Double-blind, randomized, parallel-group, monocentric, placebo-blind study of the effect of an extract of *Epilobium angustifolium* L. with high oenothein B content on benign prostatic hypertrophy (BPH)

INFORMATION SHEET
and
INFORMED CONSENT

Proposal for the use of food supplement based on *E. angustifolium* L. extract with high oenothein B content in the treatment of mild/moderate benign prostatic hyperplasia (BPH).

Dear Sir
the Ethics Committee (EC) gave a positive opinion to conduct a scientific study on the effects of a food supplements based on *E. angustifolium* extract with high oenothein B content, an ingredient legally approved in food supplements by Italian Legislation, used to have beneficial effects in the treatment of mild/moderate BPH. In order to carry out this study, we need the cooperation of people like you, that have the right characteristics for the clinical trial that we will explain to you. So that you can give a possible consent to participate in the study, it is important that you understand the purpose of this study and what a possible participation (in terms of benefits, risks and inconveniences, due to the necessity to follow accurately the procedures, specified inside the protocol) will lead to you.
We ask you to read this document and, if you wish, you can take all the time that you need to discuss about it with your family and with your own doctor. We invite you to ask for any explanation if the information supplied to you are not clear or if you need any kind of clarifications.

REASONS AND OBJECTIVES THAT THE STUDY AIMS TO REACH

This study aims to define the effects of a food supplement containing *E. angustifolium* extract in the treatment of mild/moderate BPH in the absence of other food supplements for the urinary tract at the time of recruitment and in the previous two weeks.
In particular, the monitoring of the effects after the intake of the food supplement based on *E. angustifolium* in the treatment of mild/moderate BPH, will be conducted through the determination of:
post-void residual (PVR) and prostate volume (and weight) obtained by prostate ultrasound (primary outcome); PSA, neutrofile/lymphocyte ratio (N/L) derived from blood tests; urinations number during the night before the clinical visit, and IPSS (secondary outcome) .

You presents:

- Prostate volume ≥ 25cc and ≤ 70cc;
- PVR between 30 mL and 200 mL;
- PSA ≤ 4ng/ml

In an effort to get a significant improvement in symptoms, and the improvement of urinary flow from mild/moderate BPH, we propose you a treatment that uses a food supplement containing *E. angustifolium*.

PROPOSED TREATMENT

In this clinical trial, we propose the use of a **food supplement containing** *E. angustifolium* as an alternative to drugs or other food supplements**.** It is important that you know that the available data on the efficiency of food supplement used in this study, for the reduction of symptoms associated with BPH, are still limited.
The food supplement proposed in this study, will be given to the different subjects with the same dose.
We hope that the food supplement containing *E. angustifolium* would give you benefit also in your case, although we are aware that there is always a sort of variability in the individual responses. The scientific data available are too limited to be able to say that the treatment is certainly effective, or to assure you all the effects.

The food supplement containing *E. angustifolium* **or placebo will be administered according to the following regimen:**

- **one hard gastro-resistant capsule per day containing 0.5 g of Epilobium corresponding to 2 g of aerial parts of *E. angustifolium*, or placebo for at least 5 months.**

The Ethics Committee of the ASL of Benevento has previously assessed and authorized what we're proposing you today.

RISKS AND SIDE EFFECTS

The subjects will be monitored diligently and, in case of side effects during the study, the subject will suspend the consumption of the food supplements and the same will ends the study. In the clinical trial hepatic and renal toxicity tests have been studied. In particular, blood tests to evaluate creatinine (CRE), bilirubin (BR direct/indirect/total), prothrombin, aspartate transaminase (AST), alanine transaminase (ALT), and cholinesterase (CHE) were performed at t0, t1, t2, t3.
For the evaluation of tolerance and safety of the intervention (*E. angustifolium* food supplement capsules), adverse events were monitored throughout the intervention period through spontaneous reporting of adverse events (AEs) by the participants to the relative physicians. At the end of the intervention period all subject data were evaluated by the principal investigator to determine the presence or absence of AEs

POSSIBLE BENEFITS TO PARTICIPATE TO THE CLINICAL TRIAL

It is supposed the improvement in symptoms and the urinary flow from mild/moderate BPH in the following 5 months of treatment.

FREE CHOICE TO PARTICIPATE TO THE CLINICAL TRIAL

The decision to participate to the project or is completely up to you. If you decide to participate, we will provide you the informed consent that you have to sign.
The possible participation will be covered by an insurance policy (n ._____ and valid until _____).

IF YOU DECIDES TO NOT TAKE PART OR TO INTERRUPT THE STUDY

If you choose to not take part or to interrupt the study, you can do it freely warning the investigator, without giving any justification and without changing your health care in this centre.
Similarly, always in yours interest, the test may be interrupted, if the principal doctor believe that the treatment is not good for you or if there are some undesirable and / or unpredictable effects.
In this case you will be immediately informed of your state of health and possible treatments available to restore it.

INVESTIGATIONS REQUIRED FOR PARTICIPATION TO THE STUDY

If you agree to participate to this study, you will do a first visit to verify if you can be part of this study. During this visit it will be verified post-void residual (PVR) and prostate volume (and weight) obtained by prostate ultrasound; PSA, neutrofile/lymphocyte ratio (N/L) derived from blood tests; urinations number during the night before the clinical visit, and IPSS score were registered.

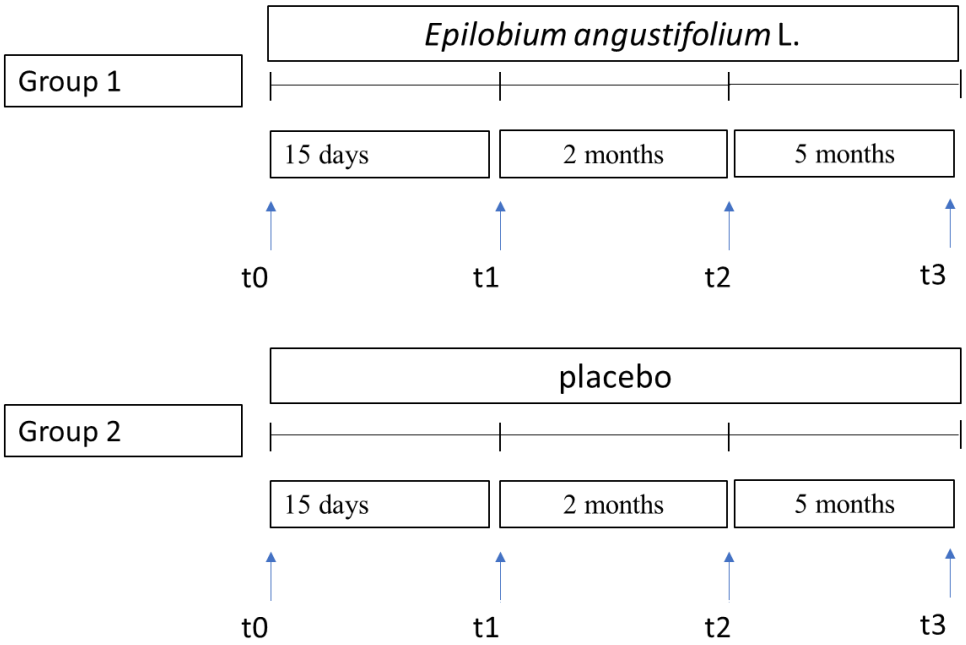

Figure 1. Type of study adopted

EXPENDITURE RELATIVE TO THE STUDY.

From participation to this study there aren't any for you and the food supplements will be free.

CONTACT PERSONS

If you have any problems or questions, the medical investigator is at your disposal and he can be contacted as follows:
Name of the Medical Investigator_____

Phone _____

This document about the clinical trial was prepared in accordance with standards of Good Clinical Practice of the European Union and the current revision of the Declaration of Helsinki, and was approved by the EC ASL Benevento, which you can contact to report any kind of event that you see.
The EC's telephone number is: +39 (0)824308419/421
EC Headquarters Via Oderisio, n1, 82100, Benevento, Italy).

We left you all the time that you need to evaluate all the information and to ask any kind of explanations.
And you will receive a copy of the information sheet and informed consent signed by the doctor.

DECLARATION OF CONSENT AND SIGNATURE

I, the undersigned (full name) _____

_____ Age Sex M birth date __ / __ / __

Address: Street / _____
Square

CAP _____ City _____

tel _____

I certify that:

- participate voluntarily in the study: " **Double-blind, randomized, parallel-group, monocentric, placebo-blind study of the effect of an extract of Epilobium angustifolium L. with high oenothein B content on benign prostatic hypertrophy (BPH)** "with the aim to define the effects of a food supplement containing *E. angustifolium* in the treatment of mild/moderate BPH in the absence of with other food supplements for the urinary tract at the time of recruitment and in the previous two weeks.

- I received from the investigator Doctor all the information in a clear and comprehensive way on the purposes and procedures of the trial;
- I have read and understood the information sheet that was handed to me early enough and that confirms what they have been told me verbally;
- I had the opportunity to ask clarification and satisfactory answers, as well as to have had the opportunity to discuss the details of the study with a trusted person;
- being inform to the results that I gain and the risks or reasonably expected disruption, and to have had enough time to decide;
- be aware:
  - that be part of this study is a voluntary decision and I can left the study of my own free will without giving reasons, having received the assurance that leave the clinical study will not have any effects on my health care in future;
  - that my clinical data could be examined or used for scientific publications, but will remain strictly confidential in accordance with the local regulations and the subsequent amendments and additions;
  - that the Ethics Committee ASL Benevento (of which i have the phone number) approved the experimental protocol of the study;

  - I'll be made aware, during the trial, about any new data that may compromise the security of the food supplement and the method of treatment;
  - Aware of my rights to have free access to the documentation concerning to the trial (insurance, clinical-scientific, drug-therapy) and to the assessment made by the Ethics Committee, who I could contact if desire;
- which it was signed an Insurance Policy in favour of the subjects being part of the study for any damages with the society insurer _____with a maxime compensation;
- having to sign two identical modules of this informed consent: the original one will be preserved by the investigator (and stored for at least 15 years) and the second one will be delivered to me;
- I'll have to contact for any type of problems or for additional information to:
- Dr./prof. _____
  Address_____
  Phone _____
- that in my interest the investigator will decide my exclusion from the study.
- I express my consent to the processing of my personal data for statistical purposes in accordance with Regulation (EU) 2016/679.

Therefore I freely agree to be part in this study.
The signature on this document will not have any effect on my legal rights.

_____ _____
Signature of the person who is included into the study Date

I declare that I have explained in a complete and exhaustive way the aspects of this treatment to the patient and / or to the person who's authorized to give consent to the patient's name.

_____ _____ _____
Signature of Medical Director Name and Surname Date