Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Spasmodex-P

2. Qualitative and quantitative composition

Each film coated tablet contains paracetamol 500mg and Hyoscine butylbromide 10mg
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet

4. Clinical particulars

4.1 Therapeutic indications

Hyoscine butylbromide + Paracetamol is an antispasmodic-analgesic combination used for the relief from the pain of stronger abdominal cramps including menstrual cramps and urinary tract spasm.

4.2 Posology and method of administration

Posology
The following doses are recommended: Adults: 1-2 tablets, 3 times daily. The total daily dose should not exceed 6 tablets.
Pediatric population: Not suitable for children under 10 years of age.
Hyoscine butylbromide + Paracetamol should not be taken over prolonged period of time (for more than 3 days) without a prescription from the physician.

Method of administration
For oral administration only.
Should be swallowed whole with adequate water.

4.3 Contraindications

Hypersensitivity to any of Excipients listed in section 6.1.
Myasthenia gravis
Mechanical stenosis in the gastrointestinal tract
Paralytic or obstructive ileus
Megacolon
Severe hepatocellular insufficiency (Child-Pugh C)

4.4 Special warnings and precautions for use

Seek medical advice in case of persisting severe, unexplained abdominal pain w/ symptoms eg, fever, nausea, vomiting, changes in bowel movement, abdominal tenderness, decreased BP, fainting or blood in stool.

Hyoscine butylbromide + Paracetamol should be used with caution in: glucose-6-phosphatedehydrogenase deficiency, hepatic dysfunction (e.g. due to chronic alcohol abuse, hepatitis), impaired renal function, Gilbert's syndrome, and hepatocellular insufficiency (Child-Pugh A/B).

Hyoscine butylbromide + Paracetamol should not be taken for more than 3 days unless directed by a physician. The patient should be instructed to seek medical advice, if pain persists or gets worse, if new symptoms occur, or if redness or swelling is present because these could be signs of a serious condition.

Patients prone to narrow-angle glaucoma, susceptible to intestinal or urinary outlet obstructions & inclined to tachyarrhythmia.

To prevent overdosing, it should be ensured that any other drugs taken concurrently do not contain paracetamol, one of the active components of Hyoscine butylbromide + Paracetamol. Liver damage may result if the recommended dosage for paracetamol is exceeded

4.5 Interaction with other medicinal products and other forms of interaction

Long-term use of paracetamol in patients being treated with oral anti-coagulants is only advisable under medical supervision.

The anticholinergic effect of drugs such as tri- and tetracyclic antidepressants, antihistamines, antipsychotics, quinidine, amantadine, disopyramide and other anticholinergics (e.g. tiotropium, ipratropium, atropine-like compounds) may be intensified by Hyoscine butylbromide + Paracetamol .

Concomitant treatment with dopamine antagonists such as metoclopramide may result in diminution of the effects of both drugs on the gastrointestinal tract. The tachycardic effects of beta-adrenergic agents may be enhanced by Hyoscine butylbromide + Paracetamol. Long-term use of paracetamol in patients being treated with oral anti-coagulants is only advisable under medical supervision.

Hyoscine butylbromide + Paracetamol can be taken together with other drugs but not with the following: certain hypnotics and anti-epileptics (e.g. glutethimide, phenobarbital, phenytoin, carbamazepine) as well as rifampicin. The same applies to potentially hepatotoxic substances and alcohol abuse.

4.6 Fertility, Pregnancy and Lactation

<u>Pregnancy</u>

There are limited data from the use of hyoscine butylbromide in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. As a precautionary measure Hyoscine Butylbromide Tablets are not recommended during pregnancy.

Lactation
There is insufficient information on the excretion of hyoscine butylbromide and its metabolites in human milk. A risk to the breastfeeding child cannot be excluded. Use of Hyoscine Butylbromide Tablets during breastfeeding is not recommended.

Fertility
No studies on the effects on human fertility have been conducted

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Because of possible visual accommodation disturbances patients should not drive or operate machinery if affected.

4.8 Undesirable effects

Table 1: undesirable effects

System Organ class	Frequency	Undesirable Effect
Immune system disorders	Not Known*	Anaphylactic shock, anaphylactic reactions, dyspnoea, other hypersensitivity
Cardiac disorders	Uncommon	Tachycardia
Gastrointestinal disorders	Uncommon	Dry mouth
Skin and subcutaneous tissue disorders	Uncommon	Skin reactions (e.g. urticaria, pruritus), abnormal sweating
	Not Known*	Rash, erythema
Renal and urinary disorders	Rare	Urinary retention
Hepatobiliary	Rare	Transaminases increase

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 Healthcare professionals are asked to report any suspected adverse reactions via Pharmacy and Poisons Board- Pharmacovigilance Electronic Reporting System (PvERS); *https://pv.pharmacyboardkenya.org* .

4.9 Overdose

Paracetamol

Symptoms normally occur during the first 24 hours and include pallor, nausea, vomiting, anorexia and abdominal pain. Patients may then experience a temporary subjective improvement but mild abdominal pain possibly indicative of liver damage may persist.
A single dose of paracetamol of approximately 6g or more in adults or 140 mg/kg in children may cause hepatocellular necrosis. This may lead to complete irreversible necrosis and subsequently to hepatocellular insufficiency, metabolic acidosis and encephalopathy, which may in turn progress to coma and death. Concurrent rises in liver transaminases (AST, ALT), lactate dehydrogenase and bilirubin and an increase in prothrombin time, occurring 12 - 48 hours after ingestion, have been observed. Clinical symptoms of liver damage are normally apparent after 2 days and reach a maximum after 4 - 6 days.
Overdosage with paracetamol may cause hepatic cytolysis which can lead to hepatocellular insufficiency, gastrointestinal bleeding, metabolic acidosis, encephalopathy, disseminated intravascular coagulation, coma, and death.

Treatment

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines (see BNF overdose section).

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem, oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patients who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit.

Further measures will depend on the severity, nature and course of clinical symptoms of paracetamol intoxication and should follow standard intensive care protocols.

Hyoscine butylbromide

Serious signs of poisoning following acute overdosage have not been observed in man. In the case of overdosage, anticholinergic effects such as urinary retention, dry mouth, reddening of the skin, tachycardia, inhibition of gastrointestinal motility and transient visual disturbances may occur, and Cheynes-Stokes respiration has been reported.

Treatment

In the case of oral poisoning, gastric lavage with medicinal charcoal should be followed by magnesium sulfate (15%). Symptoms of Hyoscine Butylbromide Tablets overdosage respond to parasympathomimetics. For patients with glaucoma, pilocarpine should be given locally. Cardiovascular complications should be treated according to usual therapeutic principles. In case of respiratory paralysis, intubation and artificial respiration should be considered. Catheterisation may be required for urinary retention.

In addition, appropriate supportive measures should be administered as required.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Hyoscine butylbromide and Paracetamol/Acetaminophen, which relieves abdominal pain and cramps. Hyoscine butylbromide is an anti-cholinergic which works by relaxing the muscles in your stomach and gut (intestine). It stops sudden muscle contractions (spasms), thereby relieving cramps, pain, bloating, and discomfort. Paracetamol/Acetaminophen is an analgesic (pain reliever) which works by blocking the release of certain chemical messengers that cause pain.

5.2 Pharmacokinetic properties

Hyoscine butylbromide

Absorption

As a quaternary ammonium compound, hyoscine butylbromide is highly polar and hence only partially absorbed following oral (8%) or rectal (3%) administration. After oral administration of single doses of hyoscine butylbromide in the range of 20 to 400 mg, mean peak plasma concentrations between 0.11 ng/ml and 2.04 ng/ml were found at approximately 2 hours. In the same dose range, the observed mean $AUC_{0\text{-}tz}$-values varied from 0.37 to 10.7 ng h/ml. The median absolute bio-availabilities of different dosage forms, i.e. coated tablets, suppositories and oral solution, containing 100 mg of hyoscine butylbromide each were found to be less than 1%.

Distribution

Because of its high affinity for muscarinic receptors and nicotinic receptors, hyoscine butylbromide is mainly distributed on muscle cells of the abdominal and pelvic area as well as in the intramural ganglia of the abdominal organs. Plasma protein binding (albumin) of hyoscine butylbromide is approximately 4.4%. Animal studies demonstrate that hyoscine butylbromide does not pass the blood-brain barrier, but no clinical data to this effect is available. Hyoscine butylbromide (1 mM) has been observed to interact with the choline transport (1.4 nM) in epithelial cells of human placenta in vitro.

Biotransformation and elimination

Following oral administration of single doses in the range of 100 to 400 mg, the terminal elimination half-lives ranged from 6.2 to 10.6 hours. The main metabolic pathway is the hydrolytic cleavage of the ester bond. Orally administered hyoscine butylbromide is excreted in the faeces and in the urine. Studies in man show that 2 to 5% of radioactive doses is eliminated renally after oral, and 0.7 to 1.6% after rectal administration. Approximately 90% of recovered radioactivity can be found in the faeces after oral administration. The urinary excretion of hyoscine butylbromide is less than 0.1% of the dose. The mean apparent oral clearances after oral doses of 100 to 400 mg range from 881 to 1420 L/min, whereas the corresponding volumes of distribution for the same range vary from 6.13 to 11.3 x 10^5 L, probably due to very low systemic availability. The metabolites excreted via the renal route bind poorly to the muscarinic receptors and are therefore not considered to contribute to the effect of the hyoscine butylbromide.

Paracetamol BP

Absorption

Paracetamol is readily absorbed from the gastrointestinal tract.

Distrubution

Peak plasma concentrations occur about 10 to 60 minutes after oral doses. Paracetamol is distributed into most body tissues. It crosses the placenta and is present in breast milk. Plasma-protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

Biotransformation

It is metabolised in the liver. A minor hydroxylated metabolite which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause tissue damage.

Elimination

It is excreted in the urine, mainly as the glucuronide and sulfate conjugates. The elimination half-life varies from about 1 to 4 hours.

5.3 Preclinical safety data

Hyoscine butylbromide

In limited reproductive toxicity studies hyoscine butylbromide showed no evidence of teratogenicity in rats at 200 mg/kg in the diet or in rabbits at 200 mg/kg by oral gavage or 50 mg/kg by subcutaneous injection. Fertility in the rat was not impaired at doses of up to 200 mg/kg in the diet.

Paracetamol

In toxicity studies in rats and mice, gastrointestinal lesions, changes in blood counts, degeneration of hepatic and renal parenchyma, and necrosis have been observed. These changes are attributed to both the mechanism of action and the metabolism of paracetamol.
Extensive research has not shown any relevant genotoxic risk of paracetamol at therapeutic dose.
Long-term studies in rats and mice showed no relevant carcinogenic effects at non-hepatotoxic doses of paracetamol.
Paracetamol passes the placental barrier.
Studies in animals have shown no reproductive toxicity.

6. Pharmaceutical Particulars

6.1 List of Excipients

Citric Acid BP
Titanium dioxide
Maize Starch BP
PVPK-30 BP
Magnesium Stearate BP
Colloidal silicon DioxideBP
Crosscarmellose Sodium BP
Pregelatinised Starch BP
Instamoist Shield IC-MS- 2398

Instaglow IH
Isopropyl Alcohol BP
Methylene Chloride BP

6.2 Incompatibilities
None stated

6.3 Shelf-Life
36 months

6.4 Special Precautions for storage
Store in a cool dry place below 30°C.
Keep medicines out of reach of children.

6.5 Nature and Content of container
3 X 10 Tablet are packed in carton along with product insert

6.6 Special precautions for disposal and other handling
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder
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8. Marketing Authorization Number
CTD8340

9. Date of first authorization/renewal of the authorization
18/04/2024

10. Date of revision of the text
5/5/2025