ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cuprymina 925 MBq/mL radiopharmaceutical precursor, solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL of solution contains 925 MBq of copper (^{64}Cu) chloride at calibration time (01h00 a.m. Central European Time [CET]), corresponding to at least 0.25 micrograms of Copper-64. The calibration time is set between the end of the synthesis time and the expiry time.

Each vial contains an activity ranging from 925 MBq to 2,770 MBq (at calibration time) which corresponds to an amount of 0.25 to 0.75 micrograms of Copper-64. The volume varies from 1 to 3 mL.

The minimal specific activity is 3,700 MBq Copper-64/micrograms of Copper at the expiry date and time.
Copper-64 has a half-life of 12.7 hours.
Copper-64 decays by an emission of β^+ (17.6 %) with a maximum energy of 0.66 MeV, an emission of β^- (38.5 %) with a maximum energy of 0.58 MeV and electronic capture (43.9 %).
Copper-64 decays in stable Nickel ^{64}Ni (61 %) by an emission of β^+ (18 %) or by an electronic capture (43 %). Copper-64 decays also in stable Zinc (^{64}Zn) by emission of β^- (39 %).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Radiopharmaceutical precursor, solution.
Clear, colourless solution, free of particulate matter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cuprymina is a radiopharmaceutical precursor. It is not intended for direct use in patients. This medicinal product must be used only for the radiolabelling of carrier molecules, which have been specifically developed and authorised for radiolabelling with this radionuclide.

4.2 Posology and method of administration

Cuprymina is only to be used by specialists experienced with *in vitro* radiolabelling

Posology

The quantity of Cuprymina required for radiolabelling and the quantity of Copper-64-labelled medicinal product that is subsequently administered will depend on the medicinal product radiolabelled and its intended use.
Refer to the Summary of Product Characteristics/package leaflet of the particular medicinal product to be radiolabelled.

Paediatric population

Copper-64-labelled medicinal products should not be used in children and adolescents up to 18 years. For more information concerning paediatric use of Copper-64-labelled medicinal products refer to the Summary of Product Characteristics/package leaflet of the radiolabelled medicinal product.

Method of administration

Cuprymina is intended for *in vitro* radiolabelling of medicinal products, which are subsequently administered by the approved route.
Cuprymina should not be administered directly to the patient.
For instruction on preparation of the medicinal product, see section 12.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Established or suspected pregnancy or when pregnancy has not been excluded (see section 4.6).

For information on contraindications to particular Copper-64-labelled medicinal products prepared by radiolabelling with Cuprymina refer to the Summary of Product Characteristics/package leaflet of each particular medicinal product to be radiolabelled.

4.4 Special warnings and precautions for use

Individual benefit/risk justification

Cuprymina is not to be administered directly to the patient but must be used for the radiolabelling of carrier molecules, such as monoclonal antibodies, peptides or other substrates.

General warnings

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.

Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

For information concerning special warnings and special precautions for use of Copper-64-labelled medicinal products refer to the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled. It must be considered that the radiolabelled medicinal product emits high intensity Auger electrons.

Regarding the dose for a person in close contact with the patient, this is entirely due to the gamma rays (Cuprymina emits 2 gamma rays at 511.0 Kev and 1,345.77 Kev), because β+ and β- emissions have no role due to their very short range.
The Copper-64 gamma dose constant is 3.6×10^{-5} mSv x MBq^{-1} x h at a distance of 1 meter. Assuming the worst case that the whole maximum activity (2,770 MBq) is injected to the patient and Copper-64 is labelled to a molecule with infinite biological half-life (no disposal by the patient) the person is continuously exposed at a distance of 2 meters. With these assumptions the estimated dose for a person in close contact with the patient is 0.46 mSv, which is less than one half of the limit of not exposed people (1 mSv/year).
Special precautions for relatives, carers and hospital staff are provided in section 6.6.

Disappearance of radioactivity

Considering that each MBq of Copper-64 causes a dose rate of 9 nSv/h (at a distance of 2 meters) and that the maximum injected activity is of 2,770 MBq, the initial dose rate is 24,930 nSv/h.
Assuming that the environmental background value is of 150 nSv/h, and requiring that the dose rate due to Copper-64 is lower than the environmental background the condition of negligible radioactivity in the patient is reached, in practice, 4 days after injection (dose rate 132 nSv/h) as shown in table 1.

Table 1 – Condition of negligible radioactivity in the patients

Days after injection (2,770 MBq)	0	1	2	3	4	5
Dose rate (nSv/h)	24,930	6,727	1,815	490	132	37

4.5 Interactions with other medicinal products and other forms of interaction

No interactions studies of Copper-64 chloride with other medicinal products have been performed.
The possible use of chelating therapies could interfere with the use of Copper-64-labelled medicinal products.
For information concerning interactions associated with the use of Copper-64-labelled medicinal products refer to the Summary of Product Characteristics/package leaflet of the radiolabelled medicinal product.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.
Before the use of Copper-64-labelled medicinal products, pregnancy should be excluded using an adequate/validated test.

Pregnancy

The use of Copper-64-labelled medicinal products is contraindicated during established or suspected pregnancy or when pregnancy has not been excluded (see section 4.3).

Breast-feeding

Before administering radiopharmaceuticals to a mother who is breast-feeding, consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breast-feeding, and to the choice of the most appropriate radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, a breast-feeding mother should be advised to stop breast-feeding.
The duration of stopping will depend on the particular radiolabelled medicinal product.
Further information concerning the use of Copper-64-labelled medicinal products in pregnancy and breast-feeding is specified in the Summary of Product Characteristics of the medicinal product to be radiolabelled.

Fertility

According to literature reports, it may be considered that both spermatogenetic and genetic damage in male test is are unlikely at the dose of 1,000 MBq.
Further information concerning the effect on fertility of the use of Copper-64-labelled medicinal products is specified in the Summary of Product Characteristics of the medicinal product to be radiolabelled.

4.7 Effects on ability to drive and use machines

Effects on ability to drive and to use machines following treatment by Copper-64-labelled medicinal products is specified in the Summary of Product Characteristics/package leaflet of the particular medicinal product to be radiolabelled.

4.8 Undesirable effects

Adverse reactions following the intravenous administration of Copper-64-labelled medicinal products prepared by radiolabelling with Cuprymina, will be dependent on the specific medicinal product being used. Such information is supplied in the Summary of Product Characteristics/package leaflet of the medicinal product to be radiolabelled.
For each patient, exposure to ionising radiation must be justifiable on the basis of likely clinical benefit. The activity administered must be such that the resulting radiation dose is as low as reasonably achievable bearing in mind the need to obtain the intended result.

The radiation dose to the patient resulting from exposure after administration may result in higher incidence of cancer and mutations. In all cases, it is necessary to ensure that the risks of the radiation are less than from the disease itself.
Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

The presence of free copper (^{64}Cu) chloride in the body after an inadvertent administration of Cuprymina will lead to increased hepatotoxicity.
Therefore, in case of an inadvertent administration of Cuprymina, the radiotoxicity for the patient must be reduced by immediate (i. e. within 1 hour) intravenous administration of preparations containing chelators like Ca-DTPA or Ca-EDTA in order to increase the elimination of the radionuclide from the body.

The following preparations must be available in medical institutions, which use Cuprymina for labelling of carrier molecules:
- Ca-DTPA (Trisodium calcium diethylenetriaminepentaacetate) or
- Ca-EDTA (Calcium disodium ethylenediaminetetraacetate)

These chelating agents help elimination of copper radiotoxicity by an exchange between the calcium ion and the copper due to their capacity of forming water soluble complexes with the chelating ligands (DTPA, EDTA).

These complexes are rapidly eliminated by the kidneys.
1 g of the chelating agents should be administered by slow intravenous injection over 3 – 4 minutes or by infusion (1 g in 100-250 mL of glucose, or sodium chloride 9 mg/mL (0.9 %) solution for injection).
The chelating efficacy is greatest immediately or within one hour of exposure when the radionuclide is circulating in or available to tissue fluids and plasma. However, a post-exposure interval > 1 hour does not preclude the administration and effective action of chelator, even if with reduced efficiency.
Intravenous administration should not be protracted over more than 2 hours.

In any case the blood parameters of the patient have to be monitored and the appropriate actions immediately taken if there is evidence of damages.

The toxicity of the free Copper-64 due to *in vivo* release from the labelled biomolecule in the body during therapy could be reduced by post-administration of chelating agents.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: various diagnostic radiopharmaceuticals, ATC code: Not yet assigned

The pharmacodynamic properties of Copper-64-labelled medicinal products prepared by radiolabelling with Cuprymina, prior to administration, will be dependent on the nature of the medicinal product to be radiolabelled. Refer to the Summary of Product Characteristics/package leaflet of the particular medicinal product to be radiolabelled.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of the studies with Cuprymina in all subsets of the paediatric population on grounds of lack of significant therapeutic benefit over existing treatments. This waiver does however not extend to any diagnostic or therapeutic uses of the medicinal product when linked to a carrier molecule.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of Copper-64-labelled medicinal products prepared by radiolabelling with Cuprymina, prior to administration, will be dependent on the nature of the medicinal product to be radiolabelled.
Pharmacokinetics of Cuprymina was investigated in mice. Following intravenous administration, at the beginning most organs contained an amount of radioactivity which represented their content of Copper-64-laden blood. Liver, kidney and the intestinal tract reached their maximal content of Copper-64 within the first few hours, and then radioactivity steadily diminished. Part of the decrease can be attributed to excretion of Copper-64 into the bile, urine and faeces.
Blood radioactivity decreased from 60.3 % to 3.4 % after 1 hour, and then it decreased of 1 % after 6 hours, and increased to 5.6 % and 4.9 % after 12-24 hours.
Copper chloride ($^{64}CuCl_2$) is distributed mainly in the liver and kidney and the pattern of radioactivity in the blood parallels the pattern of radioactivity in the liver. Almost the entire $^{64}CuCl_2$ rapidly leaves the blood and enters the liver and kidney.
Maximum liver uptake was 4 hours after injection with 57.7 %. Then copper re-emerges in plasma and is distributed to other organs.

Pharmacokinetic data on Cuprymina relate to free copper

When the precursor is bound to a carrier molecule the content of radioactive free copper is supposed to be less than the stated amounts depending on the carrier used. Relevant data is included in the Summary of Product Characteristics of the labelled medicinal products.

5.3 Preclinical safety data

The toxicological properties of Copper-64-labelled medicinal products prepared by radiolabelling with Cuprymina prior to administration will be dependent on the nature of the medicinal product to be radiolabelled.
No animal toxicity studies were conducted with Cuprymina.
Toxicity of copper compounds has been extensively investigated both in human and in animals. Liver, gastrointestinal tract and kidney are the target organs for copper toxicity after single and repeated doses administration. Many international bodies assessed copper genotoxicity and carcinogenicity concluding that there is no conclusive evidence that copper may be mutagenic or carcinogenic The Scientific Committee on Food of the European Commission (2003) recommend a Dietary Allowances of 0.9 mg copper/day in adult males and females and established a Tolerable Upper Uptake level of 5 mg/day, allowing a huge safety margin in comparison to copper amount administered by Cuprymina.

Non-clinical data reveal no special hazard for humans based on available published data.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid (0.1 N)
Water for injections

6.2 Incompatibilities

Radiolabelling of carrier molecules, such as peptides, monoclonal antibodies, or other substrates, with Copper (^{64}Cu) chloride is very sensitive to the presence of trace metal impurities.
It is important that all glassware, syringe needles etc, used for the preparation of the radiolabelled compound are thoroughly cleaned to ensure freedom from such trace metal impurities. Only syringe needles (for example, non-metallic) with proven resistance to dilute acid should be used to minimise trace metal impurity levels.

6.3 Shelf life

48 hours from date and time of End of Synthesis (EOS).

6.4 Special precautions for storage

Store in the original package that provides protection from radiation.
Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

6.5 Nature and contents of container

The radiopharmaceutical precursor solution is packaged in a colourless, type I glass 10 mL vial, closed with bromobutyl rubber stopper and aluminium overseal.
The volume of one vial ranges from 1 to 3 mL solution (corresponding to 925 to 2,770 MBq at calibration time).
The vials are packed into a tungsten or lead container for protective shielding.
Each pack contains 1 vial in a tungsten or lead container.

6.6 Special precautions for disposal and other handling

Cuprymina is not intended for direct use in patients.

Cuprymina is a sterile solution.

General warning
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.
Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

For instruction on preparation of the medicinal product, see section 12.
If at any time in the preparation of this medicinal product the integrity of this container is compromised it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory. The surface dose

rates and the accumulated dose depend on many factors. Measurements on the location and during work are critical and should be practiced for more precise and instructive determination of overall radiation dose to the staff. Healthcare personnel are advised to limit the time of close contact with patients injected with Copper-64-radiopharmaceuticals. The use of television monitor systems to monitor the patients is recommended. Given the long half-life of Copper-64 it is specially recommended to avoid internal contamination. For this reason it is mandatory to use protective high quality (latex/nitrile) gloves in any direct contact with the radiopharmaceutical (vial/syringe) and with the patient. For minimising radiation exposure with repeated exposition there is no recommendation except the strict observance of the above ones.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spill of urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Any unused medicinal product or waste material must be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

A.C.O.M. -ADVANCED CENTER ONCOLOGY MACERATA -S.R.L.
Località Cavallino 39 A/B
62010 Montecosaro (MC)
Italy
Tel.: 0039.0733.229739
Fax: 0039.0733.560352
E-mail: amministrazione@acompet.it

8. MARKETING AUTHORISATION NUMBER

EU/1/12/784/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 august 2012
Date of latest renewal: 19 july 2017

10. DATE OF REVISION OF THE TEXT

11. DOSIMETRY

The radiation dose received by the various organs following intravenous administration of a Copper-64-labelled medicinal product is dependent on the specific molecule being radiolabelled.
Information on radiation dosimetry of each different medicinal product following administration of the radiolabelled preparation is available in the Summary of Product Characteristics/package leaflet of the particular medicinal product to be radiolabelled.
The dosimetry table below is presented in order to evaluate the contribution of non-conjugated Copper-64 to the radiation dose following the administration of Copper-64-labelled medicinal product or resulting from an accidental intravenous injection of Cuprymina.
The dosimetry estimates were based on a mouse distribution study and the calculations were effected using OLINDA (Organ Level INternal Dose Assessment Code) (see Table 2). Time points for

measurements were 2 minutes, 30 minutes, 1 hour, 4 hours, 6 hours, 12 hours, 24 hours, 2 days, 4 days, 6 days.
Table 2: Absorbed dose per unit activity administered

absorbed dose per unit activity administered (mGy/MBq)							
organ	**adult male (70 kg)**	**adult female (60 kg)**	**15 years**	**10 years**	**5 years**	**1 years**	**newborn**
adrenals	0.00	0.00	0.00	0.00	0.00	0.00	0.00
brain	0.00	0.00	0.00	0.00	0.00	0.00	0.00
breasts	0.000596	0.000730	0.000732	0.00133	0.00204	0.00384	0.00776
gallbladder wall	0.00192	0.00230	0.00219	0.00278	0.00453	0.00917	0.0158
LLI wall	0.0149	0.0160	0.0195	0.0340	0.0569	0.112	0.291
small Intestine	0.00	0.00	0.00	0.00	0.00	0.00	0.00
stomach Wall	0.00	0.00	0.00	0.00	0.00	0.00	0.00
ULI wall	0.00	0.00	0.00	0.00	0.00	0.00	0.00
heart wall	0.00	0.00	0.00	0.00	0.00	0.00	0.00
kidneys	0.00885	0.00969	0.0107	0.0151	0.0224	0.0401	0.106
liver	0.0211	0.0282	0.0283	0.0436	0.0649	0.126	0.294
lungs	0.00178	0.00233	0.00245	0.00351	0.00526	0.00999	0.0240
muscle	0.00	0.00	0.00	0.00	0.00	0.00	0.00
ovaries	0.00	0.00314	0.00	0.00	0.00	0.00	0.00
pancreas	0.00267	0.00310	0.00365	0.00716	0.00955	0.0199	0.0637
red marrow	0.00581	0.00565	0.00670	0.0118	0.0242	0.0586	0.198
osteogenic cells	0.00202	0.00269	0.00263	0.00426	0.00718	0.0172	0.0549
skin	0.00	0.00	0.00	0.00	0.00	0.00	0.00
spleen	0.00	0.00	0.00	0.00	0.00	0.00	0.00
testes	0.0463	0.00	0.114	0.907	1.05	1.41	2.02
thymus	0.00	0.00	0.00	0.00	0.00	0.00	0.00
thyroid	0.000129	0.000156	0.000189	0.000292	0.000593	0.00113	0.00178
urinary bladder wall	0.00	0.00	0.00	0.00	0.00	0.00	0.00
uterus	0.00	0.00	0.00	0.00	0.00	0.00	0.00
effective dose (Sv/1 GBq administered)							
	adult male	**adult female**	**15 years**	**10 years**	**5 years**	**1 years**	**newborn**
	0.0962	0.0712	0.168	0.854	1.05	1.56	2.73

For this medicinal product, the effective dose resulting from an intravenously injected activity of 925 MBq is 65.86 mSv for a 60-kg female adult and 88.99 mSv for a 70-kg male adult.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Before use, packaging and radioactivity must be checked. Activity may be measured using an ionisation chamber. Copper-64 is a beta emitter. Activity measurements using an ionisation chamber are very sensitive to geometric factors and, therefore, should be performed only under geometric conditions which have been appropriately validated.
Usual precautions regarding sterility and radioactivity must be respected.
The vial should never be opened and must be kept inside its shielded container. The medicinal product must be aseptically withdrawn through the stopper using sterilised single-use needle and syringe after disinfecting the stopper.
Appropriate aseptic precautions must be taken, in order to maintain the sterility of Cuprymina and to maintain sterility throughout the labelling procedures.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

ACOM S.r.l. (Advanced Center Oncology Macerata)
Località Cavallino
IT-62010 MONTECOSARO (MC)
Italy

SPARKLE S.r.l
Contrada Calò, snc
IT-73042 Casarano (LE)
Italy

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of (PSURs) for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorization holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

TUNGSTEN OR LEAD CONTAINER

1. NAME OF THE MEDICINAL PRODUCT

Cuprymina 925 MBq/mL radiopharmaceutical precursor, solution

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each mL of solution contains 925 MBq of Copper (^{64}Cu) chloride at calibration time (01h00 a.m. CET), corresponding to at least 0.25 micrograms (^{64}Cu). The calibration time is set between the EOS time and the Expiry time.
Specific activity ≥ 3,700 MBq Cu-64/ micrograms of copper.

3. LIST OF EXCIPIENTS

Hydrochloric acid (0.1 N).
Water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Radiopharmaceutical precursor, solution
Volume: {Z} mL
Activity: (Y) MBq Calibration time: {DD/MM/YYYY} 01h00 a.m. CET

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Not intended for direct administration to patients.
For *in vitro* radiolabelling.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

Shelf-life: 48 hours from date/time of End of Synthesis (EOS).
EXP {DD/MM/YYYY} hh:mm CET

9. SPECIAL STORAGE CONDITIONS

Store in the original package that provides protection from radiation, according to local regulation.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose in accordance with local requirements.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MAH:

A.C.O.M. -ADVANCED CENTER ONCOLOGY MACERATA -S.R.L.
Località Cavallino 39 A/B
62010 Montecosaro

Manufacturer:
ACOM S.r.l. Italy

SPARKLE S.r.l Italy

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/12/784/001

13. BATCH NUMBER

Batch
Ref. N°

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

TYPE I VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cuprymina 925 MBq/mL radiopharmaceutical precursor, solution.
Copper (^{64}Cu) chloride

2. METHOD OF ADMINISTRATION

For *in vitro* radiolabelling.
Not intended for direct administration to patients.

3. EXPIRY DATE

EXP {DD/MM/YYYY} (hh:mm CET)

4. BATCH NUMBER

Batch
Ref. N°

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Volume: {Z} mL
Activity: {Y}_____MBq Cal.: {DD/MM/YYYY} 01h00 a.m. CET

6. OTHER

Manufacturer:

ACOM S.r.l.

SPARKLE S.r.l

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Cuprymina 925 MBq/mL radiopharmaceutical precursor, solution
Copper (^{64}Cu) chloride

Read all of this leaflet carefully before you are given the medicine combined with Cuprymina because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your nuclear medicine doctor who will supervise the procedure.
- If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Cuprymina is and what it is used for

Cuprymina is not a medicine and it is not intended to be used on its own.

Cuprymina is a type of medicine called a radiopharmaceutical precursor. It contains the active substance copper (^{64}Cu) chloride. Copper-64 is a radioactive form of the chemical element copper, which emits the radiation needed for certain procedures that may be carried out on you.

Cuprymina is used for radiolabelling, a technique in which a substance is tagged (radiolabelled) with a radioactive compound. Cuprymina is used to label certain medicines that have been specially developed and authorised for use with the active substance copper (^{64}Cu) chloride. These medicines act as a carrier to take the radioactivity to where it is needed. These may be substances that have been designed to recognise a particular type of cell in the body, including tumour cells.

The use of Copper-64-labelled medicines involves exposure to small amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the radiopharmaceutical outweighs the risk from radiation.

Please refer to the package leaflet of the medicine that is to be radiolabelled with Cuprymina.

2. What you need to know before the medicine radiolabelled with Cuprymina is used

The medicine radiolabelled with Cuprymina must not be used:
- If you are allergic to copper or any of the other ingredients of this medicine listed in section 6.
- If you are pregnant or believe you may be pregnant.

Warnings and precautions
Talk to your nuclear medicine doctor before using the medicine that is radiolabelled with Cuprymina.
Cuprymina should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.
Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiation safety and pharmaceutical quality requirements.

It must be considered that the radiolabelled medicine emits high intensity Auger electrons.
The condition of negligible radioactivity in the patient is reached, in practice, 4 days after injection.

Children and adolescents
Medicines radiolabelled with Cuprymina should not be used in children and adolescents up to 18 years.

Other medicines and medicines radiolabelled with Cuprymina
Tell your nuclear medicine doctor if you are taking, have recently taken or might take any other medicines since they may interfere with the interpretation of the images.
It is not known whether copper (^{64}Cu) chloride may interact with other medicines as specific studies have not been carried out.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your nuclear medicine doctor for advice before you are given medicines radiolabelled with Cuprymina.

You must inform the nuclear medicine doctor before the administration of medicines radiolabelled with Cuprymina if there is a possibility you might be pregnant, if you have missed your period or if you are breast-feeding.
When in doubt, it is important to consult your nuclear medicine doctor who will supervise the procedure.

If you are pregnant
Medicines radiolabelled with Cuprymina must not be administered if you are pregnant.

If you are breast-feeding
You will be asked to stop breast-feeding if you need to receive a medicine radiolabelled with Cuprymina.
Please ask your nuclear medicine doctor when you can resume breast-feeding.

Driving and using machines
There could be effects on your ability to drive and to use machines due to the medicine used in combination with Cuprymina. Please read the package leaflet of that medicine carefully.

3. How the medicine radiolabelled with Cuprymina is used

There are strict laws on the use, handling and disposal of radiopharmaceutical products. Medicines radiolabelled with Cuprymina will only be used in special, controlled areas. This medicinewill only be handled and given to you by people who are trained and qualified to use it safely. These persons will take special care for the safe use of this medicineand will keep you informed of their actions.

The nuclear medicine doctor supervising the procedure will decide on the quantity of medicine radiolabelled with Cuprymina to be used in your case. It will be the smallest quantity necessary to achieve the appropriate outcome, depending on the co-administered medicine and its intended use.

Administration of the medicine radiolabelled with Cuprymina and conduct of the procedure
Cuprymina must be used only in combination with another medicine which has been specifically developed and authorised for being combined with Cuprymina, and will be administered subsequently.

Duration of the procedure
Your nuclear medicine doctor will inform you about the usual duration of the procedure before the administration of the medicine radiolabelled with Cuprymina.

After administration of the medicine radiolabelled with Cuprymina has been performed

The nuclear medicine doctor will inform you if you need to take any special precautions after receiving the medicine radiolabelled with Cuprymina. Contact your nuclear medicine doctor if you have any questions.

If you have been given more medicine radiolabelled with Cuprymina than you should
Since the medicine radiolabelled with Cuprymina is handled by a nuclear medicine doctor under strictly controlled conditions, there is only a very small chance of possible overdose. However, in the case of an overdose, you will receive the appropriate treatment.

Should you have any further question on the use of Cuprymina, please ask the nuclear medicine doctor who supervises the procedure.

4. Possible side effects

Like all medicines, the medicine radiolabelled with Cuprymina can cause side effects, although not everybody gets them.

After the medicine radiolabelled with Cuprymina is administered, it will deliver certain amounts of ionising radiation (radioactivity) which can induce a certain risk of cancer and development of hereditary defects. In all cases, the risks of the radiation should be less than from the disease itself.

For more information, refer to the package leaflet of the particular medicine to be radiolabelled.

If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet.

Reporting of side effects
If you get any side effects, talk to your nuclear medicine doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cuprymina

Keep this medicine out of the sight and reach of children.

The following information is intended for the specialist only.
Do not use this medicine after the expiry date and time which are stated on the label after EXP.
Cuprymina will be stored in the original package that provides protection from radiation.

You will not have to store this medicine. Cuprymina is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

6. Contents of the pack and other information

What Cuprymina contains
- The active substance is copper (^{64}Cu) chloride. Each mL of solution contains 925 MBq at calibration time (01h00 a.m. CET Central European Time), corresponding to at least 0.25 micrograms of copper-64. One vial contains from 925 to 2,770 MBq (corresponding to 0.25-0.75 micrograms of copper-64). (MBq: mega Becquerel, Becquerel is the unit in which radioactivity is measured)
- The other ingredients are hydrochloric acid (0.1 N) and water for injections.

What Cuprymina looks like and contents of the pack
Cuprymina is presented as a clear, and colourless solution filled in a 10 mL glass vial.
The volume of one vial ranges from 1 to 3 mL solution (corresponding to 925 to 2,770 MBq at calibration time).
This volume depends on the quantity of medicine combined with Cuprymina required for administration by the nuclear medicine doctor.
Each pack contains 1 vial in a tungsten or lead container.

Marketing Authorisation Holder

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For any information about this medicine, please contact the Marketing Authorisation Holder.

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Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

The following information is intended for medical or healthcare professionals only:

The complete Summary of Product Characteristics (SmPC) of Cuprymina is provided as a separate document in the medicine pack, with the objective to provide healthcare professionals with other additional scientific and practical information about the use of this medicine.

Please refer to the SmPC.