# CHLORAL HYDRATE 143.3 MG IN 5ML ORAL SOLUTION
# PL 21600/0001

## UKPAR

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# CHLORAL HYDRATE 143.3 MG IN 5ML ORAL SOLUTION PL 21600/0001

## LAY SUMMARY

The MHRA granted Huntley Pharmaceuticals Limited a Marketing Authorisation for the medicinal product Chloral Hydrate 143.3 mg in 5 ml Oral Solution (PL 21600/0001) on 20th March 2007. This prescription-only medicine (POM) is used in the short-term treatment of insomnia.

The active ingredient, chloral hydrate is one of a group of medicines called hypnotics that induces sleep and act on the central nervous system.

This application is identical to a previously granted application for Welldorm Elixir (PL 13374/0005, granted to Smith & Nephew Pharmaceutical Limited on 30th December 1993.

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Chloral Hydrate 143.3 mg in 5 ml Oral Solution outweigh the risks; hence a Marketing Authorisation has been granted.

The licence for this product was cancelled on 15th September 2007.

# CHLORAL HYDRATE 143.3 MG IN 5ML ORAL SOLUTION
# PL 21600/0001

## SCIENTIFIC DISCUSSION

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# INTRODUCTION

The UK granted a marketing authorisation for the medicinal product Chloral Hydrate 143.3 mg in 5 ml Oral Solution (PL 21600/0001) to Huntley Pharmaceuticals Limited on 20th March 2007. The product is a prescription-only medicine.

The application was submitted as a simple abridged application according to Article 10c of Directive 2001/83/EC, cross-referring to Welldorm Elixir (PL 13374/0005) currently authorised to Smith & Nephew Pharmaceuticals Limited, UK following a change of ownership. The reference product has been authorised in the UK since December 1993 and so the 10-year period of data exclusivity has expired.

No new data were submitted nor was it necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no Public Assessment Report (PAR) has been generated for it.

The product contains the active ingredient choral hydrate which is a hypnotic drug which acts on the central nervous system and used in the short-term treatment of insomnia.

The licence for this product was cancelled on 15th September 2007.

# PHARMACEUTICAL ASSESSMENT

**LICENCE NO:** PL 21600/0001
**PROPRIETARY NAME:** Chloral Hydrate 143.3 mg in 5 ml Oral Solution
**ACTIVE(S):** Chloral hydrate
**COMPANY NAME:** Huntley Pharmaceuticals Limited
**E.C. ARTICLE:** Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC
**LEGAL STATUS:** POM

## 1. INTRODUCTION

This is a simple, informed consent application for Chloral Hydrate 143.3 mg in 5 ml Oral Solution submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Huntley Pharmaceutical Limited, 35A High Street, Marlborough, Wiltshire, SN8 1LW, UK.

The application cross-refers to Welldorm Elixir, approved on 30th December 1993 to the marketing authorisation holder Smith & Nephew Pharmaceuticals Limited. The current application is considered valid.

## 2. MARKETING AUTHORISATION APPLICATION FORM

### 2.1 Name(s)

The proposed name of the product is Chloral Hydrate 143.3 mg in 5 ml Oral Solution. The product has been named in line with current requirements.

### 2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

The product contains chloral hydrate, equivalent to 143.3 mg per 5 ml of solution. It is to be stored in amber glass bottles with child proof plastic screw caps. The proposed shelf-life (30 months) and storage conditions ("Do not store above 25°C. Store in the original package" and "Keep the bottle in the outer carton") are consistent with the details registered for the cross-reference product.

### 2.3 Legal status

On approval, the product will be available as prescription-only medicine (POM).

### 2.4 Marketing authorisation holder/Contact Persons/Company

Huntley Pharmaceutical Limited, 35A High Street, Marlborough, Wiltshire, SN8 1LW, UK.

The QP responsible for pharmacovigilance is stated and his CV is included.

### 2.5 Manufacturers

The proposed manufacturing sites are consistent with those registered for the cross-reference product and evidence of GMP compliance has been provided.

### 2.6 Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

**2.7 Manufacturing process**
The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

**2.8 Finished product/shelf-life specification**
The proposed finished product specification is in line with the details registered for the cross-reference product.

**2.10 TSE Compliance**
No materials of animal and/or human origin are contained or used in the manufacturing process for the medicinal product. This is consistent with the cross-reference product.

## 3. EXPERT REPORTS
The applicant has included detailed expert reports in Module 2 of the application. Signed declarations and copies of the experts' CVs are enclosed in Module 1.4 for the quality, non-clinical and clinical experts. All are considered to have sufficient experience for their responsibilities.

## 4. PRODUCT NAME & APPEARANCE
See 2.1 for details of the proposed product name. The appearance of the product is identical to the cross-reference product.

## 5. SUMMARY OF PRODUCT CHARACTERISTICS
The proposed summary is consistent with the details registered for the cross-reference product.

## 6. PATIENT INFORMATION LEAFLET/CARTON
PIL
The patient information leaflet has been prepared in-line with the details registered for the cross-reference product.
The marketing authorisation holder has provided a commitment to update the marketing authorisation with a package leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups, no later than 1st July 2008.

Carton
The proposed artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements. In line with current legislation the applicant has also included the name of the product in Braille on the outer packaging and has included sufficient space for a standard UK pharmacy dispensing label.

## 7. CONCLUSIONS
The data submitted with the application are acceptable. A Marketing Authorisation should be granted.

# PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

# CLINICAL ASSESSMENT

No new clinical data have been supplied with this application and none are required for an application of this type.

## OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

### QUALITY

The data for this application is consistent with that previously assessed for the cross-reference product and as such has been judged to be satisfactory.

### PRECLINICAL

No new preclinical data were submitted and none are required for an application of this type.

### EFFICACY

Chloral hydrate is a well known drug and has been used as a hypnotic drug for many years. This application is identical to previously granted application for Welldorm Elixir (PL 13374/0005) granted to Smith & Nephew Pharmaceuticals Limited.
No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

### RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant's product is identical to the cross-reference product which, in turn, has been shown to be interchangeable with the innovator product. Extensive clinical experience with chloral hydrate is considered to have demonstrated the therapeutic value of the compound. The risk benefit is therefore considered to be positive.

# CHLORAL HYDRATE 143.3 MG IN 5 ML ORAL SOLUTION
# PL 21600/0001

## STEPS TAKEN FOR ASSESMENT

| | |
|---|---|
| 1 | The MHRA received the marketing authorisation application on 29th July 2004. |
| 2 | Following standard checks and communication with the applicant the MHRA considered the application valid on 30th November 2005. |
| 3 | Following assessment of the application the MHRA requested further information relating to the quality dossier on 12th October 2006. |
| 4 | The applicant responded to the MHRA's requests, providing further information on 13th March 2007. |
| 5 | The application was determined on 20th March 2007. |

# CHLORAL HYDRATE 143.3 MG IN 5ML ORAL SOLUTION
# PL 21600/0001

## STEPS TAKEN AFTER ASSESSMENT

| Date submitted | Application type | Scope | Outcome |
|---|---|---|---|
| 15/09/2007 | Cancellation | Cancellation of licence | Approved – 15/09/2007 |
| | | | |
| | | | |
| | | | |
| | | | |

# CHLORAL HYDRATE 143.3 MG IN 5ML ORAL SOLUTION
# PL 21600/0001
# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT
Chloral Hydrate 143.3 mg in 5 ml Oral Solution

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 5ml of Chloral Hydrate Oral Solution contains 143.3 mg of Chloral Hydrate.

For excipients see 6.1

## 3. PHARMACEUTICAL FORM
Oral Solution

Clear red oral solution.

## 4. CLINICAL PARTICULARS
### 4.1 Therapeutic Indications
Chloral Hydrate 143.3 mg in 5 ml Oral Solution is used for the short-term treatment of insomnia.

### 4.2 Posology and Method of administration
Adults: 15-45 ml taken 15-30 minutes before bedtime with water or milk. Dose should not exceed 2g chloral hydrate per day.

Elderly: Dosage as for adults except for the frail elderly or those with hepatic impairment, where a reduction in dose may be appropriate.

Children: 30-50mg/kg of bodyweight. Dose should not exceed 1g chloral hydrate per day.

### 4.3 Contra-Indications
Hypersensitivity to the active substance or to any of the excipients (see 6.1).

Chloral Hydrate 143.3 mg in 5 ml Oral Solution should not be used in patients with marked hepatic or renal impairment, or in patients with severe cardiac disease, or in patients susceptible to acute attacks of porphyria.

### 4.4 Special Warnings And Special Precautions For Use
Best avoided in the presence of gastritis and in patients who have previously exhibited an idiosyncrasy or hypersensitivity to chloral hydrate.

Patients with rare glucose-galactose malabsorption should not take this medicine.

### 4.5 Interactions with other Medicinal Products and other Forms of Interaction
Alcohol potentiates the sedative effect. Chloral hydrate followed by intravenous furosemide may result in sweating, hot flushes and variable blood pressure including hypertension due to a hypermetabolic state caused by displacement of thyroid hormone from its bound state. Delerium may occur, especially in the elderly, particularly when used in conjunction with psychotropics or anticholinergics. In patients taking anticoagulants, when chloral hydrate is added to or withdrawn from the drug regimen, or its dosage changed, careful monitoring of the prothrombin time is required.

### 4.6 Pregnancy and Lactation
Chloral Hydrate 143.3 mg in 5 ml Oral Solution should not be used in pregnancy and lactation.

### 4.7 Effects on Ability to Drive and Use Machines
Patients receiving Chloral Hydrate 143.3 mg in 5 ml Oral Solution should be warned that their ability to drive or use machinery may be impaired by drowsiness.

**4.8 Undesirable Effects**

Gastric irritation, abdominal distension and flatulence may occur. Excitement, tolerance, allergic skin reactions, headache and ketonuria have occasionally been reported. There is a danger of abuse or chronic intoxication and the possibility that habituation may develop. In such patients gastritis and parenchymatous renal injury may develop. After long term use sudden withdrawal may result in delerium.

**4.9 Overdose**

The signs and symptoms of overdose involve the cardiovascular, respiratory and central nervous systems. These may include: respiratory depression, arrhythmias, hypothermia, pin-point pupils, hypotension or coma. Gastric irritation may result in vomiting and even gastric necrosis. If the patient survives, icterus due to hepatic damage and albuminuria from renal damage may appear. Serious problems have arisen with doses as little as 4g and 10g can be fatal. Overdosage should be treated with gastric lavage or inducing vomiting to empty the stomach. Supportive measures must be used. Haemodialysis, and in some cases haemoperfusion, have been reported to be effective in promoting the clearance of trichloroethanol.

## 5. PHARMACOLOGICAL PROPERTIES

**5.1 Pharmacodynamic Properties**

Chloral Hydrate 143.3 mg in 5 ml Oral Solution is a chloral hydrate derivative, which leads to a decrease in sleep latency and in the number of awakenings. A near natural sleep is induced and the REM/Non-REM ratio is not altered.

**5.2 Pharmacokinetic Properties**

Chloral hydrate and its metabolite trichloroethanol act as central nervous system depressants. Chloral hydrate is rapidly absorbed from the stomach, and starts to act within 30 minutes. It is widely distributed throughout the body, and is metabolised to trichloroethanol, also an active hypnotic, and trichloroacetic acid in the erythrocytes, liver and other tissues. It is excreted partly in the urine as trichloroethanol and its glucuronide, urochloralic acid, and as trichloroacetic acid. Significant amounts are also excreted in bile. Trichloroethanol has a plasma half life of the order of 8 hours. Trichloroacetic acid has a half-life of several days. In infants the half lives are longer. The value for trichloroethanol is 35 hours whilst for trichloroacetic acid the half life exceeds 6 days, with significant plasma concentrations present at 14 days.

**5.3 Pre-clinical Safety Data**

Chloral hydrate induces liver tumours in male mice, with no tumourigenic effects in rats. The mechanism of tumour induction is not known, but in the absence of clear evidence of mutagenic and clastogenic potential it is unlikely to be relevant in man.

## 6. PHARMACEUTICAL PARTICULARS

**6.1 List of Excipients**

Glycerol
Liquid glucose
Sodium benzoate
Saccharin sodium
Sunset yellow FCF (E110)
Ponceau 4R (E124)
Essence of passion fruit containing natural and artificial flavouring, and propylene glycol (E1520)
Purified water

**6.2 Incompatibilities**

None known

**6.3 Shelf-Life**

30 months

**6.4 Special Precautions for Storage**

Store below 25°C. Store in the original packaging. Keep the bottle in the outer carton.

**6.5 Nature and Contents of Container**

Amber glass bottle with child-proof plastic screw cap, containing 150ml of Chloral Hydrate 143.3 mg in 5 ml Oral Solution, presented in a carton.

**6.6 Instructions for Use, Handling and Disposal**

Syrup BP should be used as a diluent.

**7. MARKETING AUTHORISATION HOLDER**

Huntley Pharmaceuticals Ltd
35A High Street
Marlborough
Wiltshire
SN8 1LW

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

PL 21600/0001

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

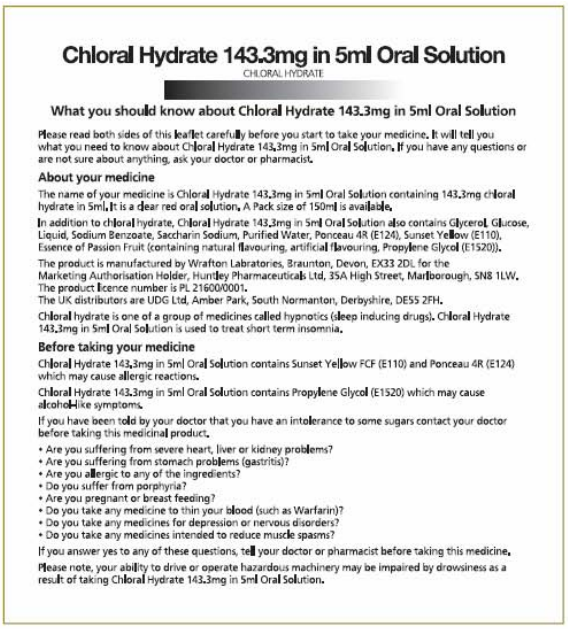
20/03/2007

**10 DATE OF REVISION OF THE TEXT**

20/03/2007

# CHLORAL HYDRATE 143.3 MG IN 5ML ORAL SOLUTION
# PL 21600/0001

## PATIENT INFORMATION LEAFLET



### Chloral Hydrate 143.3mg in 5ml Oral Solution

CHLORAL HYDRATE

**What you should know about Chloral Hydrate 143.3mg in 5ml Oral Solution**

Please read both sides of this leaflet carefully before you start to take your medicine. It will tell you what you need to know about Chloral Hydrate 143.3mg in 5ml Oral Solution. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

**About your medicine**

The name of your medicine is Chloral Hydrate 143.3mg in 5ml Oral Solution containing 143.3mg chloral hydrate in 5ml. It is a clear red oral solution. A Pack size of 150ml is available.

In addition to chloral hydrate, Chloral Hydrate 143.3mg in 5ml Oral Solution also contains Glycerol, Glucose, Liquid, Sodium Benzoate, Saccharin Sodium, Purified Water, Ponceau 4R (E124), Sunset Yellow (E110), Essence of Passion Fruit (containing natural flavouring, artificial flavouring, Propylene Glycol (E1520)).

The product is manufactured by Wrafton Labratories, Braunton, Devon, EX33 2DL for the Marketing Authorisation Holder, Huntley Pharmaceuticals Ltd, 35A High Street, Marlborough, SN8 1LW. The product licence number is PL 21600/0001.
The UK distributors are UDG Ltd, Amber Park, South Normanton, Derbyshire, DE55 2FH.

Chloral hydrate is one of a group of medicines called hypnotics (sleep inducing drugs). Chloral Hydrate 143.3mg in 5ml Oral Solution is used to treat short term insomnia.

**Before taking your medicine**

Chloral Hydrate 143.3mg in 5ml Oral Solution contains Sunset Yellow FCF (E110) and Ponceau 4R (E124) which may cause allergic reactions.

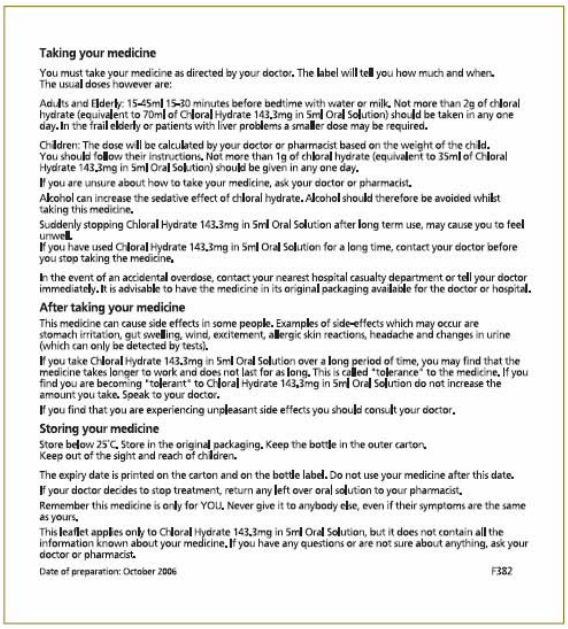
Chloral Hydrate 143.3mg in 5ml Oral Solution contains Propylene Glycol (E1520) which may cause alcohol-like symptoms.

If you have been told by your doctor that you have an intolerance to some sugars contact your doctor before taking this medicinal product.

- Are you suffering from severe heart, liver or kidney problems?
- Are you suffering from stomach problems (gastritis)?
- Are you allergic to any of the ingredients?
- Do you suffer from porphyria?
- Are you pregnant or breast feeding?
- Do you take any medicine to thin your blood (such as Warfarin)?
- Do you take any medicines for depression or nervous disorders?
- Do you take any medicines intended to reduce muscle spasms?

If you answer yes to any of these questions, tell your doctor or pharmacist before taking this medicine.

Please note, your ability to drive or operate hazardous machinery may be impaired by drowsiness as a result of taking Chloral Hydrate 143.3mg in 5ml Oral Solution.



**Taking your medicine**

You must take your medicine as directed by your doctor. The label will tell you how much and when. The usual doses however are:

Adults and Elderly: 15-45ml 15-20 minutes before bedtime with water or milk. Not more than 2g of chloral hydrate (equivalent to 70ml of Chloral Hydrate 143.3mg in 5ml Oral Solution) should be taken in any one day. In the frail elderly or patients with liver problems a smaller dose may be required.

Children: The dose will be calculated by your doctor or pharmacist based on the weight of the child. You should follow their instructions. Not more than 1g of chloral hydrate (equivalent to 35ml of Chloral Hydrate 143.3mg in 5ml Oral Solution) should be given in any one day.

If you are unsure about how to take your medicine, ask your doctor or pharmacist.

Alcohol can increase the sedative effect of chloral hydrate. Alcohol should therefore be avoided whilst taking this medicine.

Suddenly stopping Chloral Hydrate 143.3mg in 5ml Oral Solution after long term use, may cause you to feel unwell.
If you have used Chloral Hydrate 143.3mg in 5ml Oral Solution for a long time, contact your doctor before you stop taking the medicine.

In the event of an accidental overdose, contact your nearest hospital casualty department or tell your doctor immediately. It is advisable to have the medicine in its original packaging available for the doctor or hospital.

**After taking your medicine**

This medicine can cause side effects in some people. Examples of side-effects which may occur are stomach irritation, gut swelling, wind, excitement, allergic skin reactions, headache and changes in urine (which can only be detected by tests).

If you take Chloral Hydrate 143.3mg in 5ml Oral Solution over a long period of time, you may find that the medicine takes longer to work and does not last for as long. This is called "tolerance" to the medicine. If you find you are becoming "tolerant" to Chloral Hydrate 143.3mg in 5ml Oral Solution do not increase the amount you take. Speak to your doctor.

If you find that you are experiencing unpleasant side effects you should consult your doctor.

**Storing your medicine**

Store below 25°C. Store in the original packaging. Keep the bottle in the outer carton.
Keep out of the sight and reach of children.

The expiry date is printed on the carton and on the bottle label. Do not use your medicine after this date.

If your doctor decides to stop treatment, return any left over oral solution to your pharmacist.

Remember this medicine is only for YOU. Never give it to anybody else, even if their symptoms are the same as yours.

This leaflet applies only to Chloral Hydrate 143.3mg in 5ml Oral Solution, but it does not contain all the information known about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

Date of preparation: October 2006 F382

# CHLORAL HYDRATE 143.3 MG IN 5ML ORAL SOLUTION
# PL 21600/0001

## LABELLING

## CARTON