1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

1. Name of the medicinal product

DROTAVERINE HYDROCHLORIDE AND PARACETAMOL TABLETS

2. Qualitative and quantitative composition

ACTIVE INGREDIENTS				
APPROVED NAME	SPECIFICATION OR REFERENCE TEXT	QTY/ TABLET		% OVERAGES
		MG/ TABLET	%W/W/ TABLET	
Drotaverine Hydrochloride	INHOUSE	80.000 mg	8.839 %	0.00 %
Paracetamol	BP	500.000 mg	55.248 %	0.00 %
INACTIVE INGREDIENTS				
APPROVED NAME	SPECIFICATION OR REFERENCE TEXT	QTY/ TABLET		REASON FOR INCLUSION
		MG/ TABLET	%W/W/ TABLET	
Dibasic Calcium Phosphate	BP	50.000 mg	5.524 %	Diluent
Maize Starch	BP	110.000 mg	12.154 %	Diluent
Microcrystalline Cellulose	BP	71.000 mg	7.845 %	Diluent
Demineral Water	INHOUSE	0.030 ml	0.003 %	Vehicle
Maize Starch	BP	40.000 mg	4.419 %	Binder
Povidone	BP	15.000 mg	1.657 %	Binder
Magnesium Stearate	BP	8.000 mg	0.883 %	Lubricant
Purified Talc	BP	14.000 mg	1.546 %	Glidant
Croscarmellose Sodium	BP	10.000 mg	1.104 %	Disintegrant
Colloidal Silicon Dioxide	USP	2.000 mg	0.220 %	Glidant
Isopropyl Alcohol*	BP	0.500 ml	-	Solvent
Acetone*	BP	0.500 ml	-	Solvent
Iron Oxide Yellow colour	INHOUSE	1.000 mg	0.110 %	Colour
Wesco Coating Material	INHOUSE	3.500 mg	0.386 %	Coating
Titanium Dioxide	BP	0.500 mg	0.055 %	Colour

*Evaporates during manufacturing, does not remain in final formulation.

3. Pharmaceutical form

Oral Tablet

4. Clinical particulars

4.1 Therapeutic indications

Drotaverine Hydrochloride and Paracetamol Tablet is indicated for treatment of a wide range of gastrointestinal disorders, including such conditions as peptic ulcer, gastritis, hyperchlorhydria, functional diarrhea, irritable or spastic colon, pyloroduodenal irritability, pylorospasm, acute nonspecific gastroenteritis, biliary dyskinesia and chronic cholelithiasis, duodenitis, gastrointestinal spasm; it may also be used to treat genitourinary spasm.

4.2 Posology and method of administration

Adult dose: Oral: 80 - 500 mg tablet twice daily or as directed by physician
Children: 80 - 500 mg/day in 3 divided doses or as directed by physician. Dose is depending upon the age of the patient.

4.3 Contraindications

Hypersensitivity to the active component or to an excipient
Drotaverine: Severe hepatic or renal failure, severe heart failure, AV blockade II and III grades, cardiogenic shock, arterial hypotension, childish age younger 12.
Paracetamol: Severe and active hepatic impairment.

4.4 Special warnings and precautions for use

Drotaverine: Caution should be exercised when Drotaverine is prescribed at the same time with Magnesium hydroxide cause increase in drug absorption.
Caution should be exercised when prescribing Drotaverine to patients with lithium toxicity as it increases lithium toxicity which can be fatal.
Drotaverine for which dosage adjustments may be required in patients with renal impairment since drotaverine and its metabolites are excreted by kidneys.
Drotaverin has the potential to decrease the antiparkinsonian effect of levodopa resulting in increase in rigidity and tremor. In patients of parkinson Drotaverine is not recommended.
Paracetamol: Keep out of reach of children.

- Do not take if allergic to paracetamol.
- Patients should contact their health careprovider if symptomspersist.
- Paracetamol should be given with care to patients with impaired kidney or liver function.
- Large doses should be avoided in patients with hepatic impairment. Paracetamol overdose may harm the liver.
- Do not exceed recommended dose.
- It should be given with care to patients with alcohol dependence.
- Paracetamol provides symptomatic relief only, additional therapy to treat the cause of the pain or fever should be instituted when necessary.

4.5 Interaction with other medicinal products and other forms of interaction

Drotaverine: It enhances other spasmolytics effect, hypotension caused by three-cyclic anti-depressants, quinidine, procainamide. It reduces the morphine spasmogenic activity, anti-parkinsonic properties of levodopa rigidity increase. Phenobarbital improves the spasm removal reliability.

Paracetamol: Substances that induce or regulate hepatic cytochrome enzyme CYP2E1 may alter the metabolism of acetaminophen and increase its hepatotoxic potential.
Acetaminophen injection should be administered only as a 15 minute anticoagulant.

4.6 Pregnancy and lactation

Drotaverine: Drotaverine should not to be used in pregnancy.

Paracetamol:
Use in pregnancy:
- Considered to be the analgesic of choice in pregnant patients.
- Although it crosses placenta, paracetamol is considered to be safe in normal therapeutic doses for short term use as a minor analgesic/antipyretic in pregnancy.
  Use in lactation:
- Excreted in breast milk.
- Maternal ingestion of paracetamol in normal therapeutic doses does not appear to present a risk to the nursing infant.

4.7 Effects on ability to drive and use machines

If you experience drowsiness, dizziness, hypotension or a headache as side-effects when using Drotaverine Hydrochloride / Paracetamol medicine then it may not be safe to drive a vehicle or operate heavy machinery.

4.8 Undesirable effects

Drotaverine: After the oral dose appearance of feeling of heat, dizziness, headache, insomnia are possible; arrhythmia, hypotension, tachycardia, sweating, nausea, constipation may be observed. In some patients, especially in persons being hypersensitive to bisulphites allergic reactions – allergic dermatitis as a rule – are possible; extremely rarely in asthmatic patients or in those having had allergic reactions in the anamnesis anaphylactic reactions, bronchospasm are possible.
Paracetamol: Adverse effects of paracetamol are rare and usually mild, although haematological reactions have been reported. Skin rashes and other hypersensitivity reactions occur occasionally.

4.9 Overdose

Drotaverine:
- Do not use more than prescribed dose. Taking more medication will not improve your symptoms; rather they may cause poisoning or serious side-effects. If you suspect that you or anyone else who may have overdosed of _Drotaverine tablet, please go to the emergency department of the closest hospital or nursing home. Bring a medicine box, container, or label with you to help doctors with necessary information.
- Do not give your medicines to other people even if you know that they have the same condition or it seems that they may have similar conditions. This may lead to overdosage.

Paracetamol:

Symptoms: Toxic symptoms include vomiting, abdominal pain, hypotension and sweating. The most serious adverse effect of acute overdose of paracetamol is a dose-dependent, potentially fatal hepatic necrosis. Clinical and laboratory evidence of hepatoxicity may be delayed for up to one week. Major manifestations of liver failure such as jaundice, hypoglycemia and metabolic acidosis may take at least 3 days to develop.
Treatment: In cases of overdose, methods of reducing the absorption of ingested drug are important. Gastric lavage is essential even if several hours have elapsed. Prompt administration of 50g activated charcoal and 500ml iced mannitol 20% by mouth, may reduce absorption.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Drotaverine: Drotaverine is a spasmolytic agent by inhibiting PDE4 in smooth muscle cells.
Drotaverine inhibits phosphodiesterases hydrolysing cAMP, thereby increasing cAMP concentration, decreasing Ca uptake of the cells and changing the distribution of calcium among the cells. It may also have minor allosteric calcium channel blocking properties.
Paracetamol: Acetaminophen (USAN) or Paracetamol (INN) is a widely used analgesic and antipyretic drug that is used for the relief of fever, headaches, and other minor aches and pains. It is a major ingredient in numerous cold and flu medications and many prescription analgesics. It is extremely safe in standard doses, but because of its wide availability, deliberate or accidental overdoses are not uncommon. Acetaminophen, unlike other common analgesics such as aspirin and ibuprofen, has no anti-inflammatory properties or effects on platelet function, and it is not a member of the class of drugs known as non-steroidal anti-inflammatory drugs or NSAIDs. At therapeutic doses acetaminophen does not irritate the lining of the stomach nor affect blood coagulation, kidney function, or the fetal ductus arteriosus (as NSAIDs can). Like NSAIDs and unlike opioid analgesics, acetaminophen does not cause euphoria or alter mood in any way. Acetaminophen and NSAIDs have the benefit of being completely free of problems with addiction, dependence, tolerance and withdrawal. Acetaminophen is used on its own or in combination with pseudoephedrine, dextromethorphan, chlorpheniramine, diphenhydramine, doxylamine, codeine, hydrocodone, or oxycodone.

5.2 Pharmacokinetic properties

Drotaverine: Drotaverine 95 – 98% of it fixes with plasma proteins. It is distributed evenly in tissues, penetrates into non-striated muscles cells. It does not pass through the HEB. The preparation is excreted mostly by the kidneys, in a smaller volume with the bile.
Paracetamol: Oral administration of paracetamol is rapidly absorbed.
Paracetamol absorption takes place mainly in the small intestine and therefore the rate of absorption is depending on the rate of gastric emptying. It has been shown that drugs which delay gastric emptying also delay the absorption of paracetamol whereas metoclopramide accelerates absorption of the analgesic through the total amount absorbed doses not increase.
The presence of food in the stomach has also been reported to reduce the rate of absorption of paracetamol. Alterations in gastric pH have no appreciable effect on paracetamol absorption.
During absorption, the amount of paracetamol which is inactivated is negligiable and it has been shown that paracetamol does not affect gastric mucosal permeability and does not produce

mucosal bleeding. Peak plasma concentrations are reached 1 hour after absorption. The plasma half-life is 1 to 3 hours.
Paracetamol penetrates the brain and is present in breast milk of human.
Paracetamol is metabolized by the microsomal enzyme system of the liver. This metabolism is mainly to the glucuronide and sulphate conjugates, accounting for approximately 49% and 26% of the ingested dose respectively. About 4% is excreted as free paracetamol. Other minor pathways include the production of catechol derivatives and cysteine conjugates (via glutathione). Paracetamol excretion is rapid.

5.3 Preclinical safety data

No Data Found.

6. Pharmaceutical particulars

6.1 List of Excipients

- Dibasic Calcium Phosphate
- Maize Starch
- Microcrystalline Cellulose
- Demineral Water
- Povidone
- Magnesium Stearate
- Purified Talc
- Croscarmellose Sodium
- Colloidal Silicon Dioxide
- Isopropyl Alcohol
- Acetone
- Iron Oxide Yellow colour
- Wesco Coating Material
- Titanium Dioxide

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store in a dry place at a temperature below 30°C.

6.5 Nature and contents of container

1 X 10 Tablets Alu-Alu pack, packed in printed and laminated carton.

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing authorisation holder

West Coast Pharmaceutical Works Ltd, Ahmedabad

8. Marketing authorisation number(s)

Not applicable.

9. Date of first authorisation/renewal of the authorisation

Not applicable.

10. Date of revision of the text

January, 2018