

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## **1. NAME OF THE MEDICINAL PRODUCT**

Cuprior 150 mg film-coated tablets

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each film-coated tablet contains trientine tetrahydrochloride equivalent to 150 mg trientine.

For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Film-coated tablet (tablet)

Yellow, 16 mm x 8 mm oblong film-coated tablet with a score line on each side.

The tablet can be divided into equal doses.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Cuprior is indicated for the treatment of Wilson's disease in adults, adolescents and children  $\geq 5$  years intolerant to D-penicillamine therapy.

### **4.2 Posology and method of administration**

Treatment should only be initiated by specialist physicians with experience in the management of Wilson's disease.

#### Posology

The starting dose would usually correspond to the lowest dose in the range and the dose should subsequently be adapted according to the patient's clinical response (see section 4.4).

#### Adult

The recommended dose is between 450 mg and 975 mg (3 to 6 and a half film-coated tablets) per day in 2 to 4 divided doses.

#### Paediatric population

The starting dose in paediatrics is lower than for adults and depends on age and may be calculated using body weight. The dose should subsequently be adapted according to the child's clinical response (see section 4.4).

#### *Children and adolescents ( $\geq 5$ years to 18 years)*

The dose is usually between 225 mg and 600 mg per day (1 and a half to 4 film-coated tablets) in 2 to 4 divided doses.

#### *Children aged $< 5$ years*

The safety and efficacy of trientine in children aged  $< 5$  years have not been established. The pharmaceutical form is not suitable for administration to children  $< 5$  years.

The recommended doses of Cuprior are expressed as mg of trientine base (i.e. not in mg of the trientine tetrahydrochloride salt).

#### Special populations

##### *Elderly*

No dose adjustment is required in elderly patients.

##### *Renal impairment*

There is limited information in patients with renal impairment. No specific dose adjustment is required in these patients (see section 4.4).

#### Method of administration

Cuprior is for oral use. The film-coated tablets should be swallowed with water. The scored film-coated tablet can be divided in two equal halves, if required, to provide a more precise dose or facilitate administration.

It is important that Cuprior is given on an empty stomach, at least one hour before meals or two hours after meals and at least one hour apart from any other medicinal product, food, or milk (see section 4.5).

### **4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

### **4.4 Special warnings and precautions for use**

When switching a patient from another formulation trientine, caution is advised because doses expressed in trientine base may not be equivalent (see section 4.2).

Trientine is a chelating agent which has been found to reduce serum iron levels. Iron supplements may be necessary in case of iron deficiency anaemia and should be administered at a different time (see section 4.5).

The combination of trientine with zinc is not recommended. There are only limited data on concomitant use available and no specific dose recommendations can be made.

In patients who were previously treated with D-penicillamine, lupus-like reactions have been reported during subsequent treatment with trientine, however it is not possible to determine if there is a causal relationship with trientine.

#### Monitoring

Patients receiving Cuprior should remain under regular medical supervision and be monitored for appropriate control of symptoms and copper levels in order to optimise the dose (see section 4.2).

The aim of maintenance treatment is to maintain free copper levels in the serum within acceptable limits. The most reliable index for monitoring therapy is the determination of serum free copper which is calculated using the difference between the total copper and the ceruloplasmin-bound copper (normal level of free copper in the serum is usually 100 to 150 microgram/L).

The measurement of copper excretion in the urine may be performed during therapy. Since chelation therapy leads to an increase in urinary copper levels, this may/will not give an accurate reflection of the excess copper load in the body but may be a useful measure of treatment compliance.

Worsening of clinical symptoms, including neurological deterioration, may occur at the beginning of chelation therapy due to excess of free serum copper during the initial response to treatment. Close monitoring is required to optimise the dose or to adapt treatment if necessary.

#### Special populations

Overtreatment carries the risk of copper deficiency. Monitoring for manifestations of overtreatment should be undertaken, particularly when copper requirements may change, such as in pregnancy (see section 4.6) and in children where appropriate control of copper levels are required to ensure proper growth and mental development.

Patients with renal impairment receiving trientine should remain under regular medical supervision for appropriate control of symptoms and copper levels. Close monitoring of renal function is also recommended in these patients (see section 4.2).

#### Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free.'

### **4.5 Interaction with other medicinal products and other forms of interaction**

No interaction studies have been performed.

Trientine has been found to reduce serum iron levels, possibly by reducing its absorption, and iron supplements may be required. Since iron and trientine may inhibit absorption of each other, iron supplements should be taken after at least two hours have elapsed from the administration of trientine.

As trientine is poorly absorbed following oral intake and the principal mechanism of action requires its systemic exposure (see section 5.1), it is important that the film-coated tablets are taken on empty stomach at least one hour before meals or 2 hours after meals and at least one hour apart from any other medicinal product, food, or milk (see section 4.2). This maximises the absorption of trientine and reduces the likelihood of the medicinal product binding to metals in the gastrointestinal tract. However, no food interaction studies have been performed and so the extent of the food effect on systemic trientine exposure is unknown.

Although there is no evidence that calcium or magnesium antacids alter the efficacy of trientine, it is good practice to separate their administration.

### **4.6 Fertility, pregnancy and lactation**

#### Pregnancy

There is a limited amount of data from the use of trientine in pregnant women.

Studies in animals have shown reproductive toxicity, which was probably a result of trientine-induced copper deficiency (see section 5.3).

Cuprior should only be used in pregnancy after careful consideration of the benefits compared with the risks of treatment in the individual patient. Factors which need to be born in mind include the risks associated with the disease itself, the risk of those alternative treatments which are available and the possible teratogenic effects of trientine (see section 5.3).

Since copper is required for proper growth and mental development, dose adjustments may be required to ensure that the foetus will not become copper deficient and close monitoring of the patient is essential (see section 4.4).

The pregnancy should be closely monitored in order to detect possible foetal abnormality and to assess maternal serum copper levels throughout the pregnancy. The dose of trientine used should be adjusted in order to maintain serum copper levels within the normal range.

Babies born to mothers being treated with trientine should be monitored for serum copper levels where appropriate.

#### Breast-feeding

It is unknown whether trientine is excreted in human milk. A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Cuprior therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

#### Fertility

It is unknown whether trientine has an effect on human fertility.

### **4.7 Effects on ability to drive and use machines**

Cuprior has no or negligible influence on the ability to drive and use machines.

### **4.8 Undesirable effects**

#### Summary of the safety profile

The most commonly reported adverse reaction with trientine is nausea. Serious iron deficiency anaemia and severe colitis may occur during treatment.

#### Tabulated list of adverse reactions

The following adverse reactions have been reported with the use of trientine for Wilson's disease. Frequencies are defined as: very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); very rare ( $< 1/10,000$ ); not known (cannot be estimated from the available data).

<b>System organ class</b>	<b>Adverse reactions</b>
Blood and lymphatic system disorders	<i>Uncommon:</i> sideroblastic anaemia. <i>Not known:</i> iron deficiency anaemia.
Gastrointestinal disorders	<i>Common:</i> nausea. <i>Not known:</i> duodenitis, colitis (including severe colitis).
Skin and subcutaneous tissue disorder	<i>Uncommon:</i> skin rash, pruritus, erythema. <i>Not known:</i> urticaria.

#### 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**

Occasional cases of trientine overdose have been reported. In cases up to 20 g of trientine base there were no apparent adverse effects reported. A large overdose of 40 g of trientine base resulted in self-

limiting dizziness and vomiting with no other clinical sequelae or significant biochemical abnormalities reported.

There is no antidote for trientine acute overdose.

Chronic over treatment can lead to copper deficiency and reversible sideroblastic anaemia. Overtreatment and excess copper removal can be monitored using values of urine copper excretion and of non-ceruloplasmin bound copper. Close monitoring is required to optimise the dose or to adapt treatment if necessary (see section 4.4).

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Other alimentary tract and metabolism products, various alimentary tract and metabolism products, ATC code: A16AX12.

#### Mechanism of action

Trientine is a copper-chelating agent whose principal mechanism of action is to eliminate absorbed copper from the body by forming a stable complex that is then eliminated through urinary excretion. Trientine may also chelate copper in the intestinal tract and so inhibit copper absorption.

### **5.2 Pharmacokinetic properties**

#### Absorption

The absorption of trientine following oral administration is low and variable in patients with Wilson disease. The pharmacokinetic profile of Cuprior has been evaluated after a single oral dose of 450 mg, 600 mg and 750 mg trientine in healthy male and female subjects. Plasma levels of trientine rose rapidly following administration with the median peak level reached after 1.25 to 2 hours. The trientine plasma concentration then declined in a multiphasic manner, initially rapidly, followed by a slower elimination phase. The overall pharmacokinetic profiles were similar between males and females, although males had higher levels of trientine.

#### Distribution

Little is known on the distribution of trientine in organs and tissues.

#### Biotransformation

Trientine is acetylated in two major metabolites, N(1)-acetyltriethylenetetramine (MAT) and N(1),N(10)-diacetyltriethylenetetramine (DAT). MAT may also participate to the overall clinical activity of Cuprior, however the extent of MAT to the overall effect of Cuprior on copper levels remains to be determined.

#### Elimination

Trientine and its metabolites are rapidly excreted in the urine, although low levels of trientine could still be detected in the plasma after 20 hours. Unabsorbed trientine is eliminated through faecal excretion.

#### Linearity/non-linearity

Plasma exposures in humans have shown a linear relationship with oral doses of trientine.

### 5.3 Preclinical safety data

Preclinical data obtained with trientine have shown adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use as follows:

#### Repeat dose toxicity

In mice administered in drinking water, trientine displayed increased frequencies of inflammation of the lung interstitium and liver periportal fatty infiltration. Hematopoietic cell proliferation was seen in the spleen of males. Kidney and body weights were reduced in males as was the incidence of renal cytoplasmic vacuolisation. The NOAEL was established at approximately 92 mg/kg/day for males and 99 mg/kg/day for females. In rats administered oral trientine doses, up to 600 mg/kg/day for 26 weeks, histopathology revealed a dose-related incidence and severity of focal chronic interstitial pneumonitis accompanied by fibrosis of the alveolar wall. The microscopic changes in lung were considered indicative of a persistent inflammatory reaction or persistent toxic effect on alveolar cells. Taking into account that trientine has irritating properties, it was estimated that the observed chronic interstitial pneumonitis was explained by a cytotoxic effect of trientine upon accumulation into bronchiolar epithelial cells and alveolar pneumocytes. These findings were not reversible. The rat NOAEL was considered 50 mg/kg/day for females, a NOAEL was not established for males. Dogs receiving oral doses of trientine up to 300 mg/kg/day, showed neurological and/or musculo-skeletal clinical symptoms (abnormal gait, ataxia, weak limbs, body tremors) in repeat-dose toxicity studies, attributed to the copper-depleting activity of trientine. The NOAEL was established at 50 mg/kg/day resulting in safety margins of about 4 in males and 17 in females, towards human therapeutic exposures.

#### Genotoxicity

Overall, trientine has shown positive effects in *in vitro* genotoxicity studies, including the Ames test and genotoxicity tests in mammalian cells. *In vivo*, trientine was however negative in the mouse micronucleus test.

#### Reproductive and developmental toxicity

When rodents were fed throughout pregnancy a diet containing trientine, the frequency of resorptions and the frequency of abnormal fetuses at term showed a dose-related increase. These effects are possibly due to trientine induced-copper and zinc deficiency.

#### Local tolerance

*In silico* data predict that trientine displays irritating and sensitising properties. Positive results for sensitization potential in Guinea pig maximization tests were reported.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

#### Tablet core

Mannitol  
Colloidal anhydrous silica  
Glycerol dibehenate

#### Tablet film-coating

Polyvinyl alcohol  
Talc  
Titanium dioxide (E 171)  
Glycerol monocaprylocaprate (Type I)  
Iron oxide yellow (E 172)  
Sodium laurilsulfate

#### **6.2 Incompatibilities**

Not applicable.

#### **6.3 Shelf life**

3 years.

#### **6.4 Special precautions for storage**

This medicinal product does not require any special storage conditions.

#### **6.5 Nature and contents of container**

oPA/Alu/PVC//Alu blisters, each blister contains 8 film-coated tablets.  
Pack size: 72 or 96 film-coated tablets.  
Not all pack sizes may be marketed.

#### **6.6 Special precautions for disposal**

No special requirements.

### **7. MARKETING AUTHORISATION HOLDER**

Orphalan  
226 Boulevard Voltaire  
75011 Paris  
France

### **8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/17/1199/001 72 film-coated tablets  
EU/1/17/1199/002 96 film-coated tablets

### **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 5 September 2017  
Date of latest renewal: 17 August 2022

### **10. DATE OF REVISION OF THE TEXT**

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

Delpharm Evreux  
5 rue du Guesclin  
27000 Evreux  
France

**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 authorisation 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****OUTER CARTON****1. NAME OF THE MEDICINAL PRODUCT**

Cuprior 150 mg film-coated tablets  
trientine

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each film-coated tablet contains trientine tetrahydrochloride equivalent to 150 mg trientine.

**3. LIST OF EXCIPIENTS****4. PHARMACEUTICAL FORM AND CONTENTS**

Film-coated tablet  
72 film-coated tablets  
96 film-coated tablets

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use.  
Package leaflet online at *QR code to be included* <http://www.cuprior.com>

Oral use.

**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**

Take on an empty stomach, at least one hour before meals or two hours after meals and at least one hour apart from any other medicine, food, or milk.

**8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

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

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Orphalan  
226 Boulevard Voltaire  
75011 Paris, France

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/17/1199/001 72 film-coated tablets  
EU/1/17/1199/002 96 film-coated tablets

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

Cuprior 150 mg

**17. UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.

**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC  
SN  
NN

<b>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</b>
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<b>BLISTER</b>
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<b>1. NAME OF THE MEDICINAL PRODUCT</b>
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Cuprior 150 mg film-coated tablets  
trientine

<b>2. NAME OF THE MARKETING AUTHORISATION HOLDER</b>
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Orphalan

<b>3. EXPIRY DATE</b>
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EXP

<b>4. BATCH NUMBER</b>
------------------------

Lot

<b>5. OTHER</b>
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## **B. PACKAGE LEAFLET**

## **Package leaflet: Information for the patient**

### **Cuprior 150 mg film-coated tablets** trientine

**Read all of this leaflet carefully before you start taking this medicine 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 doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

#### **What is in this leaflet**

1. What Cuprior is and what it is used for
2. What you need to know before you take Cuprior
3. How to take Cuprior
4. Possible side effects
5. How to store Cuprior
6. Contents of the pack and other information

#### **1. What Cuprior is and what it is used for**

Cuprior is a medicine used to treat Wilson's disease that contains the active substance trientine.

Wilson's disease is an inherited condition in which the body cannot transport copper around the body in the normal way or remove copper in the normal way as a secretion from the liver into the gut. This means that the small amounts of copper from food and drink build up to excessive levels and can lead to liver damage and problems in the nervous system. This medicine mainly works by attaching to copper in the body which then allows it to be removed in the urine instead, helping to lower copper levels. It may also attach to copper in the gut and so reduce the amount taken up into the body. Cuprior is given to adults, adolescents and children aged 5 years and over who cannot tolerate another medicine that is used to treat this disease, called penicillamine.

#### **2. What you need to know before you take Cuprior**

##### **Do not take Cuprior**

- if you are allergic to trientine or any of the other ingredients of this medicine (listed in section 6).

##### **Warnings and precautions**

Talk to your doctor or pharmacist before taking Cuprior.

If you were already taking another trientine medicine, your doctor may modify your daily dose, the number of tablets or the number of intake in the day when switching to Cuprior treatment.

Your symptoms may initially get worse after starting the treatment. If this happens, you must tell your doctor.

Your doctor will regularly check your blood and urine to ensure that you receive the right dose of Cuprior to properly control your symptoms and copper levels.

You should tell your doctor if you get any side effects as this may indicate that your dose of Cuprior needs to be adjusted up or down.

This medicine may also reduce the level of iron in your blood and your doctor may prescribe iron supplements (see section “Other medicines and Cuprior” below).

If you have kidney problems, your doctor will regularly check that the treatment dose is appropriate and does not affect the functioning of your kidney.

The association of trientine with another medicine that contains zinc is not recommended.

Lupus-like reactions (symptoms may include persistent rash, fever, joint pain, and tiredness) have been reported in some patients switched to trientine medicine after penicillamine medicine. However it was not possible to determine if the reaction was due to trientine or to previous penicillamine treatment.

### **Children and adolescents**

Your doctor will carry out checks more frequently to ensure your copper levels are maintained at a suitable level for normal growth and mental development.

This medicine is not recommended for children aged below 5 years of age.

### **Other medicines and Cuprior**

Tell your doctor if you are taking, have recently taken, or might take any other medicines.

In particular, you must tell your doctor if you are already taking iron supplements or if you take indigestion remedies (medicines that reduce discomfort after eating). If you take these medicines you may need to take Cuprior at a different time in the day because otherwise Cuprior may not be as effective. If you take iron supplements, make sure that at least two hours have passed between taking Cuprior and taking your iron supplements.

### **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 doctor for advice before taking this medicine.

It is very important to continue treatment to reduce copper during pregnancy. You and your doctor should fully discuss the potential benefits of treatment whilst considering any possible risks that there may be. Your doctor will advise you which treatment and which dose is best in your situation.

If you are pregnant and taking Cuprior, you will be monitored throughout your pregnancy for any effects on the baby or changes in your copper levels. When your baby is born, the copper level in the baby's blood will also be monitored.

It is not known if Cuprior can pass into breast milk. It is important to tell your doctor if you are breast-feeding or plan to do so. Your doctor will then help you decide whether to stop breast-feeding or to stop taking Cuprior, considering the benefit of breast-feeding to the baby and the benefit of Cuprior to the mother. Your doctor will decide which treatment and which dose is best in your situation.

### **Driving and using machines**

Cuprior is not expected to affect your ability to drive a car or use any tools or machines.

### **Cuprior contains sodium**

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free.’

### 3. How to take Cuprior

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

#### Adults

In adults of all ages, the recommended total daily dose is 3 to 6 and a half tablets per day (making a total of between 450 and 975 mg). This daily total will be divided into 2 to 4 smaller doses to be taken during the day. Your doctor will tell you how many tablets you should take and how often in the day. Tablets can be divided in half if needed.

#### Use in children and adolescents (5 to 18 years)

The dose that you will take is usually lower than for an adult and depends on your age and body weight.

The usual total daily dose is between 225 and 600 mg (1 and a half to 4 tablets daily), which will be divided into 2 to 4 smaller doses to be taken during the day. Your doctor will tell you how many tablets you should take and how often in the day. Tablets can be divided in half if needed.

Once you have started the treatment, your doctor may adjust the dose based on the response to treatment.

Swallow the tablets with water. Take this medicine on an empty stomach, at **least one hour before meals or two hours after meals** and at least one hour apart from any other medicines, food, or milk.

If you take iron supplements, take them at least two hours after taking a dose of Cuprior.

#### If you take more Cuprior than you should

Take Cuprior only as it is prescribed for you. If you think you may have taken more Cuprior than you were told to, contact your doctor or pharmacist.

If you take more than you should, you may get nausea, vomiting and dizziness.

#### If you forget to take Cuprior

Do not take a double dose to make up for a forgotten dose. Skip the missed dose and take your next dose at its usual scheduled time.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

#### If you stop taking Cuprior

This medicine is for long-term use. Do not stop your treatment without the advice of your doctor even if you feel better because Wilson's disease is a life-long condition.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

### 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been reported:

*Common (may affect up to 1 in 10 people)*

- feeling sick (nausea)

*Uncommon (may affect up to 1 in 100 people)*

- skin rashes
- reddening of the skin (erythema)
- itching

- anaemia

*Not known (frequency cannot be estimated from available data)*

- stomach upsets and discomfort, including severe stomach pains (duodenitis)
- inflammation of the gut which may lead to e.g. abdominal pain, recurring diarrhoea and blood in stools (colitis)
- decrease in the number of red blood cells due to low iron level in your blood (iron deficiency)
- urticaria (nettle rash or hives).

### **Reporting of side effects**

If you get any side effects, talk to your doctor or pharmacist. 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 Cuprior**

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

Do not use this medicine after the expiry date which is stated on the carton and blister after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## **6. Contents of the pack and other information**

### **What Cuprior contains**

- The active substance is trientine. Each film-coated tablet contains trientine tetrahydrochloride equivalent to 150 mg trientine.
- The other ingredients are:

Tablet core: mannitol, colloidal anhydrous silica and glycerol dibehenate.

Tablet film-coating: polyvinyl alcohol, talc, titanium dioxide (E 171), glycerol monocaprylocaprate (Type I), iron oxide yellow (E 172) and sodium laurilsulfate (see section 2 “Cuprior contains sodium”).

### **What Cuprior looks like and contents of the pack**

Cuprior are yellow, 16 mm x 8 mm oblong film-coated tablets with a score line on each side.

Cuprior is available in blisters containing 72 or 96 film-coated tablets.

Not all pack sizes may be marketed.

### **Marketing Authorisation Holder**

Orphalan  
226 Boulevard Voltaire  
75011 Paris  
France

### **Manufacturer**

Delpharm Evreux  
5 rue du Guesclin  
27000 Evreux  
France

**This leaflet was last revised in.**

You can find the information also when flashing the QR code below with a smartphone or via the website *QR code to be included* <http://www.cuprior.com>

**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site: <http://www.ema.europa.eu>. There are also links to other websites about rare diseases and treatments.