

**SOMNWELL 707MG FILM-COATED TABLETS  
PL 21600/0002**

**UKPAR**

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**SOMNWELL 707MG FILM-COATED TABLETS  
PL 21600/0002**

**LAY SUMMARY**

The MHRA granted Huntley Pharmaceuticals Limited a Marketing Authorisation (licence) for the medicinal product Somnwell 707mg Film-Coated Tablets on 20<sup>th</sup> March 2007. This product, to be available by prescription only (POM), contains chloral betaine and is used for the short-term treatment of insomnia.

The active ingredient chloral betaine is part of a group of medicines called hypnotics (sleeping tablets).

This application is a duplicate of a previously granted application for Welldorm Tablets, which were originally approved on 4<sup>th</sup> October 1988 to Chauvin Pharmaceuticals Limited (PL 00033/0032R). The current marketing authorisation holder for this product is Alphashow Limited (PL 21618/0001).

No new or unexpected safety concerns arose from this simple application and it was, therefore, judged that the benefits of taking Somnwell 707mg Film-Coated Tablets outweigh the risks, hence a Marketing Authorisation has been granted.

**SOMNWELL 707MG FILM-COATED TABLETS  
PL 21600/0002**

**SCIENTIFIC DISCUSSION**

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## **INTRODUCTION**

The UK granted a marketing authorisation for the medicinal product Somnwell 707mg Film-Coated Tablets (PL 21600/0002) to Huntley Pharmaceuticals Limited on 20<sup>th</sup> March 2007. The product is available as a prescription only medicine (POM).

The application was submitted as a simple abridged application according to Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC, cross-referring to Welldorm Tablets, which were originally approved on 4<sup>th</sup> October 1988 to Chauvin Pharmaceuticals Limited (PL 00033/0032R), but have since undergone a change of ownership on 30<sup>th</sup> December 1993 to Smith and Nephew Pharmaceuticals Limited (PL 13374/0004), followed by another change of ownership to the current marketing authorisation holder Alphashow Limited (PL 21618/0001) on 10<sup>th</sup> August 2004.

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 PAR was generated for it.

The active ingredient is chloral betaine, which completely dissociates in solution to give chloral hydrate and trimethylglycine (betaine). Chloral hydrate and its metabolite trichloroethanol act as central nervous system depressants, leading 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.

Somnwell 707 mg Film-coated Tablets are used for the short-term treatment of insomnia.

This application was subsequently cancelled on 5<sup>th</sup> September 2007.

# **PHARMACEUTICAL ASSESSMENT**

**LICENCE NO:** PL 21600/0002

**PROPRIETARY NAME:** Somnwell 707mg Film-Coated Tablets

**ACTIVE(S):** Chloral Betaine

**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, piggy back application for Somnwell 707mg Film-Coated Tablets submitted under Article 10c (formerly Article 10.1(a)(i)) of Directive 2001/83/EC. The proposed MA holder is Huntley Pharmaceuticals Ltd, 35A High Street, Marlborough, Wiltshire, SN8 1LW.

The application cross-refers to Welldorm Tablets, which were originally approved on 4<sup>th</sup> October 1988 to Chauvin Pharmaceuticals Limited (PL 00033/0032R), but have since undergone a change of ownership on 30<sup>th</sup> December 1993 to Smith and Nephew Pharmaceuticals Limited (PL 13374/0004), followed by another change of ownership to the current marketing authorisation holder Alphashow Limited (PL 21618/0001) on 10<sup>th</sup> August 2004.

The current application is considered valid.

## **2. MARKETING AUTHORISATION APPLICATION FORM**

### **2.1 Name(s)**

The proposed name of the product is Somnwell 707mg Film-Coated Tablets. 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 betaine, equivalent to 707mg. It is to be stored in a polyvinylidene chloride/polyvinylchloride/aluminium blisters in pack sizes of 56 tablets. The proposed shelf-life (3 years) and storage conditions (store in original package, do not refrigerate and store below 25 degrees) are consistent with the details registered for the cross-reference product.

### **2.3 Legal status**

On approval, the products will be available as prescription-only medicines (POM).

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

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

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.

## **2.9 Drug substance specification**

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

## **2.10 TSE Compliance**

No materials of animal or human origin are included in the 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.

### **Carton and blister**

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**

As this is a duplicate application, no new clinical data have been supplied and none are required.

## **OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT**

### **QUALITY**

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

### **PRECLINICAL**

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

### **EFFICACY**

This application is identical to a previously granted application for Welldorm Tablets (PL 00790/0100), currently authorised to Alphashow Limited (PL 21618/0001).

No new or unexpected safety concerns arise from these applications.

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. Extensive clinical experience with chloral betaine is considered to have demonstrated the therapeutic value of the compound. The risk:benefit is, therefore, considered to be positive.

**SOMNWELL 707MG FILM-COATED TABLETS  
PL 21600/0002**

**STEPS TAKEN FOR ASSESMENT**

1	The MHRA received the marketing authorisation application on 31/08/2004.
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 16/09/2004.
3	Following assessment of the application the MHRA requested further information on 12/01/2005, 24/02/2005 and 12/10/2006.
4	The applicant responded to the MHRA's requests, providing further information on 15/03/2005, 30/11/2005 and 13/03/2007.
5	The application was determined on 20/03/2007

**SOMNWELL 707MG FILM-COATED TABLETS  
PL 21600/0002**

**STEPS TAKEN AFTER ASSESSMENT**

<b>Date submitted</b>	<b>Application type</b>	<b>Scope</b>	<b>Outcome</b>

# SOMNWELL 707MG FILM-COATED TABLETS

## PL 21600/0002

### SUMMARY OF PRODUCT CHARACTERISTICS

#### 1 NAME OF THE MEDICINAL PRODUCT

Somnwell 707 mg Film-coated Tablets

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Somnwell Film-coated Tablet contains 707 mg Cloral betaine, equivalent to 414 mg of Chloral Hydrate.

For excipients, see 6.1.

#### 3 PHARMACEUTICAL FORM

Film-coated tablet

Elongated, bluish-purple coloured tablets with a smooth film coat.

#### 4 CLINICAL PARTICULARS

##### 4.1 Therapeutic indications

Somnwell 707 mg Film-coated Tablets are used for the short-term treatment of insomnia.

##### 4.2 Posology and method of administration

Route of administration: oral.

Adults: The hypnotic dose is one to two tablets 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: Somnwell 707 mg Film-coated Tablets are not suitable for use in children under 12 years of age. An oral solution of Chloral Hydrate is available.

##### 4.3 Contraindications

Somnwell 707 mg Film-coated Tablets should not be used in patients with a marked hepatic or renal impairment, or in patients with severe cardiac disease. Should not be used in patients susceptible to acute attacks of porphyria.

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

Best avoided in the presence of gastritis and in patients who have previously exhibited an idiosyncrasy or hypersensitivity to chloral hydrate.

##### 4.5 Interaction 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.

Delirium 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

Somnwell 707 mg Film-coated Tablets should not be used in pregnancy and lactation.

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

Patients receiving Somnwell 707 mg Film-coated Tablets 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 delirium.

#### **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**

Somnwell 707 mg Film-coated Tablets are 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 betaine completely dissociates in solution to give chloral hydrate and trimethylglycine (betaine). 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.

#### **5.3 Preclinical safety data**

Chloral betaine is hydrolysed in the stomach to chloral hydrate, which 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**

##### Tablet core

Povidone  
Maize starch  
Sodium citrate  
Purified talc  
Magnesium stearate

##### Film-coat

Hypromellose (E464)  
Hydroxypropyl cellulose (E463)  
Macrogol 400  
Macrogol 8000  
Disodium edatate  
Azorubine Carmoisine (E122)  
Titanium dioxide (E171)

Brilliant blue FCF aluminium lake (E133)  
Sodium methyl parahydroxybenzoate (E219)  
Sodium propyl parahydroxybenzoate (E217)

**6.2 Incompatibilities**

None known

**6.3 Shelf life**

3 years

**6.4 Special precautions for storage**

Store below 25°C.

Do not refrigerate.

Store in the original package.

**6.5 Nature and contents of container**

Aluminium foil topped opaque PVC-PVdC blister packs each containing 14 Somnwell Film-coated Tablets, presented in a carton, a pack size 56 is available.

**6.6 Special precautions for disposal**

No special requirements.

**7 MARKETING AUTHORISATION HOLDER**

Huntley Pharmaceuticals Ltd

35A High Street

Marlborough

Wiltshire

SN8 1LW

**8 MARKETING AUTHORISATION NUMBER(S)**

PL 21600/0002

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

20/03/2007

**10 DATE OF REVISION OF THE TEXT**

20/03/2007

**SOMNWELL 707MG FILM-COATED TABLETS  
PL 21600/0002**

# Somnwell 707mg Film-coated tablets (Cloral Betaine)



## What you should know about Somnwell 707mg Film-coated tablets, (Cloral Betaine)

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 SOMNWELL 707mg Film-coated tablets. 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 SOMNWELL 707mg Film-coated tablets. They are elongated, bluish-purple coloured tablets with a smooth film coat containing 707mg of Cloral Betaine (equivalent to 414mg chloral hydrate) per tablet. A pack size of 56 blister packed tablets is available.

In addition to Cloral Betaine, SOMNWELL 707mg Film-coated tablets contain Povidone, Maize Starch, Sodium Citrate, Purified Talc, Magnesium Stearate, Hydromellose (E464), Hydroxypropyl Cellulose (E463), Macrogol 400, Macrogol 8000, Disodium Edetate, azorubine carmoisine (E122), Brilliant Blue FCF aluminium lake (E133), Titanium Dioxide (E171), Sodium methyl parahydroxybenzoate (E219), Sodium propyl parahydroxybenzoate (E217).

Ashton Pharmaceuticals Limited, Vale of Bardsley, Ashton-under-Lyne, Lancashire manufacture SOMNWELL 707mg Film-coated tablets for the Product Licence holder, Huntley Pharmaceuticals Ltd, 35A High Street, Marlborough, SN8 1LW. The Product Licence number is PL 21600/0002. The UK distributors are UDG Ltd, Amber Park, South Normanton, Derbyshire, DE55 2FH.

Chloral hydrate is one of a group of medicines called hypnotics ('sleeping tablets'). SOMNWELL 707mg Film-coated tablets are used for the short-term treatment of insomnia.

### Before taking your medicine

Somnwell 707mg Film-coated tablets contain azorubine carmoisine (E122), which may cause an allergic reaction. Somnwell 707mg Film-coated tablets contain Sodium methyl parahydroxybenzoate (E219) and Sodium propyl parahydroxybenzoate (E217) which may cause allergic reactions (possibly delayed).

- 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?
- Are you under 12 years old?
- 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 SOMNWELL 707mg Film-coated tablets.



## **Taking your medicine**

You must use your medicine as directed by your doctor. Swallow the tablets with water or milk. The label will tell you how many and when. The usual adult dose is 1-2 tablets 15-30 minutes before bedtime. The dose should not exceed 4 tablets per day. The dose for elderly people is the same as for adults. Frail elderly people or those with liver problems may require a lower dose. *Children: SOMNWEELL 707mg Film-coated tablets are not suitable for children under 12 years of age. An oral solution of CHLORAL HYDRATE is available.* 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 SOMNWEELL 707mg Film-coated tablets after long term use, may cause you to feel unwell. If you have used SOMNWEELL 707mg Film-coated tablets for a long time, contact your doctor before you stop taking the tablets.

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 the urine (which can only be detected by tests).

If you take SOMNWEELL 707mg Film-coated tablets over a long period of time, you may find that the tablets take longer to work and do not last for as long. This is called "tolerance" to the medicine. If you find you are becoming "tolerant" to SOMNWEELL 707mg Film-coated tablets do not increase the number 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 your medicine below 25°C. Do not refrigerate. Store in the original package. Keep out of the sight and reach of children.

The expiry date is printed on the side panel of the carton and on the tablet blisters. Do not use your medicine after this date.

If your doctor decides to stop treatment, return any left over tablets 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 SOMNWEELL 707mg Film-coated tablets, 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

P1150B

**SOMNWELL 707MG FILM-COATED TABLETS  
PL 21600/0002**

**LABELLING**

**HP** Huntley Pharmaceuticals Ltd.

Store below 25°C. Do not refrigerate.  
Store in the original package.

**Somnwell 707mg**  
Film Coated Tablets  
(CLORAL BETAINE)

Also contains azorubine carmoisine (E122),  
Sodium methyl parahydroxybenzoate (E219)  
and Sodium propyl parahydroxybenzoate (E217)

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