SUMMARY OF SAFETY AND CLINICAL PERFORMANCE

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The SSCP is not intended to replace the Instructions For Use as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following information is intended for users/healthcare professionals.

Following this information there is a summary intended for patients.

Manufacturer's reference number for the SSCP - **8032472LENOby232_SSCP**

1. Device identification and general information

1.1. Device trade name(s) of Antidiarroico pediatric

LENODIAR PEDIATRIC, LENODIAR KINDER

1.2. Manufacturer's name and address

Aboca S.p.A. Società Agricola - Loc. Aboca 20 – 52037 Sansepolcro (AR) – Italy

1.3. Manufacturer's single registration number (SRN)

IT-MF-000029499

1.4. Basic UDI-DI

8032472LENOby232

1.5. Medical device nomenclature description / text

G0401 - ORALLY ADMINISTERED DEVICES FOR THE THERAPY OF GASTRO-INTESTINAL DISORDERS

1.6. Class of device

Class III

1.7. Year when the first certificate (CE) was issued covering the device

2017 (certification according to Directive 93/42/EEC)

1.8. Authorised representative if applicable; name and the SRN

Not applicable

1.9. NB's name (the NB that will validate the SSCP) and the NB's single identification number

Eurofins Product Testing Italy S.r.l. – 0477

2. INTENDED USE OF THE DEVICE

2.1. Intended purpose

Antidiarroico pediatric is indicated for the treatment of acute diarrhoea and relapses of chronic diarrhoea.

2.2. Indication(s) and target population(s)

Antidiarroico pediatric is indicated for infants and children from 6 months to 12 years of age.

2.3. Contraindications and/or limitations

The device shall not be used in case of individual hypersensitivity or allergy to one or more components of the product.

Consult physician if symptoms persist for more than 7 days.

There are no known interactions of Antidiarroico pediatric with other medications, medical devices or food.

3. DEVICE DESCRIPTION

3.1. Description of the device

Antidiarroico pediatric is a medical device available in granular sticks for children and infants starting from 6 months to 12 years of age.

Antidiarroico pediatric works by normalizing the consistency of the stools in case of acute diarrhoea and relapses of chronic diarrhoea and by reducing the frequency of diarrheal discharges and the inflammation of the intestinal mucosa, while respecting the functionality of the intestine.

The composition of the device is described below:

One 2 g sachet contains: plant complex Actitan-F® 92 mg, based on Tannins (extractive fractions of Agrimony and Tormentilla - 57 mg) and Flavonoids (extract fraction of Chamomile 35 mg); Juice of Blueberry, Blackberry and Elderberry; Cane sugar; Natural flavor and natural Lemon aroma; Lemon essential oil; Arabic gum.

3.2. A reference to previous generation(s) or variants if such exist, and a description of the differences

A previous generation of Antidiarroico pediatric has been certified according to Directive 93/42/EEC since 2017.

The device is available in different packaging sizes in the following dosage form: granular stick whose content has to be dissolved in a small quantity of water before ingestion.

3.3. Description of any accessories which are intended to be used in combination with the device

Not applicable – no accessories are intended to be used in combination with Antidiarroico pediatric.

3.4. Description of any other devices and products which are intended to be used in combination with the device

Not applicable as there are no devices and products intended to be used in combination with Antidiarroico pediatric.

4. RISKS AND WARNINGS

4.1. Residual risks and undesirable effects

The main residual risks identified for Antidiarroico pediatric are the following:

- Subjective allergic reaction of the user – although the product is non-sensitising, it is possible that a small number of people may be allergic to one or more components of the product; the labelling and the instructions for use list the components of the product, so the user has all the information needed in order to verify the ingredients and therefore the safe use in cases of allergies.
- Microbial contamination in case of poor storage and/or use of the product – in order to minimize this risk, the storage conditions of the product are clearly reported on the labelling and instructions for use.

Antidiarroico pediatric is normally well tolerated, however, if the user notices an adverse effect attributable to the product or its use, it is recommended to inform a doctor and/or pharmacist and the Manufacturer Aboca. In case of serious incident, the competent authority of the user's Country should be informed.

4.2. Warnings and precautions

Do not use in case of individual hypersensitivity or allergy to one or more components.

Consult physician if symptoms persist for more than 7 days.

4.3. Other relevant aspects of safety, including a summary of any field safety corrective action (FSCA including FSN) if applicable

No FSCA have been taken for Antidiarroico Pediatric in any country of the world for safety reasons.

5. SUMMARY OF CLINICAL EVALUATION AND POST-MARKET CLINICAL FOLLOW-UP (PMCF)

5.1. Summary of clinical data related to equivalent device, if applicable

Not applicable to Antidiarroico Pediatric.

5.2. Summary of clinical data from conducted investigations of the device before the CE-marking, if applicable

Not applicable.

5.3. Summary of clinical data from other sources

As part of the post-market surveillance activities, one pilot, randomized, controlled clinical trial and two surveys were conducted on Antidiarroico Pediatric.

A summary of the clinical trial is reported below.

Trial : ***"Clinical trial: Oral administration of tannins and flavonoids in children with acute diarrhea: a pilot, randomized, control-case study"*** [1]

The aim of this pilot study was to evaluate the efficacy and the compliance of Antidiarroico pediatric, a natural molecular complex of tannins (from Agrimony and Tormentil) and flavonoids (Chamomile), added-on to standard oral rehydration (SOR), in a pediatric population (range 3 months - 12 years old) affected by Acute gastroenteritis (AG).

Study outcomes

The primary outcome was to evaluate the efficacy of Antidiarroico pediatric, added to SOR as compared to SOR only in infants and children with AG.
The secondary outcome was to assess safety, tolerability and compliance of the study product for short-term treatment.

Endpoints of the study

The primary endpoint was the duration of diarrhoea, defined as "the number of stools after 24 h of treatment or the time needed to normalize number and consistency of stools (compared with the period before the

[1] Marina Russo Vincenzo Coppola, Eleonora Giannetti, Roberta Buonavolontà, Antonio Piscitelli and Annamaria Staiano. Oral administration of tannins and flavonoids in children with acute diarrhea: a pilot, randomized, control-case study. Italian Journal of Pediatrics, 2018; 44(64); 2-6.

onset of diarrhoea)". Secondary endpoints were the evaluation of vomiting, body weight, possible need of hospitalization, compliance to therapy.

Study design and Methods

The study included 60 children (mean age: 3.1 yrs., range 3 months - 12 years) with a diagnosis of AG, referred between April and July 2017 to the Department of Translational Medicine, section of Pediatric, University of Naples Federico II. Patients enrolled were children from 3 months to 12 years old, with a diagnosis of acute diarrhoea appeared less than 7 days before the admission, capability to oral rehydration, mild to moderate dehydration.
Patients with diarrhoea over 7 days, serious somatic pathology and severe dehydration were excluded.
The study was approved by the Institutional Review Board of the University of Naples "Federico II" with the protocol number 25/17. At admission, written informed consent was obtained from participants' parents and from all patients older than 10 years. At first visit, a medical history was collected by one of the authors and all patients underwent clinical evaluation, including body weight and body temperature.
Frequency of bowel movements, stool consistency measured through the Bristol Stool Form Scale (BSFS) and other associated gastrointestinal symptoms, including nausea, vomiting, abdominal pain and rectal bleeding, were accurately recorded. The BSFS is the most commonly used, standardized instrument to rate stool consistency in children. On admission, the degree of dehydration was clinically determined for each patient, based on WHO recommendations and data were recorded on a scale from 1 to 3 (1 for mild or < 5%; 2 for moderate or 5 to 10%; 3 for severe or 10% and more). All enrolled children were randomly divided into two groups: Group 1 was treated with Antidiarroico pediatric and standard oral rehydration (SOR) whereas Group 2 was treated with SOR only ad libitum for 7 days. SOR is a reduced osmolarity oral solution (50/60 mmol/L Na), which is the first line therapy recommended by ESPGHAN guideline for Acute Diarrhea. Antidiarroico pediatric, instead, was orally administrated at dose of 1 sack every 4 h, maximum 4 sacks/ day for 7 days.
Caregivers were instructed to administer the daily dose after mixing the contents of the sachet with a small amount of water. At home, all parents had to fulfil a daily diary to record number and consistency of stools, presence of fever, vomiting and children compliance with the therapy. During the final visit, scheduled after 7 days, the interim history was assessed, daily diaries were reviewed and discussed, and a physical evaluation was performed.

Summary of results

All patients completed the study.
The median number of stools per day at baseline was 5 in both groups (range: 3 to 8 in Group 1 and 2 to 10 in Group 2) ($p = 0.63$). As for stool consistency, at day 6, the percentage of patients reporting formed stools was significantly higher in the group treated with *Antidiarroico pediatric* (Group 1) as compared to the group treated with SOR only (Group 2) (76.9% vs 50%; $p = 0.028$).
The difference between the two groups in the number of stools after 24 h was not statistically significant ($p = 0.4$); however, the change of the number of stools, from baseline to 24 h of treatment, was significant ($p < 0.0001$) in the group treated with *Antidiarroico pediatric*.
After 24 h of treatment, it has been found that the most of children (23/30, 76%) in Group 1, by their own choice, interrupted the assumption of SOR and continued to take *Antidiarroico pediatric* only.
Stool consistency from baseline to 24 h improved similarly in both groups, as the percentage of patients with liquid stools decreased from 89.7% and 86.7% in Group 1 and Group 2, respectively, to 60% and 73.3% ($p = 0.34$).The presence of vomiting at baseline was 73.3% (22 children out of 30) for Group 1 and 43.3% (13 children out of 30) for the Group 2; at 24 h vomiting was present in 46.6% of the Group1 and 16% of the Group 2 with no statistically significant difference.

Bloody diarrhoea was found in only 10% and 6% of patients at baseline in Group 1 and Group 2, respectively; at the end of treatment, no patient presented blood in the stool in both groups. As for weight and fever, the authors didn't any statistically significant difference between the groups. No one was hospitalized.

Compliance and patient acceptance of treatment

Concerning compliance with therapy, similar proportions of patients in the two groups (8/30, 26% in Group 1 and 10/30, 30%, in Group 2) refused to take Antidiarroico pediatric and SOR, respectively (p = 0.77). Regarding the perception of the treatment efficacy, parents of children in Group 1 evaluated the
As for perception of improvement after 24 h, it has been found a tendency toward significance favouring *Antidiarroico pediatric* treatment (p = 0.07). No adverse events in both groups were reported during the study.

Conclusions

The clinical trial shows that Antidiarroico pediatric is an effective treatment in reducing the duration of acute diarrhoea and no major concerns on safety arose. In particular, after six days of treatment, 76.9% of children treated with Antidiarroico pediatric reported formed stools compared with 50% of patients treated with SOR alone (p=0.028). Also the compliance with administration of Antidiarroico pediatric was good.
Thus, it can be concluded that *Antidiarroico pediatric* may offer a safe and effective therapeutic approach to acute diarrhoea in infants and children.

Surveys

In addition to the clinical trial above reported, as part of the post-market surveillance activities, one survey was conducted through a validated electronic platform to obtain Real World clinical data on Antidiarroico pediatric.

Such RWD on-line platform[2] hosts validated digital questionnaires specifically developed for patients, physicians and pharmacists. It has been developed for Aboca by a Contract Research Organization (CRO) and designed to collect spontaneously delivered data via web framework page through a GxP validated software to assure the integrity and reliability of collected data.

Data refer to the period from September 2021 to October 2022; during that time, in total about 1142 questioners on Antidiarroico pediatric were collected from parents/care givers, pharmacists and physicians. Data collection is still ongoing at the present time and the data presented are meant to substantiate the clinical evidence of the Medical Devices as per EU Reg 2017/745 art. 83.

This survey aims to collect and process the information coming from patients, pharmacists and physicians, using or prescribing the product. Overall, with a high level of agreement across all questionnaires Antidiarroico pediatric received a very positive assessment in terms of effectiveness and satisfaction with its use. Also, an excellent level of safety and tolerability was reported by responders. Thus, an extremely positive benefit/risk ratio of the product was consistently indicated by parents or tutors of children/patients (352 responders), pharmacists (459 responders) and physicians (331 responders).

[2] Cioeta R, Cossu A, Giovagnoni E, Rigoni M and Muti P (2022), A new platform for post-marketing surveillance and real-world evidence data collection for substance-based medical devices. Front. Drug. Saf. Regul. 2:992359.

The survey was conducted on a large scale and aimed at evaluating the experience of use with Antidiarroico pediatric. As a matter of fact, about 98% of people who used or administered the product to children (tutors/care givers) were satisfied with the effectiveness of Antidiarroico pediatric.

Overall, parents/tutors mostly used the product to treat acute diarrhoea of various origins (about 70% of responders) and, a lower percentage of responders (about 15%), used it for treating functional diarrhoea.

In addition, the majority of parents/tutors, pharmacists and physicians noticed a rapid improvement of symptoms. Indeed, about 23% of responders noticed symptoms improvement within few hours from product intake. It is worth to note that most responders (about 60% of total answers parents/tutors) reported that symptoms improved within 12 hours from the product intake.

Another important aspect of this survey is the concordance among parents/tutors, pharmacists and physicians concerning the tolerability and safety of the product. In fact, tolerability was always in the "excellent" and "good" range in all categories. About 99% of pharmacists and physicians didn't observe any interactions between the product and other treatments. In addition, 96% of the patients rated the safety of the product at least good. All these data were also confirmed by the evaluations collected over the doctors and pharmacists.

In addition, no interactions with other concomitant treatments or Undesirable Side Effect have been recorded. Potential systematic misuses of the product and off-label use were not reported as well.

Also the Quality of life (QoL), for both child and parents/tutors after treatment reported by all groups of participants, was assessed through two general questions: one regarding the effect of treatment on mood, crying, eating, ability to play and sleep of the children and the other regarding the effect of the product on the parents/tutors who take care of young patients. Overall, a high percentage of all responders agreed reporting high scores of QoL improvement.

These data were consistent with those reported by the physicians and pharmacists who prescribed and advised the Antidiarroico pediatric. The data from this Survey were published[3].

In addition, another survey was conducted on Antidiarroico pediatric, aimed to collect data from healthcare professionals (HCPs) concerning the safety and effectiveness of the medical device.

The survey conducted on HCPs confirmed the high level of tolerability, efficacy and ease of use of Antidiarroico pediatric which was considered "good" or "excellent" by almost all the participants. The perceived effectiveness and tolerability of the product, was, again, very positive, with the degree of action of the medical device considered at least "good" or "excellent" for all the age groups (from 2 to 12 years).

One of the key parts of the post-marketing surveillance questionnaire was the collection of potential adverse effects: no relevant adverse reactions related to Antidiarroico pediatric were mentioned by the specialists questioned.

Thus, all surveys available confirm a favourable benefit/risk profile of the product.

Other clinical data

[3]Cioeta, Ret al. Actitan: A Natural Complex for Managing Diarrhea—Insights from Cross Sectional Survey Research Involving Patients, Pharmacists and Physicians. Gastrointest. Disord. 2024, 6, 753–764. https://doi.org/10.3390/gidisord6030051.

The safety data collected from the Vigilance system of Aboca can confirm that the Benefit-Risk determination is unchanged, taking into account the following findings:

- No new and unexpected risks, including off-label or misuse, were identified during the various post-market surveillance activities in any relevant Country;
- No evidence of relevant undesirable side-effects that affected the safety profile of the product were identified.

Since no serious related incidents were registered, no cases were reported to Competent Authorities because they did not match the criteria of reportability for Antidiarroico pediatric. Furthermore, no trend or safety signal have been identified.

Therefore, it can be concluded that the use of the Antidiarroico pediatric medical devices can be considered safe.

5.4. An overall summary of the clinical performance and safety

The safe and effective profile of the medical device was demonstrated clinically by the post-market activities conducted on the product consisting in one clinical trial and two surveys. Such profile is supported also by the Vigilance data, as well as by pre-clinical testing and assessments available on the product.

5.5. Ongoing or planned post-market clinical follow-up

Post market activities have been planned for Antidiarroico pediatric, legacy MDs, with the aim to gather information, monitor and follow-up on the clinical efficacy and safety of the product.

Among these, is included:

- a Post Marketing Clinical Evaluation(double-blind, placebo-controlled, parallel-group investigation) in order to collect clinical evidence on efficacy and safety of Antidiarroico pediatric in children aged 1-5 years;
- the continuously ongoing survey conducted through the electronic validated platform cited in section 5.3 the collection and analysis of Vigilance data through the manufacturer system;
- the collection and analysis of Vigilance data through the manufacturer system.

6. POSSIBLE DIAGNOSTIC OR THERAPEUTIC ALTERNATIVES

Diarrhoeal disorders[4] often represent a challenge for clinicians, particularly when the symptoms are long-standing. Indeed, a myriad of possible causative factors should be carefully considered until a diagnosis is established.
Making an accurate diagnosis is central as the patient may benefit of an effective management.
In children acute diarrhea mostly withdraws spontaneously, thus the treatment basis consists of replacement of lost water and electrolytes and adequate nutrition. Probiotics and symbiotics can be useful, while the application of antibiotics is justified only in certain cases.

Principles of management of chronic diarrhoea in children involve accurate and timely diagnosis and specific treatment of underlying cause. In patients presenting with dehydration, electrolyte abnormalities or oedema, fluid resuscitation and electrolyte correction should be initiated as necessary. Nutritional rehabilitation is the most important aspect of managing a child with chronic diarrhoea.

[4] Roberto Corinaldesi et al. Clinical approach to diarrhoea. Intern Emerg Med (2012) 7 (Suppl 3):S255–S262. DOI 10.1007/s11739-012-0827-4.

Antidiarroico pediatric is a therapeutic option for the non-pharmacological treatment of acute diarrhoea and relapses of chronic diarrhoea in children. This clinical benefit takes place thanks to a non-pharmacological mode of action of the whole product[5], which is able to normalize stool consistency, to reduce the stool frequency and to indirectly counteract the inflammation of the intestinal mucosa eventually present, while respecting the functionality of the intestine.

7. SUGGESTED PROFILE AND TRAINING FOR USERS

The device is intended for lay users.

8. REFERENCE TO ANY HARMONISED STANDARDS AND CS APPLIED

- EN ISO 14971:2019 “Medical devices - Application of risk management to medical devices”
- EN ISO 10993-9:2021 “Biological evaluation of medical devices - Part 9: Framework for identification and quantification of potential degradation products”
- EN ISO 10993-10:2023 “Biological evaluation of medical devices - Part 10: Tests for skin sensitization”
- EN ISO 10993-17:2023 “Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances”
- EN ISO 10993-18:2020 “Biological evaluation of medical devices - Part 18: Chemical characterization of medical device materials within a risk management process”
- EN ISO 10993-23:2021 “Biological evaluation of medical devices - Part 23: Tests for irritation”
- EN ISO 15223-1:2021 “Medical devices - Symbols to be used with medical device labels, labelling and information to be supplied - Part 1 - General Requirements”
- EN ISO 13485:2016 “Medical devices - Quality management systems - Requirements for regulatory purposes”

9. REVISION HISTORY

SSCP revision number	Date issued	Change description	Revision validated by the Notified Body
1	21/04/2023	First issue	
2	05/11/2024	Data updated	Yes. Validation language: English

[5] The concept of non-pharmacological mechanism of action in medical devices made of substances in practice: what pharmacology can do to promote the scientific implementation of the European medical device regulation Pharmadvances 2020 01s: 4-12 doi:10.36118/pharmadvances.01.2020.02s.

[Break page]

SUMMARY OF SAFETY AND CLINICAL PERFORMANCE

A summary of the safety and clinical performance of the device, intended for patients, is given below.

Document revision: 2

Date issued: 05/11/2024

This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device. The information presented below is intended for patients or lay persons. A more extensive summary of its safety and clinical performance prepared for healthcare professionals is found in the first part of this document.

The SSCP is not intended to give general advice on the treatment of a medical condition. Please contact your healthcare professional in case you have questions about your medical condition or about the use of the device in your situation. This SSCP is not intended to replace an Implant card or the Instructions For Use to provide information on the safe use of the device.

1. DEVICE IDENTIFICATION AND GENERAL INFORMATION

o Device trade name of Antidiarroico pediatric

LENODIAR PEDIATRIC, LENODIAR KINDER

o Manufacturer; name and address

Aboca S.p.A. Società Agricola - Loc. Aboca 20 – 52037 Sansepolcro (AR) – Italy

o Basic UDI-DI

8032472LENOby232

o Year when the device was first CE-marked

2017 (certification according to Directive 93/42/EEC)

2. Intended use of the device

o Intended purpose

Antidiarroico pediatric is indicated for the treatment of acute diarrhoea and relapses of chronic diarrhoea.

o Indications and intended patient groups

Antidiarroico pediatric is indicated for infants and children from 6 months to 12 years of age.

o Contraindications

The device shall not be used in case of individual hypersensitivity or allergy to one or more components of the product.

3. DEVICE DESCRIPTION

o Device description and material/substances in contact with patient tissues

Antidiarroico pediatric is a medical device available in granular sticks for children and infants starting from 6 months to 12 years of age.

Antidiarroico pediatric works by normalizing the consistency of the stools and by reducing the frequency of diarrheal discharge and the inflammation of the intestinal mucosa, while respecting the functionality of the intestine.

The composition of the device is described below:

One 2 g sachet contains: plant complex Actitan-F® 92 mg, based on Tannins (extractive fractions of Agrimony and Tormentilla - 57 mg) and Flavonoids (extract fraction of Chamomile 35 mg); Juice of Blueberry, Blackberry and Elderberry; Cane sugar; Natural flavor and natural Lemon aroma; Lemon essential oil; Arabic gum.

o Information about medicinal substances in the device, if any

Not applicable – the device does not contain medicinal substances.

o Description of how the device is achieving its intended mode of action

Antidiarroico pediatric works by normalizing the consistency of the stools and by reducing the frequency of diarrheal discharge and inflammation of the intestinal mucosa.

Antidiarroico pediatric acts with a physiological mechanism of action through the following actions:

- ASTRINGENT
- ANTIOXIDANT

Thanks to the synergy of its actions, Antidiarroico pediatric promotes the recovery of intestinal function and the balance of bacterial flora (microbiota).

o Description of accessories, if any

Not applicable – no accessories are intended to be used in combination with Antidiarroico pediatric

4. RISKS AND WARNINGS

Contact your healthcare professional if you believe that you are experiencing side effects related to the device or its use or if you are concerned about risks. This document is not intended to replace a consultation with your healthcare professional if needed.

o How potential risks have been controlled or managed

The manufacturer manages the risk analysis and risk control according to the relevant harmonised standards.

o Remaining risks and undesirable effects

The main residual risks identified for Antidiarroico pediatric are the following:

- Subjective allergic reaction of the user – although the product is non-sensitising, it is possible that a small number of people may be allergic to one or more components of the product; the labelling and the instructions for use list the components of the product, so the user has all the information needed in order to verify the ingredients and therefore the safe use in cases of allergies.

- Microbial contamination in case of poor storage and/or use of the product – in order to minimize this risk, the storage conditions of the product are clearly reported on the labelling and instructions for use.

Antidiarroico pediatric is normally well tolerated, however, if the user notices an adverse effect attributable to the product or its use, it is recommended to inform a doctor and/or pharmacist and the Manufacturer Aboca. In case of serious incident, the competent authority of the user's Country should be informed.

o Warnings and precautions

Do not use if there is hypersensitivity or individual allergy to one or more components.

Consult physician if symptoms persist for more than 7 days.

o Summary of any field safety corrective action, (FSCA including FSN) if applicable

No FSCA have been taken for Antidiarroico pediatric in any country of the world for safety reasons.

5. SUMMARY OF CLINICAL EVALUATION AND POST-MARKET CLINICAL FOLLOW-UP

o Background of the device

Antidiarroico pediatric is a medical device indicated for the treatment of acute diarrhoea and relapses of chronic diarrhoea and it is able to reduce the frequency of diarrheal discharges and to respect the functionality of the intestine.

The product is suitable for infants and children from 6 months to 12 years of age.

The product works by normalizing the consistency of the stools and by reducing the frequency of diarrheal discharge and the inflammation of the intestinal mucosa.

Antidiarroico pediatric acts with a physiological mechanism of action through the following actions:

ASTRINGENT: aspecific interaction with intestinal, mucus and mucosal proteins, increasing fecal consistency and forming a mucoadhesive film which favours:

• the protection of the mucosa from irritants, inflammatory mediators and microorganisms

• the restoration of the integrity of the mucosa, when damaged.

ANTIOXIDANT: counteracts the action of free radicals, protecting the mucosa from oxidative damage.

Thanks to the synergy of its actions, Antidiarroico pediatric promotes the rapid recovery of intestinal function and the balance of bacterial flora (microbiota).

Antidiarroico pediatric is 100% natural and biodegradable and contains no artificial substances.

- **The clinical evidence of Antidiarroico pediatric on safety and efficacy**

The efficacy and safety profile of Antidiarroico pediatric is demonstrated by clinical data coming from:

- one clinical trial
- surveys in a real-world setting addressed to both healthcare professionals (physicians and pharmacists) and patients
- safety data collected from the manufacturer's Vigilance system

A pilot, randomized, case-controlled trial was conducted to investigate the efficacy and safety of Antidiarroico pediatric associated, according to WHO recommendations, with standard oral rehydration (SOR) versus only SOR, in 60 children aged 3 months - 12 years old affected by Acute gastroenteritis (AG). Both groups received treatment for seven days, respectively.

The study shows that Antidiarroico pediatric is an effective treatment in reducing the duration of acute diarrhoea and no major concerns on safety arose. In particular, after six days of treatment, 76.9% of children

treated with Antidiarroico pediatric reported formed stools compared with 50% of patients treated with SOR alone (p=0.028). Also the compliance with administration of Antidiarroico pediatric was good. In addition, patients treated with Antidiarroico pediatric stopped for their own choice, SOR after the first 24 hours and continued only with Antidiarroico pediatric.

In the whole trial any adverse event in children were observed in both groups, and this confirms the safe profile of the product in the pediatric population.

In conclusions, Antidiarroico pediatric in association with SOR, may offer a safe and cost-effective approach to acute gastroenteritis in infants and children.

In addition to a clinical trial, as part of the post-market surveillance activities, two surveys have been performed. The first one was conducted on the product in a Real-World setting and gathered through a validated electronic platform[1].

Such RWD on-line platform hosts validated digital questionnaires specifically developed for patients, physicians and pharmacists, and it has been designed to collect spontaneously delivered data via web framework page through a GxP validated software to assure the integrity and reliability of data collected, developed for Aboca by a Contract Research Organization (CRO).

The data gathered refer to the period from September 2021 to October 2022; during that time, in total about 1142 questioners have been collected from patients or care givers, pharmacists and physicians for Antidiarroico pediatric. However, the data collection is still ongoing at the present time and the data presented are meant to substantiate the clinical evidence of the Medical Devices involved as per EU Reg 2017/745 art. 83.

The high level of agreement across all questionnaires supported the evidence that the MD is associated with positive assessment of its effectiveness, high level of performance satisfaction and excellent level of safety and tolerability with an exceptionally positive benefit/risk ratio as concordantly described by parents/tutors who administered the product to children (352 responders), pharmacists (459 responders) and physicians (331 responders).

The survey was conducted on a large scale and aimed at evaluating the experience of use gained with Antidiarroico pediatric: 98% of parents/tutors who used or administered the product to children were satisfied with the effectiveness of Antidiarroico pediatric; in fact, a benefit was found within a few hours of its use and in the majority of cases, within 12 hours.

Furthermore, Antidiarroico pediatric was found to be safe and tolerable by all users and finally, 97% of people reported an overall improvement in their quality of life.

These data were also consistent with the ones from about 800 doctors and pharmacists. The data from this Survey were published[2].

In addition, another survey was conducted on Antidiarroico pediatric, aimed to collect data from healthcare professionals (HCPs) concerning the safety and effectiveness of the medical device. This survey was

[1] Cioeta R, Cossu A, Giovagnoni E, Rigoni M and Muti P (2022), A new platform for post-marketing surveillance and real-world evidence data collection for substance-based medical devices. Front. Drug. Saf. Regul. 2:992359.

[2]Cioeta, Ret al. Actitan: A Natural Complex for Managing Diarrhea—Insights from Cross Sectional Survey Research Involving Patients, Pharmacists and Physicians. Gastrointest. Disord. 2024, 6, 753–764. https://doi.org/10.3390/gidisord6030051.

conducted on HCPs and confirmed the high level of tolerability, efficacy and ease of use of Antidiarroico pediatric which was considered "good" or "excellent" by almost all the participants. The perceived effectiveness and tolerability of the product, was, again, very positive, with the degree of action of the medical device considered at least "good" or "excellent" for all the age groups analysed (from 2 to 12 years).

Thus, all surveys available confirm that the risk / benefit profile of the products is favourable.

The safety profile of the product in all its intended users is further confirmed by the Vigilance Data recorded for Antidiarroico pediatric through the Vigilance system, where no serious reportable incidents or safety issues related to the use of the product were identified.

Several activities have been planned for Antidiarroico pediatric with the aim to gather information, monitor and follow-up on the clinical efficacy and safety of the product.

Furthermore, the safety profile of the product will be continuously monitored through the collection and analysis of Vigilance data.

6. POSSIBLE DIAGNOSTIC OR THERAPEUTIC ALTERNATIVES

When considering alternative treatments, it is recommended to contact your healthcare professional who can take into account your individual situation.

o General description of therapeutic alternatives

Diarrhoeal disorders[3] often represent a challenge for clinicians, particularly when the symptoms are long-standing. Indeed, a myriad of possible causative factors should be carefully considered until a diagnosis is established.
Making an accurate diagnosis is central as the patient may benefit of an effective management.
In children acute diarrhea mostly withdraws spontaneously, thus the treatment basis consists of replacement of lost water and electrolytes and adequate nutrition. Probiotics and symbiotics can be useful, while the application of antibiotics is justified only in certain cases.

Principles of management of chronic diarrhoea in children involve accurate and timely diagnosis and specific treatment of underlying cause. In patients presenting with dehydration, electrolyte abnormalities or oedema, fluid resuscitation and electrolyte correction should be initiated as necessary. Nutritional rehabilitation is the most important aspect of managing a child with chronic diarrhoea.

Antidiarroico pediatric is a therapeutic option for the non-pharmacological treatment of acute diarrhoea and relapses of chronic diarrhoea. This clinical benefit takes place thanks to a non-pharmacological mode of action of the whole product[4], which is able to normalize stool consistency, to reduce the stool frequency and to indirectly counteract the inflammation of the intestinal mucosa eventually present, while respecting the functionality of the intestine.

7. SUGGESTED TRAINING FOR USERS

The device is intended for lay users. No training is required.

[3] Roberto Corinaldesi et al. Clinical approach to diarrhoea. Intern Emerg Med (2012) 7 (Suppl 3):S255–S262. DOI 10.1007/s11739-012-0827-4.
[4] The concept of non-pharmacological mechanism of action in medical devices made of substances in practice: what pharmacology can do to promote the scientific implementation of the European medical device regulation Pharmadvances 2020 01s: 4-12 doi:10.36118/pharmadvances.01.2020.02s.