PRODUCT INFORMATION

1.3 Product Information

1.3.1 Summary of Product Characteristics

Summary of product characteristic is attached.

SUMMARY OF PRODUCT CHARACTERISTICS

1. Trade name of medicinal product

Udihep Tablets

2. Qualitative and Quantitative Composition

S. No.	Name of Excipients	Concentration (mg/tablet)	Reference to Standard	Function
1.	Ursodeoxycholic Acid	150.00	BP	Gall Stone solubilizing agent
2.	Croscarmellose Sodium (Ac-Di-Sol)	5.00	BP	Disintegrant
3.	Colloidal Anhydrous Silica (Aerosil -200)	0.60	BP	Lubricant
4.	Lactose	20.40	BP	Diluent
5.	Magnesium Stearate	3.50	BP	Glidant & Lubricant
6.	Microcrystalline Cellulose (Avicel PH-102)	12.50	BP	Diluent
7.	Povidone (K-30)	8.00	BP	Binder
	Total	200		

3. Pharmaceutical form

Oral Tablets

4. Clinical Particulars

4.1 Therapeutic indications

1. For the treatment of patient with chronic cholestatic liver diseases in particular primary billiary cirrhosis, primary sclerosing cholangitis and cholestasis associated with cystic fibrosis.
2. For the dissolution of radiolucent, non-calcified gall bladder stones (which are less than 10 mm in diameter) in patients with functional gall bladder. It is also indicated in patients for whom elective cholecystectomy cannot be undertaken due to presence of increased surgical risk due to systemic diseases, advanced age, idiosyncratic reaction to general anaesthesia, or for those patients who refuse surgery.
3. For the prevention of gall stone formation in obese patients experiencing rapid weight loss due to intensive dieting and for patients who are prone to developing gall bladder stones.

4. For relief of symptoms of cholestasis in the management of chronic hepatitis, intrahepatic cholestasis of pregnancy and cirrhosis.
5. For relief of symptoms of cholestasis in post-liver transplant rejection, graft-versus-host disease, alcoholic and non alcoholic steatohepatitis, and viral hepatitis.

4.2 Posology and Method of Administration

The recommended adult dose for Udihep in treatment of primary billiary cirrhosis is 13 to 15 mg/kg/day administered in four divided doses with food.

Gall Stone Treatment- The recommended dose of Udihep treatment of radiolucent gall bladder stones is 8-15 mg/kg of body weight/day given in 2-4 divided doses. Bedtime administration is advocated; the rationale is to enhance bile acid secretion during the night, when it normally is lowest and cholesterol saturation is highest.

Ultrasound images of the gall-bladder should be obtained at 6-months intervals for the first year of Udihep therapy to monitor gall stone response. If gallstones appear to have dissolved, Udihep therapy should be continued and dissolution confirmed on a repeat ultrasound examination within 1 to 3 months. Most patients who eventually achieve complete stone dissolution will show partial or complete dissolution at the first on-treatment re-evaluation. If partial stone dissolution is not seen by 12 months of Udihep therapy, the likelihood of success is greatly reduced.

Gall Stone Prevention- The recommended dose of Udihep for gall stone prevention in patients undergoing rapid weight loss is 600 mg/day (300 mg BID).

The recommended dose for cholestasis is 8-15 mg/kg/day, in 2-4 divided doses, after meals.

In a placebo-controlled cross over study, administration of Ursodiol for 4 weeks led to reduction in serum bilirubin levels, as well as serum aminotransferases, gamma-glutamyl transpeptidase and alkaline phosphatase levels in patients with alcoholic liver cirrhosis who continued to drink. Treatment of non-alcoholic steatohepatitis with ursodiol for 12 months resulted in significant improvement in alkaline phosphatase, ALT, GGT and hepatic steatosis.
Ursodiol has been successfully used in the treatment of cholestasis of pregnancy with no ill effects to the mother or the baby. The usual starting dose is 12- 15 mg/kg/day.
Ursodiol has been used in the treatment of acute viral hepatitis using a daily dose of 600 mg for a period of 4 months.

In a controlled trial, prophylactic treatment with Ursodiol at a dose of 600-900 mg/day significantly decreased the incidence of veno-occlusive disease (VOD) after allogeneic bone marrow trans-plantation.

4.3 Contraindications

Hypersensitivity to bile acids; radio-opaque stones; non-functioning gall bladder.

4.4 Special warnings and special precautions for use

Pregnancy: Category-B. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be appraised of potential risk to the fetus.

Lactation: It is not known whether ursodiol is excreted in human milk. Caution should be exercised when ursodiol is administered to a nursing mother.

4.5 Interaction with other medicinal products and other forms of Interaction

Cholestyramine or colestipol may interfere with the action of ursodiol by reducing its absorption. Aluminium based antacids have been shown to absorb bile acid *in vitro* and may be expected to interfere with ursodiol in the same manner as the sequestering agents. Estrogens, oral contraceptives and fibrates increase biliary cholesterol secretion and hence may counteract the effectiveness of ursodiol.

4.6 Pregnancy and lactation

Pregnancy: Category-B. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be appraised of potential risk to the fetus.

Lactation: It is not known whether ursodiol is excreted in human milk. Caution should be exercised when ursodiol is administered to a nursing mother.

4.7 Effects on ability to drive and use machines

Not Applicable

4.8 Side effects

The following side effects have been reported with the use of ursodeoxycholic: diarrhoea, exacerbation of pre-existing psoriasis, rash, urticaria, dry skin, sweating, hair thinning, leucopenia, stomatitis, flatulence, headache, fatigue, anxiety, depression, sleep disorder, arthralgia, myalgia, back pain, cough and rhinitis.

4.9 Overdose and its treatment

Accidental or intentional over dosage of ursodiol has not been reported and would probably result only in self-limiting acute diarrhoea, which should be treated symptomatically. Monitor liver function tests. May use ion-exchange resins.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Ursodeoxycholic Acid (ursodiol) is a naturally occurring bile acid. The various mechanisms of action of this hydrophilic bile acid include direct cytoprotection, detergent action on dysfunctional microtubules, immunomodulation and induction of hypercholeresis.

5.2 Pharmacokinetic properties

About 90% of a therapeutic dose of ursodiol is absorbed in the small bowel after oral administration. After absorption, ursodiol enters the portal vein and undergoes extraction from portal blood by the liver (i.e., "first-pass" effect) where it is conjugated with either glycine or taurine and is then secreted into the hepatic bile ducts. Ursodiol in bile is concentrated in the gall bladder and expelled into the duodenum in gallbladder bile via the cystic and common ducts by gallbladder contractions produced by physiological responses to eating.

Small quantities of ursodiol appear in the systemic circulation and very small amounts are excreted into urine. A small portion of orally administered drug undergoes bacterial degradation with each cycle of enterohepatic circulation. Ursodiol can be both oxidized and reduced, yielding either 7-keto-lithocholic acid or Lithocholic acid, respectively. Free Ursodiol, 7-keto-lithocholic acid and Lithocholic acids are relatively insoluble in aqueous media and larger proportions of these compounds are excreted via the feces. Reabsorbed free ursodiol is reconjugated by the liver. Eighty percent of the Lithocholic acid formed in the small bowel is excreted in the feces, but the 20% that is absorbed is sulfated in the liver to relatively insoluble lithocholyl conjugates

which are excreted into bile and lost in feces. Absorbed 7-keto-lithocholic acid is stereo specifically reduced in the liver to chenodiol.

5.3 Preclinical safety data

Single oral doses of Ursodiol at 10, 5 and 10 g/kg in mice, rats and dogs, respectively were not lethal. A single oral dose of Ursodiol at 1.5 g/kg was lethal in hamsters. Symptoms of acute toxicity were salivation and vomiting in dogs, and ataxia, dyspnea, ptosis, agonal convulsions and coma in hamsters.

6. Pharmaceutical Particulars

6.1 List of Excipients

S. No.	Name of Excipients
1.	Croscarmellose Sodium (Ac-Di-Sol)
2.	Colloidal Anhydrous Silica (Aerosil -200)
3.	Lactose
4.	Magnesium Stearate
5.	Microcrystalline Cellulose (Avicel PH-102)
6.	Povidone (K-30)

6.2 Incompatibilities

None of the incompatibilities has been reported.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C, protected from light & moisture.

6.5 Nature and content of container

Primary Packaging

Udihep Tablets are packed in blister strips made up of printed aluminium foil (width 80 mm × thickness 0.025 mm) and Clear PVC rigid film (width 84 mm × thickness 0.25 mm).

Secondary Packaging

The blister strip of 3 x 10s is packaged in an outer carton comprising of Laminated Indian duplex board with tucking on both sides and contain a package insert comprising of Cream wove art paper.

Pack size

Box of 3x 10's

6.6 Instructions for use/handling

Keep the medicine out of reach of the children
The tablets should be swallowed whole and not chewed.

7.0 MARKETING AUTHORISATION HOLDER

Win-Medicare Pvt. Ltd.

8.0 MARKETING AUTHORISATION NUMBER(S)

B4-1236

9.0 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28th Nov 2013

10.0 DATE OF REVISION OF THE TEXT

12th Dec.2019

1.3.2 Labelling (outer & inner labels)

Please find the enclosed mock ups of Udihep tablets.

Rx 150 mg 30 Tablets

Udihep™

Ursodeoxycholic Acid Tablets BP

Rx Udihep™ 150 mg

Win-Medicare*

Manufactured by :
WIN-MEDICARE PVT. LTD.
Modipuram-250 110, U.P., India.

8 901815 002376

MMP 9335

PMCA310 Ed. III / 06.16

Rx

Udihep™

Ursodeoxycholic Acid Tablets BP

Each uncoated tablet contains :
Ursodeoxycholic Acid BP : 150 mg

Dosage : As directed by the physician.

For full prescribing information, please consult package insert.

Keep out of reach of children.

Store at a temperature not exceeding 30°C, protected from light and moisture.

WARNING : To be sold by retail on the prescription of a Registered Medical Practitioner only.

Mfg. Lic. No. 14/84

NAFDAC Reg. No: B4-1236

Imported and Distributed by :
Phillips Pharmaceuticals (Nigeria) Limited.
122-132, Afprint Industrial Estate,
Apapa-Oshodi Expressway,
Iyana-Isolo, Lagos, Nigeria.

Marketed by :
Win-Medicare
WIN-MEDICARE PVT. LTD.
Office :
1400, Modi Tower, 98, Nehru Place,
New Delhi-110 019, India.

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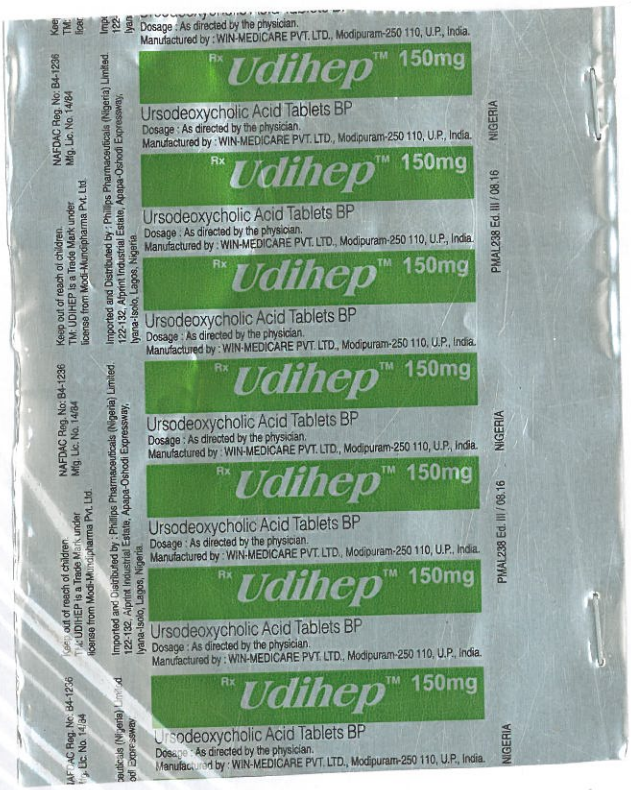
TM: UDIHEP is a Trade Mark under license from Modi-Mundipharma Pvt. Ltd.

* : Trade Mark in India of Win-Medicare Pvt. Ltd.


Dosage : As directed by the physician.
Manufactured by : WIN-MEDICARE PVT. LTD., Modipuram-250 110, U.P., India.
Rx Udihep™ 150mg
Ursodeoxycholic Acid Tablets BP
Dosage : As directed by the physician.
Manufactured by : WIN-MEDICARE PVT. LTD., Modipuram-250 110, U.P., India.
NAFDAC Reg. No: 04-1236
Mfg. Lic. No. 14/84
Keep out of reach of children.
TM: UDIHEP is a Trade Mark under license from Modi-Mundipharma Pvt. Ltd.
Imported and Distributed by : Phillips Pharmaceuticals (Nigeria) Limited. 122-132, Alprint Industrial Estate, Apapa-Oshodi Expressway, Iyana-Isolo, Lagos, Nigeria.
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1.3.3 Packaging Insert (also known as patient information PIL)

Pack insert of Udihep tablets is enclosed.

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory.

Rx

Udihep™

Ursodeoxycholic Acid Tablets BP

Composition :
Each uncoated tablet contains :
Ursodeoxycholic Acid BP : 150 mg

Actions :
Ursodeoxycholic Acid (Ursodiol) is a naturally occurring bile acid. The various mechanisms of action of this hydrophilic bile acid include direct cytoprotection, detergent action on dysfunctional microtubules, immunomodulation and induction of hypercholeresis.

Indications :
1. For the treatment of patients with chronic cholestatic liver diseases in particular primary biliary cirrhosis, primary sclerosing cholangitis and cholestasis associated with cystic fibrosis.
2. For the dissolution of radiolucent, non-calcified gall bladder stones (which are less than 10 mm in diameter) in patients with functional gall bladder. It is also indicated in patients for whom elective cholecystectomy cannot be undertaken due to presence of increased surgical risk due to systemic diseases, advanced age, idiosyncratic reaction to general anaesthesia, or for those patients who refuse surgery.
3. For the prevention of gall stone formation in obese patients experiencing rapid weight loss due to intensive dieting and for patients who are prone to developing gall bladder stones.
4. For relief of symptoms of cholestasis in the management of chronic hepatitis, intrahepatic cholestasis of pregnancy and cirrhosis.
5. For relief of symptoms of cholestasis in post-liver transplant rejection, graft-versus-host disease, alcoholic and non-alcoholic steatohepatitis, and viral hepatitis.

Pharmacokinetics :
About 90% of a therapeutic dose of ursodiol is absorbed in the small bowel after oral administration. After absorption, ursodiol enters the portal vein and undergoes extraction from portal blood by the liver (ie, "first-pass" effect) where it is conjugated with either glycine or taurine and is then secreted into the hepatic bile ducts. Ursodiol in bile is concentrated in the gall bladder and expelled into the duodenum in gall bladder bile via the cystic and common ducts by gall bladder contractions produced by physiological responses to eating.

Small quantities of ursodiol appear in the systemic circulation and very small amounts are excreted into urine. A small portion of orally administered drug undergoes bacterial degradation with each cycle of enterohepatic circulation. Ursodiol can both be oxidized and reduced, yielding either 7-keto-lithocholic acid or lithocholic acid, respectively. Free Ursodiol, 7-keto-lithocholic acid and lithocholic acid are relatively insoluble in aqueous media and larger proportions of these compounds are excreted via the feces. Reabsorbed free ursodiol is reconjugated by the liver. Eighty percent of lithocholic acid formed in the small bowel is excreted in the feces, but the 20% that is absorbed is sulphated in the liver to relatively insoluble lithocholyl conjugates which are excreted into the bile and lost in the feces. Absorbed 7-keto-lithocholic acid is stereospecifically reduced in the liver to chenodiol.

Dosage and Administration:
The recommended adult dosage for Udihep™ in the treatment of Primary biliary cirrhosis is 13-15 mg/kg/day administered in four divided doses with food.

Gall Stone Treatment-The recommended dose of Udihep™ treatment of radiolucent gall bladder stones is 8-15 mg/kg of body weight/day given in 2 - 4 divided doses. Bedtime administration is advocated; the rationale is to enhance bile acid secretion during the night, when it normally is lowest and cholesterol saturation is highest.

Ultrasound images of the gall bladder should be obtained at 6-months intervals for the first year of Udihep™therapy to monitor gall stone response. If gallstones appear to have dissolved, Udihep™ therapy should be continued and dissolution confirmed on a repeat ultrasound examination within 1 to 3 months. Most patients who eventually achieve complete stone dissolution will show partial or complete dissolution at the first on-treatment re-evaluation. If partial stone dissolution is not seen by 12 months of Udihep™ therapy, the likelihood of success is greatly reduced.

Gall Stone Prevention-The recommended dose of Udihep™ for gall stone prevention in patients undergoing rapid weight loss is 600 mg/day (300 mg BID).

The recommended dose for cholestasis is 8-15 mg/ kg/ day, in 2-4 divided doses, after meals.

In a placebo-controlled cross over study, administration of Ursodiol for 4 weeks led to a reduction in serum bilirubin levels, as well as serum aminotransferases, gamma- glutamyl transpeptidase and alkaline phosphatase levels in patients with alcoholic liver cirrhosis who continued to drink. Treatment of Non-alcoholic steatohepatitis with ursodiol for 12 months resulted in significant improvement in alkaline phosphatase, ALT, GGT & hepatic steatosis.

Ursodiol has been successfully used in the treatment of cholestasis of pregnancy with no ill effects to the mother or the baby. The usual starting dose is 12-15 mg/kg/day.

Ursodiol has been used in the treatment of acute viral hepatitis using a daily dose of 600 mg for a period of 4 months.

In a controlled trial, prophylactic treatment with Ursodiol at a dose of 600 – 900 mg/day significantly decreased the incidence of veno - occlusive disease (VOD) after allogeneic bone marrow trans-plantation

Contraindications :
Hypersensitivity to bile acids; radio-opaque stones; non-functioning gall bladder.

Precautions :
Pregnancy : Category - B. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be appraised of potential risk to the fetus.

Lactation : It is not known whether ursodiol is excreted in human milk. Caution should be exercised when ursodiol is administered to a nursing mother.

Drug Interactions : Cholestyramine or colestipol may interfere with the action of ursodiol by reducing its absorption. Aluminium based antacids have been shown to absorb bile acid in vitro and may be expected to interfere with ursodiol in the same manner as the sequestering agents. Estrogens, oral contraceptives and fibrates increase biliary cholesterol secretion and hence may counteract the effectiveness of ursodiol.

Side effects :
The following side effects have been reported with the use of ursodeoxycholic : diarrhoea, exacerbation of pre-existing psoriasis, rash, urticaria, dry skin, sweating, hair thinning, leucopenia, stomatitis, flatulence, headache, fatigue, anxiety, depression, sleep disorder, arthralgia, myalgia, back pain, cough and rhinitis.

Overdosage :
Accidental or intentional overdosage of ursodiol has not been reported and would probably result only in self-limiting acute diarrhoea which should be treated symptomatically. Monitor liver function tests. May use ion-exchange resins.

Storage :
Store at a temperature not exceeding 30°C, protected from light and moisture.
Keep out of reach of children.

Shelf life :
24 months from date of manufacturing.

Presentation :
Box of 30 tablets (3 strips of 10 tablets each).

TM: UDIHEP is a Trade Mark under license from Modi-Mundipharma Pvt. Ltd.

Manufactured by :
WIN-MEDICARE PVT. LTD.
Modipuram-250 110, U.P., India.

NAFDAC Reg. No: B4-1236

Imported and Distributed by :
Phillips Pharmaceuticals (Nigeria) Limited.
122-132, Afprint Industrial Estate,
Apapa-Oshodi Expressway, Iyana-Isolo, Lagos, Nigeria.

Marketed by :
Win-Medicare
WIN-MEDICARE PVT. LTD.
Office :
1400, Modi Tower, 98, Nehru Place,
New Delhi-110 019, India.

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