SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Diumide-K Continus Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Film coated, round, orange/white bilayer tablet with 'DK' on the white layer. Each tablet contains 40mg furosemide and 600mg potassium chloride within a patented controlled release system.

3. PHARMACEUTICAL FORM

Controlled release tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For patients requiring diuresis and concomitant potassium supplementation. Indications include cardiac oedema, pulmonary oedema, hepatic oedema, renal oedema and peripheral oedema of various aetiologies.

4.2 Posology and Method of administration

For all indications:

Adults:	The usual adult dose is one tablet daily, normally in the morning; this may be adjusted depending on the condition.
Children:	Not recommended.
The Elderly:	The normal adult dosage is recommended.

Administration: **Diumide-K Continus Tablets** should be swallowed whole with water, preferably prior to or during a meal. The tablets should not be chewed as this will destroy the controlled release system.

4.3 Contra-Indications

Porphyria, hyperkalaemia, precomatose states associated with liver cirrhosis, Addison's disease and concomitant administration of potassium sparing diuretics.

Although the Continus® controlled release system minimises the likelihood of oesophageal ulceration, all solid forms of potassium medication are contra-indicated in the presence of obstructions in the digestive tract (eg resulting from compression of the oesophagus due to dilation of the left atrium or from stenosis of the gut).

4.4 Special Warnings and Special Precautions for Use

Care should be exercised in patients with renal insufficiency where there is a risk of hyperkalaemia. **Diumide K Continus Tablets** should not be chewed but swallowed whole with water preferably prior to or during a meal.

4.5 Interaction with other medicinal products and other forms of interaction

Increased toxicity risk with cardiac glycosides, hypotensive agents, including ACE inhibitors and nephrotoxic antibiotics. Serum lithium levels may be increased with concomitant administration. Non-steroidal anti-inflammatory drugs antagonise the diuretic effect.

4.6 Pregnancy and Lactation

Specific experience is unavailable with **Diumide-K Continus tablets.** Rat studies have shown that the administration of furosemide (37.5 - 300mg/kg twice daily) on days 6 - 17 of gestation produced dose related increases in wavy ribs. When providing potassium chloride during the dosing period, the incidence of wavy ribs reduced by 90% indicating that the teratogenicity was probably related to hypokalaemia.

In humans, furosemide crosses the placenta. Oral doses of 25 to 40mg have produced peak cord serum concentrations after approximately 9 hours. Maternal and cord levels were equal at approximately 8 hours. Increased foetal urine production after maternal furosemide therapy has been observed in newborns exposed to furosemide shortly before birth. Urinary sodium and potassium in treated neonates have been found to be significantly greater than in non-exposed controls. Neonatal electrolyte disturbances may occur.

Whilst potassium chloride is a natural constituent of tissues and fluids, high or low levels can be detrimental to maternal and foetal cardiac function and serum levels should therefore be monitored closely.

Furosemide has been used in pregnancy, in labour and in the puerperium in cases of excessive weight gain, oedema, hypertension and toxaemia of pregnancy with satisfactory results and with no embryotoxic, foetotoxic or teratogenic effects.

Diumide-K Continus tablets should not be administered during the first trimester. Diuretics may reduce placental perfusion. After the first trimester, **Diumide-K Continus tablets** should not be administered if the adequacy of placental perfusion is suspect.

Nursing Mothers

Lactation may be inhibited due to maternal fluid depletion. Furosemide is excreted into breast milk therefore **Diumide-K Continus tablets** should be used with caution.

4.7 Effects on Ability to Drive and Use Machines

None known.

4.8 Undesirable Effects

Patients with prostatic hypertrophy or impairment of micturition have an increased risk of developing acute urinary retention. Latent diabetes may become manifest or the insulin requirements of diabetic patients may increase.

Water and electrolyte balance may be disturbed and serum calcium levels may be reduced. Raised urea and creatinine levels may occur. Bone marrow depression and acute pancreatitis have also been reported as rare complications and therapy should be withdrawn.

Bullous pemphigoid among elderly patients has also been reported as very rare complication: the therapy should be withdrawn.

4.9 Overdose

Overdosage is characterised by excessive diuresis. Replace fluids and correct electrolyte imbalance.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Diumide-K Continus Tablets contain the diuretic furosemide and potassium chloride. Furosemide is a loop diuretic, inhibiting resorption from the ascending loop of Henlé. It is used for the treatment of oedematous states of various aetiologies. Potassium chloride is present in the tablets to counteract the urinary loss of potassium induced by furosemide.

5.2 Pharmacokinetic properties

The furosemide layer has normal release characteristics. Furosemide produces a diuresis within one hour and it is complete within six hours. Furosemide has a biphasic half life in the plasma with a terminal elimination phase of up to about $1^{1}/_{2}$ hours. The potassium chloride in **Diumide-K Continus Tablets** is incorporated in the controlled release system. This ensures a prolonged release giving maximum absorption and avoiding 'flushing out' of the potassium by the action of the diuretic.

5.3 Preclinical safety data

None relevant to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The tablets also contains:

Lactose
Povidone (K25)
Pregelatinised maize starch
Talc
Hydroxyethyl cellulose
Gelatin powder
Cetostearyl alcohol
Magnesium stearate
FD & C Yellow No 6
Hydroxypropylmethyl cellulose
Polyethylene glycol 400
Purified water

6.2 Incompatibilities

None known.

6.3 Shelf Life

36 months.

6.4 Special Precautions for Storage

None.

6.5 Nature and Contents of Container

Blister pack containing 4 or 30 tablets. Securitainers with PE foam rondel containing 250 or 1000 tablets.

6.6 Instructions for Use/Handling

Not relevant.

7 MARKETING AUTHORISATION HOLDER

TEOFARMA s.r.l
Via F.lli Cervi no 8
I-27010 Valle Salimbene (PV)
Italy

8. MARKETING AUTHORISATION NUMBER

PL 16250/0001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30th June 2001

10. DATE OF (PARTIAL) REVISION OF TEXT

May 2003