# Summary of Safety and Clinical Performance for the L112 product range

Reference number for the SSCP from the manufacturer: L112_310_V3

## 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, 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-DI**
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 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.

### 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/m$^2$);
- are pregnant or breastfeeding;
- suffer from chronic constipation, intestinal obstruction etc.; or
- are on long-term medication that reduces intestinal activity.

## 3 Device Description

### 3.1 Description of the device

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 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.

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 Reference to previous generations of variants

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.

A conformity assessment procedure in accordance with Regulation (EU) 2017/745 was successfully completed with regard to the technical documentation in October 2021 and the quality management in February 2022 for both versions (biconvex 500 mg tablet; biconvex 750 mg tablet).

A version has since been developed for both tablet sizes with a slightly adjusted excipient formula. The tabletting excipients croscarmellose sodium and povidone are no longer used – sodium sulphate is now used. The composition stated under item 3.1 corresponds to this adjusted formula.

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 31 countries have been supplied over the past 20 years.

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 appliances 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 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.

The most common side effects are gastrointestinal complaints of a mild and temporary nature, as well as intolerance reactions.

The following table shows the frequency of reported side effects in relation to the packs placed on the market.

Table 1: Side effects occurred in conjunction with L112 products (IMDRF* code)

| Side effects (IMDRF*-Code) | Reporting Day + preceding 12 months (N)<br><br>2022 | N – 12 months (N2)<br><br>2021 | N2 – 12 months (N3)<br><br>2020 | N3 – 12 months (N4)<br><br>2019 |
|---|---|---|---|---|
| Gastro-intestinal complaints (E10) | 0,0045 % | 0,0034 % | 0,0032 % | 0,0015 % |
| Allergic reaction (E04) | 0,0011 % | 0,0012 % | 0,0012 % | 0,0021 % |
| General well-being (E23) | 0,0004 % | 0,0008 % | 0,0014 % | 0,0004 % |
| Other (E24) | 0 % | 0,0001 % | 0 % | 0 % |

*IMDRF = International Medical Device Regulators Forum (publishes codes for clinical signs, symptoms and conditions to categorise medical device incidents)

The reported side effects are rare isolated cases. No accumulation or trend is evident. The side effects reported had a mild course and were reversible.

**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 responsible authority.

### 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 clinical follow-up observations after placing on the market

### 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 from conducted investigations

#### 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 ($x2 = 16.04$, $P < 0.0001$). After 6 months the percentages were 67 % and 98 % ($x2 = 16.43$, $P < 0.0001$).

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 ≥ 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.

### 5.2.5 Study by Belcaro et al 2020

**Description of the study:**
58 overweight subjects with a BMI of 26-30 were selected, of which 45 were enrolled in the study: 34 men and 11 women aged between 40-50 years. The study started with an initial introductory phase of 4 weeks, in which the subjects were randomly divided into two groups of 23 and 22 subjects, respectively. Both groups followed an identical standard management (SM) protocol that included suggestions on diet and daily activity, reducing salt (NaCl) and lipids/fats in the diet, increasing vegetable and fruit intake, and adopting a healthier lifestyle that included regular exercise and stress management. A brisk walk of at least one hour/day was suggested. No other restrictions were called for.

Immediately after the first phase, a second phase of 4 weeks followed in which the subjects were assigned to polyglucosamine group A (PGA = existing product of the L112 product range (750 mg)) or polyglucosamine group B (PGB = formula with new excipient formula (750 mg) – differences see section 3.2) and received the corresponding polyglucosamine formulas in addition to the SM programme described. The two polyglucosamine formulas were administered in the same dosage of 4 tablets of 750 mg each (2 x 2) before the main meals, with a total daily dose of 3 g (corresponding to 2.4 g biopolymer L112). A weekly food intake assessment (FIA) of the main components of dietary intake was performed, including the intake of vitamin A, vitamin C and vitamin E. The main variables

of the analysis were body weight (BW), oxidative stress (OS) and body fat mass (FM %; FM kg). Abdominal circumference (AC), lipids, glucose levels and hs-CRP levels were considered as auxiliary variables. Changes in stool were also included.

**Results:**
During the run-in phase, there was a significant reduction in most of the variables. In the subsequent four-week treatment phase, the reductions in BW, AC, OS and FM were similar and statistically significant for both formulas ($p<0.05$ ANOVA [analysis of variables]). FM was significantly reduced by about 7% for PGA and PGB. Lipid levels and hs-CRP were also significantly reduced. Results of the FIA were very similar in both groups in terms of the main variables of food intake, and stool change was inconsistent in both treatments. Apart from a few cases of meteorism that lasted only one day and were clinically irrelevant, no side effects were observed. Both formulas can be considered equivalent.

As the study is an active controlled study, the validity of the study design was tested by comparing with results of clinical trials conducted with the existing product of the L112 product range in the 500 mg dosage. Initially, the reduction in BW was fairly consistent across both study phases (run-in and control phases), partly attributable to diet (involving restricted intake of salt and sweet beverages and increased intake of fruit and vegetables) and lifestyle changes. With regard to the PGA and PGB treatments, despite the very short duration of treatment, a more consistent BW reduction was achieved than in previous studies. The reduction in BW for both groups was about 1.6 kg in the run-in phase. Treatment with the L112 product range caused a weight loss of 3.5 to 3.7 kg (with PGA and PGB, respectively), indicating that there was a summative effect between SM and PG that appeared to double the effect of the diet followed.

**Authors' conclusions:**
Both formulas PGA and PGB showed almost similar reductions in BW, OS and FM. The hs-CRP concentration was also reduced, indicating a certain anti-inflammatory activity. No side effects or stool changes were reported, apart from very few cases of temporary meteorism, which were clinically irrelevant.

**Summary:**
The reason for the study by Belcaro (Belcaro et al. 2020) was to demonstrate the clinical equivalence of the new excipient formula of the L112 product range with that of the existing product from the L112 product range. In order to record any differences in efficacy as precisely as possible, comprehensive exclusion criteria were used to ensure a very homogeneous study group. Despite the comparatively short study duration of 4 weeks, a reduction in body weight was achieved by using the L112 product range, which was significantly more pronounced than the effects of the existing product biconvex tablets (500 mg) from the L112 product range. The absence of a placebo control does not limit the significance of this result. As the use of the L112 product range was preceded by a 4-week introductory phase with identical dietary and behavioural modifications, compliance with which was also monitored and documented, the additional effect achieved by the use of the L112 product range could be estimated even without a placebo control. It was shown that the subjects in the phase of using the L112 product range lost 3.5 and 3.7 kg of body weight, respectively, in 4 weeks, whereas the weight reduction in the introductory phase, also lasting 4 weeks, was only 1.6 kg for both groups. Nevertheless, the evidence level of the study is limited due to the absence of case number estimates and the lack of a definition of primary endpoints, as well as the short study duration.

### 5.2.6 Study by Cornelli (Cornelli et al. 2022)

**Description of the study:**
This randomised, double-blind, placebo-controlled study with 150 overweight and obese patients was conducted in a study centre. Both groups received individual advice and written instructions for adhering to a diet therapy with three balanced meals that covered 100 % of the energy consumption at the beginning of the diet. This was calculated using the Harris-Benedict equation (calculated with the CASIMET software) so that around 30 % of energy comes from fats, 60 % from carbohydrates and 15 % from proteins (with a minimum of around 0.8 g of protein for an ideal weight) with sodium levels controlled, which corresponds to the basis of the Mediterranean dietary model. The study medication administrated was the L112 product range with a dosage of 4 tablets of 750 mg (2 x 2) before main meals, with a total daily dose of 3 g (corresponding to 2.4 g biopolymer L112). Data collection took place at the beginning, after 45 days, and after 90 days. The study was listed on clinicaltrials.gov under the number NCT04375696.

**Results:**
Of the 150 subjects enrolled, 119 (58 in the L112 product range group, 61 in the placebo group) completed the study. This comparatively high drop-out rate compared to the long-term study by Cornelli et al. was likely due to the Coronavirus epidemic. Firstly, patients who showed COVID-19 infection were excluded from the study. On the other hand, it may be speculated that the visit to a medical institution required for the follow-up was avoided by some study participants, which was recorded as a drop-out without reason. Nevertheless, in both the intention-to-treat (ITT) evaluation and the per-protocol (PP) evaluation, a significantly higher weight reduction was observed than in the placebo group. Although this effect was of a comparable magnitude in the intention-to-treat (ITT) evaluation (placebo: -1.08 kg; verum: -3.76 kg) for the per-protocol (PP) evaluation (placebo: -1.12 kg; verum: 3.71 kg) it was only statistically significant in the per protocol evaluation. The cause of this lack of statistical significance in the ITT evaluation could have been the high rate of drop-outs (placebo: 14; verum: 17). Overall, the weight reductions observed in this study fall somewhat short of what was expected from the Belcaro 2020 equivalence study. Here too, it is likely that the restrictions of movement associated with the COVID-19 epidemic in the study region of Italy led to a reduction in activity and physical exercise levels, which had a negative impact on weight reduction, as study data from Italy shows that body weight increased during the pandemic. No changes were found in the fat-soluble vitamins (A, E, D3 and K1). Lipid levels (total cholesterol, LDL, VLDL, HDL, triglycerides) and glucosamine levels did not change over the course of the study. However, in terms of the total cholesterol level the number of cases showing a 10% reduction was significantly higher in the verum group. Tolerability of both treatments was similar, with no side effects in the placebo group (0 %) and one case of faecaloma (faecal stones) in the verum group (< 2 %).

**Authors' conclusions:**
Use of the L112 product range has been shown to be at least three times more efficacious than the use of a placebo when administered under the same conditions of diet and physical exercise. This is a clinically relevant benefit for the relatively short duration of treatment.

**Summary:**
The reason for the study was to confirm the clinical equivalence of the new excipient formula of the L112 product range with the existing L112 product. The approach of this study is of high methodological merit. The clinical endpoint is clearly defined and a case number estimate was made on this basis. In this group of subjects, the use of the L112 product range leads to a significantly higher weight reduction compared to the placebo group. The fact that this difference is only statistically significant in the PP evaluation limits the significance of the result somewhat. As both this limitation and the comparatively small observed weight reduction can be well explained by the effects of the COVID-19 pandemic, this

result, especially when viewed together with the other data on the 2020 formula, demonstrates the clinical equivalence of the adjusted formula with that of the existing product.

## 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 pre-diabetics, 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/m$^2$, 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 ± 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.

### 5.3.2 Results of the user survey 2020-2021

The safety and performance of the L112 product range were demonstrated in clinical trials (item 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 was collected using 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 for anonymised collection of, among other things, data about the users, safety, and the conditions of use.
The data from the patient survey is now available. Even though this is only data from a user survey, the performance results are within the range of the values determined in clinical investigations and are therefore solid evidence that the results achieved in clinical trials are also achieved under

everyday conditions. The frequency of reported side effects shows that the benefit-risk balance remains favourable.

The results of the studies from items 5.2 and 5.3 are summarised in the following tables. Table 2 provides an overview for weight reduction, Table 3 an overview of changes in cholesterol levels.

Table 2: Summary of study results on the efficacy of the L112 PRODUCT RANGE for weight reduction

| Study | Short description | Performance criteria | | |
|---|---|---|---|---|
| | | Change in body weight over the course of the study greater with verum than with placebo | Number of patients who, in the observation period, achieve > 5 % weight reduction | Period before 5 % weight reduction is achieved |
| Cornelli, 2017 see 5.2.1 | Comparison against placebo 12 months | Verum: -12.1 kg (-12.7 %) Placebo: -8 kg (-7.8 %) | Verum after 3 months: 55 % (27 of 49) Placebo after 3 months: 17 % (8 of 49) Verum after 6 months: 98 % Placebo after 6 months: 67 % | |
| Willers, 2012 see 5.2.2 | Comparison against placebo 1 x 2 tablets 3 months | Verum: -5.46 kg Placebo: -4.72 kg | | |
| Pokhis, 2015 see 5.2.3 | Comparison against placebo 6 months | Verum: -6.5 kg Placebo: -4.3 kg | Verum: 90 % Placebo: 55 % | Verum: 56 days (median) Placebo: 119 days (median) |
| Stoll, 2017 see 5.2.4 | Comparison against Orlistat 60 mg 3 months | Verum: -6.7 kg Orlistat: -4.8 kg | Verum: 70.4 % Orlistat: 54.8 % | |
| Belcaro, 2020 see 5.2.5 | Comparison of formulas 4 weeks | Existing product (PGA): -3.5 kg new formula (PGB): -3.7 kg | | |
| Cornelli, 2022 see 5.2.6 | Comparison against placebo 3 months | Verum formula 2020: -3.71 kg Placebo: -1.12 kg Weight reduction 3 times higher than in the placebo group | In the verum group, the number of subjects with weight reduction ≥ 5 % (14/58) is significantly higher than in the placebo group (6/61). | |
| Sanhueza, 2018 see 5.3.1 | IIT observation 12 weeks | Verum: -3 kg | | |
| PMCF survey see 5.3.2 | Duration of application individually different | L112 Extra (750 mg): Intake for weight reduction: Weight loss in 79 out of 85 participants (92.9 %) No weight loss in 6 out of 85 participants<br><br>L112 (500 mg): Intake for weight reduction: Weight loss in 83 out of 91 participants (91.2 %) No weight loss in 8 out of 91 participants | L112 Extra (750 mg): Intake for weight reduction: ≥5 % weight reduction in 41 of 85 participants<br><br>L112 (500 mg) Intake for weight reduction: ≥5% weight reduction in 43 of 91 participants | |

Table 3: Effects achieved on cholesterol levels in studies on the efficacy of the L112 PRODUCT RANGE

| Study | Development of cholesterol values | |
|---|---|---|
| | Total cholesterol | LDL cholesterol |
| Cornelli, 2017<br>see 5.2.1 | 3 months:<br>Verum: -5.0 % vs. placebo: -1.5 % (p<0.05)<br>6 months:<br>Verum: -6.6 % vs. placebo: -2.5 % (p<0.05)<br>9 months:<br>Verum: -9.1 % vs. placebo: -3.5 % (p<0.05)<br>12 months:<br>Verum: -9.6 % vs. placebo: -4.6 % (p<0.05) | 3 months:<br>Verum: -5.4 % vs. placebo: -2.7 %<br>6 months:<br>Verum: -8.8 % vs. placebo: -2.7 %<br>9 months:<br>Verum: -12.7 % vs. placebo: -4.5 % (p<0.05)<br>12 months:<br>Verum: -12.9 % vs. placebo: -5.3 % (p<0.05) |
| Willers, 2012<br>see 5.2.2 | Verum: -0.45 mmol/l (-7.4 %)<br>Placebo: -0.04 mmol/l (-0.6 %) (p= 0.011) | Verum: -0.30 mmol/l (-7.8 %)<br>Placebo: +0.01 mmol/l (+0.2 % ) (p= 0.013) |
| Belcaro 2020<br>see 5.2.5 | PGA group (existing product):<br>4 weeks run-in (standard treatment):<br>233→218 mg/dL (-6.4 %)<br>4 weeks PGA + standard treatment:<br>218→198 mg/dL (-9.2 %)<br><br>PGB group (new formula):<br>4 weeks run-in (standard treatment):<br>225→213 mg/dL (-5.3 %)<br>4 weeks PGB + standard treatment:<br>213→194 mg/dL (-8.9 %) | PGA group (existing product):<br>4 weeks run-in (standard treatment):<br>147→139 mg/dL (-5.4 %)<br>4 weeks PGA + standard treatment:<br>139→120 mg/dL (-13.7 %)<br><br>PGB group (new formula):<br>4 weeks run-in (standard treatment):<br>145→136 mg/dL (-6.2 %)<br>4 weeks PGB + standard treatment:<br>136→117 mg/dL (-14.0 %) |
| Cornelli, 2022<br>see 5.2.6 | Verum formula 2020:<br>201.75→198.52 mg/dL (-1.6 %)<br>Placebo:<br>206.13→205.10 mg/dL (-0.5 %) (p= 0.1294)<br>The number of participants with a clinically relevant drop in total cholesterol of > 10 % is significantly higher in the verum group than in the placebo group (p=0.0302) | Verum formula 2020:<br>123.17→121.10 mg/dL (-1.7 %)<br>Placebo:<br>126.39→127.00 mg/dL (+0.5 %) (p= 0.1101) |

The efficacy of the L112 product range for weight reduction is demonstrated by the clinical data identified and evaluated. Reducing body weight towards a normal weight is associated with various other health benefits, as discussed in more detail below: Overweight and obesity are risk factors for various diseases. They increase the risk of cardiovascular diseases. Weight loss of 5–10 % lowers mean blood pressure and reduces cardiovascular risk by 25–40 %. In terms of this risk, the LDL cholesterol-lowering accompanying effect also has a positive impact. Weight reduction achieved with the L112 product range therefore reduces risk factors for cardiovascular diseases.

Janhsen, K., Strube, H., & Starker, A. (2008). Themenheft 43 – Hypertonie. Gesundheitsberichterstattung des Bundes.

Joint problems are another example of the negative influence of overweight and obesity on health. Joint wear, measured by the degeneration of cartilage in the knee, progresses significantly more slowly with weight reduction, and the symptoms improve. A 5 % weight loss resulted in an 18 % improvement in the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) score for osteoarthritis in the knee and hip. The authors of a systematic review conclude: “Given the safety and effectiveness of lifestyle interventions such as weight loss and exercise, these should be advocated in all patients due to the low risk of harm.” (Charlesworth et al. 2019). Weight reduction achieved with the L112 product range helps to reduce wear on the joints.

Weight loss and risk reduction joint disease:
Gersing et al. (2019). Weight loss regimen in obese and overweight individuals is associated with reduced cartilage degeneration: 96-month data from the Osteoarthritis Initiative. Osteoarthritis Cartilage, 27(6), 863-870.
Gersing et al. (2016). Progression of cartilage degeneration and clinical symptoms in obese and overweight individuals is dependent on the amount of weight loss: 48-month data from the Osteoarthritis Initiative. Osteoarthritis Cartilage, 24(7), 1126-1134.
Charlesworth et al. (2019). Osteoarthritis- a systematic review of long-term safety implications for osteoarthritis of the knee. BMC Musculoskelet Disord, 20(1), 151.

### 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 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 demonstrated by the identified and evaluated clinical data (details: see Tables 2 and 3). In this patient target group, use of the L112 product range leads to a clearly demonstrable, clinically relevant benefit for weight reduction. The clinical benefit achieved is greater than that typically achieved with non-prescription medicines. This is the consequence of a purely physical mode of action of polyglucosamine. This effect is independent of the tabletting excipients used, so the 2020 formula 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. (Figures: see Table 1).
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 post-market clinical follow-up (PMCF)

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.

In addition, a patient survey on the experiences gained with the 2020 formula is planned.

## 6 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.

The specific success of basic therapy is very much dependent on the type of measures taken. Very few studies report weight reduction in %, even though the guideline emphasises a percentage weight reduction for achieving a health benefit. A meta-analysis of very heterogeneous studies arrived at a reduction of 6 % over a period of 12 months with nutritional advice. With a much greater restriction of calorie intake, for example through the use of formula diets, a greater reduction is possible: Under medical supervision and using formula diets, 77 % of the participants achieve a weight reduction of more than 5 % over a period of one year, and almost half a weight reduction of more than 10 %. Weight reductions of 16.1 % and 9.7 % were achieved with very severe and severe calorie restriction, respectively, using meal replacement products. The amount of weight reduction under basic therapy depends strongly on how great the restrictions are that the participants have to accept.

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.

Leitlinie 2014 der DAG: Berg A, et al. Interdisziplinäre Leitlinie der Qualität S3 zur „Prävention und Therapie der Adipositas". Deutsche Adipositas-Gesellschaft. 2014.
Meta analysis of the basic therapy: Dansinger, M. L., Tatsioni, A., Wong, J. B., Chung, M., & Balk, E. M. (2007). Meta-analysis: the effect of dietary counseling for weight loss. Ann Intern Med, 147(1), 41-50.
Study with severe restriction of calorie intake: Tsai et al. (2006). The evolution of very-low-calorie diets: an update and meta-analysis. Obesity (Silver Spring), 14(8), 1283-1293.
Cochrane-Metaanalysen:
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 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 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

- VERORDNUNG (EU) 2017/745 vom 5. April 2017 über Medizinprodukte
- Durchführungsverordnung (EU) 2017/2185 vom 23. November 2017 über das Verzeichnis der Codes und der ihnen entsprechenden Produktarten usw.
- Gesetz zur Durchführung unionsrechtlicher Vorschriften betreffend Medizinprodukte (Medizinprodukterecht-Durchführungsgesetz – MPDG) vom 28.04.2020, zuletzt geändert 28.06.2022
- Verordnung über das Errichten, Betreiben und Anwenden von Medizinprodukten Medizinprodukte-Betreiberverordnung – MPBetreibV vom 21.08.2002, zuletzt geändert 21.04.2021

- Verordnung über die Meldung von mutmaßlichen schwerwiegenden Vorkommnissen bei Medizinprodukten sowie zum Informationsaustausch der zuständigen Behörden (Medizinprodukte-Anwendermelde- und Informationsverordnung – MPAMIV) vom 21.04.2021, zuletzt geändert 21.04.2021
- DIN EN ISO 20417:2022-03, Medizinprodukte – Anforderungen an vom Hersteller bereitzustellende Informationen
- ISO 10993-1:2021-05, Biologische Beurteilung von Medizinprodukten – Teil 1: Beurteilung und Prüfungen im Rahmen eines Risikomanagementsystems.
- DIN EN ISO 13485:2021-12, Medizinprodukte – Qualitätsmanagementsysteme – Anforderungen für regulatorische Zwecke.
- DIN EN ISO 14155:2021-05, Klinische Prüfung von Medizinprodukten an Menschen – Gute klinische Praxis
- DIN EN ISO 14971:2022-04, Medizinprodukte – Anwendung des Risikomanagements auf Medizinprodukte
- DIN EN ISO 15223-1:2022-02, Bei Aufschriften von Medizinprodukten zu verwendende Symbole, Kennzeichnung und zu liefernde Informationen
- DIN EN ISO 22442-1:2021-08, Tierische Gewebe und deren Derivate, die zur Herstellung von Medizinprodukten eingesetzt werden – Teil 1: Anwendung des Risikomanagements
- DIN EN ISO 22442-2:2021-04, Tierische Gewebe und deren Derivate, die zur Herstellung von Medizinprodukten eingesetzt werden – Teil 2: Kontrollen der Beschaffung, Materialgewinnung und Handhabung
- DIN EN ISO 22442-3:2008-03, Tierische Gewebe und deren Derivate, die zur Herstellung von Medizinprodukten eingesetzt werden – Teil 3: Validierung der Eliminierung und/oder Inaktivierung von Viren und Erregern der übertragbaren spongiösen Enzephalopathie (TSE)
- DIN EN ISO 10993-2:2006-10 Biologische Beurteilung von Medizinprodukten – Teil 2: Tierschutzbestimmungen
- DIN EN ISO 10993-5:2009-10 Biologische Beurteilung von Medizinprodukten – Teil 5: Prüfungen auf In-vitro-Zytotoxizität
- DIN EN ISO 10993-9:2022-03: Biologische Beurteilung von Medizinprodukten – Teil 9: Rahmen zur Identifizierung und Quantifizierung von möglichen Abbauprodukten
- DIN EN ISO 10993-10:2014-10: Biologische Beurteilung von Medizinprodukten – Teil 10: Prüfungen auf Irritation und Hautsensibilisierung
- DIN EN ISO 10993-17:2009-08: Biologische Beurteilung von Medizinprodukten – Teil 17: Nachweis zulässiger Grenzwerte für herauslösbare Bestandteile
- DIN EN ISO 10993-18:2021-03: Biologische Beurteilung von Medizinprodukten – Teil 18: Chemische Charakterisierung von Werkstoffen
- ISO/TR 10993-22:2017-07: Biological evaluation of medical devices – Part 22: Guidance on nanomaterials
- Ph. Eur. 1774 Chitosanhydrochlorid
- Ph. Eur. 0253 Ascorbinsäure
- Ph. Eur. 0460 Weinsäure
- Ph. Eur. 0434 Hochdisperses Siliciumdioxid
- Ph. Eur. 0316 Mikrokristalline Cellulose
- Ph. Eur. 0472 Carmellose-Natrium
- Ph. Eur. 0685 Povidon
- Ph. Eur. 0229 Magnesiumstearat
- Ph. Eur. 0099 Wasserfreies Natriumsulfat
- Ph. Eur. 2.02.24.00 2.2.24 IR-Spektroskopie
- Ph. Eur. 2.09.34.00 2.9.34 Schütt- und Stampfdichte von Pulvern
- Ph. Eur. 2.09.12.00 2.9.12 Siebanalyse

- Ph. Eur. 2.09.38.00 2.9.38 Bestimmung der Partikelgrößenverteilung durch analytisches Sieben
- Ph. Eur. 2.02.32.00 2.2.32 Trocknungsverlust
- USP Monographie 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 | 09.06.2021 | Document first created | ☒ Yes<br>Language: German<br>O No |
| Version 02 | 09.03.2022 | Updating of references to applied harmonised standards and CS [common specifications], editorial processing | O Yes<br>Language: German<br>O No |
| Version 03 | 29.03.2023 | Inclusion of the changed excipients, widening of the clinical evidence in terms of changed excipients, editorial processing | ☒ Yes<br>Language: German<br>O No |

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

# Summary of Safety and Clinical Performance for the L112 product range

Revision number: 03
Date: 29.03.2023

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 L112, formoline L112 EXTRA, Sterolsan.

**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. 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 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.

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.

**Results of the user survey 2020-2021**
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 is now available. 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

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.

In addition, a patient survey on the experiences gained with the 2020 formula is planned.

### 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/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. 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.