CAPILLARY METHODS
- GB 14754-2010 National Food Safety Standard Food additive - Vitamin C (Ascorbic acid)
- GB 1886.42-2015 National food safety standard - Food additive - dl-Tartaric acid

9. Revision history

Revision number of the summary	Date	Changes	Validation by the notified body
Version 01	09.06.21	Document first created <i>ATA von P...</i>	<input checked="" type="checkbox"/> Yes Language: German <input type="checkbox"/> No

The summary of safety and clinical performance for patients is listed below:

Summary of safety and clinical performances for the L112 product range

Revision number: 01
Date: 9.6.2021

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

Trade name

Variants of the L112 product range can be marketed under the following trade names: formoline L112, formoline L112 EXTRA, Sterolsan.

Name and address of the manufacturer

Certmedica International GmbH, Magnolienweg 17, 63741 Aschaffenburg, Germany

Basic UDI

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.

Indications 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. Description of the medical device

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 (formoline L112 EXTRA) 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 β -1,4-polymer from D-glucosamine and N-acetyl-D-glucosamine from crustacean shells

Excipients: Ascorbic acid, tartaric acid, tableting excipients (plant-based cellulose, croscarmellose sodium, plant-based magnesium stearate, povidone, 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:

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.

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).

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 Palestinian MOH www.pharmacy.moh.ps.

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. If required, a multivitamin preparation can also be taken as a supplement to ensure a sufficient supply of vitamins.

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 – which is regarded as critical – saw a 12.9% decline with L112.

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. 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, doubleblind, 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 absorption 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

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 collected via an online questionnaire. For this purpose, inserts with QR codes have 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.

A study on the mode of action is being carried out in order to further clarify how the medical device works. This study is placebo-controlled, randomised and double-blind, and it is being conducted as a crossover study. This means that the participants are given both the medical device in the L112 product range and a placebo one after the other. However, it is randomly assigned (randomised) whether the participant is first given the medical device and then the placebo, or whether this is the other way around.

The purpose of this study is to investigate the influence of the L112 product range on the uptake of cholesterol from food.

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 LDL cholesterol lowering accompanying 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.

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/m²) or class II (BMI 35.0 - 39.9 kg/m²) and who also suffer from key diseases triggered by the obesity.

Conservative therapy for excess weight and obesity

Basic therapy

The basic therapy for every treatment of excess weight and obesity consists of changes to diet, exercise and behaviour. 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.