ANNEX I

LIST OF THE NAMES, PHARMACEUTICAL FORMS, STRENGTHS, ROUTES OF ADMINISTRATION, MARKETING AUTHORISATION HOLDERS, PACKAGING AND PACKAGE SIZES OF THE MEDICINAL PRODUCT IN THE MEMBER STATES

Article 30 Referral for Calcitugg (and associated names) Chewable tablets (Calcium carbonate)

Member State	MAH	Invented name	Strength	Pharmaceutical form	Route of Administration	Packaging	Package size
Belgium	Christiaens Pharma	Calci-Chew	500 mg	Chewable tablet	Oral	Polyethylene (PEHD) bottle	20, 50, 100
Finland	Oy Leiras Finland Ab	Calcichew 500 mg purutabletti	500 mg	Chewable tablet	Oral	Polyethylene (PEHD) bottle	20, 100
	Oy Leiras Finland Ab	Calcichew Spearmint 500 mg purutabletti	500 mg	Chewable tablet	Oral	Polyethylene (PEHD) bottle	20, 100
Germany	Orion Pharma GmbH	Calcimagon 500 mg	500 mg	Chewable tablet	Oral	Polyethylene (PEHD) bottle	20, 50, 100 and 10 x100
Greece	Nycomed Hellas S.A.	Calcioral	500 mg	Chewable tablet	Oral	Polyethylene (PEHD) bottle	20
Luxembourg	Christiaens Pharma	Calcichew	500 mg	Chewable tablet	Oral	Polyethylene (PEHD) bottle	20, 50, 100
Netherlands	Christiaens B.V	Calci-Chew 500 mg	500 mg	Chewable tablet	Oral	Bottle: Polyethylene (PEHD) Unit dose (blister): PVC/PVdC/PE/Al	Bottle: 15, 30, 60, 90 Unit dose (blister): 50
	Christiaens B.V	Calci-Chew 1000 mg	1000 mg	Chewable tablet	Oral	Polyethylene (PEHD) bottle Unit dose (blister): PVC/PVdC/PE/Al	30, 60, 90, 100 Unit dose (blister): 50
Spain	Altana Pharma S.A	Mastical	500 mg	Chewable tablet	Oral	Polyethylene (PEHD) bottle	60, 90
Sweden	Nycomed AB	Calcitugg	500 mg	Chewable tablet	Oral	Polyethylene (PEHD) bottle	60, 100
	Nycomed AB	Calcitugg 1000 mg	1000 mg	Chewable tablet	Oral	Polyethylene (PEHD) bottle Unit dose (blister): PVC/PVdC/PE/Al	30, 60, 90, 100 Unit dose (blister): 50

ANNEX II

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS PRESENTED BY THE EMEA

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF CALCITUGG (see Annex I)

- Quality issues

The pharmaceutical documentation (module 3) as well as well as the pharmaceutical particulars of the SPC were harmonised, except the sections, which need to be introduced nationally by the Member States when implementing the harmonised SPC (sections 6).

- Efficacy issues

Section 4.1. Therapeutic indications

After an assessment of the documentation provided by the MAH and an evaluation of the current EU-wide clinical practices relating to the use of Calcium carbonate, the following was considered to be the most suitable harmonised Section 4.1 indications text:

> **4.1 Therapeutic indications**
> Prevention and treatment of calcium deficiency. Calcium supplement as an adjunct to specific therapy in the prevention and treatment of osteoporosis. Phosphate binder in hyperphosphataemia

Section 4.2. Posology and method of administration

After an assessment of the documentation provided by the MAH and an evaluation of the current EU-wide clinical practices relating to the use of Calcium carbonate, the following was considered to be the most suitable harmonised Section 4.2 Posology text:

> **4.2 Posology and method of administration**
> *Prevention and treatment of calcium deficiency*
> Adults: 500 – 1500 mg per day
> Children: 500 – 1000 mg per day
>
> *Adjunctive therapy in osteoporosis*
> Adults: 500 – 1500 mg per day
>
> *Hyperphosphataemia*
> Individual dosage. 2-8 g calcium daily is often required divided into 2-4 doses. The tablets should be taken with meals in order to bind phosphate in the food.
>
> The tablet should be chewed or sucked.

- Safety issues

Section 4.3. Contra-indications

After an assessment of the documentation provided by the MAH and an evaluation of the current EU-wide clinical practices relating to the use of Calcium carbonate, the most suitable harmonised Section 4.3 Contraindications text was approved (See Annex III). The text in the harmonised SPC is not so dissimilar to the currently approved SPCs that it will significantly change clinical practices

Section 4.4. Special warnings and precautions for use

After an assessment of the documentation provided by the MAH and an evaluation of the current EU-wide clinical practices relating to the use of Calcium carbonate, the most suitable harmonised Section 4.4 Special Warnings and Precautions for Use text was approved (See Annex III). The text in the harmonised SPC is not so dissimilar to the currently approved SPCs that it will significantly change clinical practices

Section 4.6. Pregnancy and lactation

After an assessment of the documentation provided by the MAH and an evaluation of the current EU-wide clinical practices relating to the use of Calcium carbonate, the most suitable harmonised Section 4.6 Pregnancy was approved (See Annex III).

Section 4.8 Undesirable effects

After an assessment of the documentation provided by the MAH and an evaluation of the current EU-wide clinical practices relating to the use of Calcium carbonate, the most suitable harmonised Section 4.8 Undesirable effects was approved (See Annex III).

All other sections of the SPC were harmonised as a result of the referral procedure (except See Below; Administrative Issues).

- Administrative issues

Other sections of the SPC which were not harmonised and which need to be introduced nationally by the Member States when implementing the harmonised SPC are the following: Product name, MAH, MA number, date of first authorisation/renewal of authorisation, Date of revision of the text.

Benefit/Risk considerations
Based on the documentation submitted by the MAH and the scientific discussion within the Committee, the CPMP considered that the benefit/risk ratio of Calcitugg is favourable for use relating to prevention and treatment of calcium deficiency, for use as Calcium supplement as an adjunct to specific therapy in the prevention and treatment of osteoporosis and Phosphate binder in hyperphosphataemia.

GROUNDS FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS

Whereas,

- the scope of the referral was the harmonisation of the Summaries of Products Characteristics and additionally the harmonisation of the technical document – module 3 (quality),

- the Summary of Products Characteristic proposed by the Marketing Authorisation Holder(s) has been assessed based on the documentation submitted and the scientific discussion within the Committee,

the CPMP has recommended the amendment of the Marketing Authorisations for which the Summary of Product Characteristics is set out in Annex III of the Opinion.

ANNEX III

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product

Calcitugg and associated names (see Annex I) 500 mg/1000 mg chewable tablets

[To be implemented nationally]

2. Qualitative and Quantitative Composition

One tablet of 500 mg contains:
Elemental calcium 500 mg
as
Calcium carbonate

One tablet of 1000 mg contains:
Elemental calcium 1000 mg
as
Calcium carbonate

For excipients, see 6.1

3. Pharmaceutical Form

Chewable tablet

Round, white, uncoated and convex tablets. May have small specks.

4. Clinical Particulars

4.1 Therapeutic indications

Prevention and treatment of calcium deficiency. Calcium supplement as an adjunct to specific therapy in the prevention and treatment of osteoporosis. Phosphate binder in hyperphosphataemia.

4.2 Posology and method of administration

Prevention and treatment of calcium deficiency
Adults: 500 – 1500 mg per day
Children: 500 – 1000 mg per day

Adjunctive therapy in osteoporosis
Adults: 500 – 1500 mg per day

Hyperphosphataemia
Individual dosage. 2-8 g calcium daily is often required divided into 2-4 doses. The tablets should be taken with meals in order to bind phosphate in the food.

The tablet should be chewed or sucked.

4.3 Contraindications

- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria
- Nephrolithiasis
- Hypersensitivity to the active substance or to any of the excipients

4.4 Special warnings and special precautions for use

Calcium 500 mg and 1000 mg tablets contain aspartame and should be avoided by patients with phenylketonuria.

In renal insufficiency the tablets should be given only under controlled conditions for hyperphosphataemia. Caution should be exercised in patients with a history of renal calculi.

During high dose therapy and especially during concomitant treatment with vitamin D, there is a risk of hypercalcaemia with subsequent kidney function impairment. In these patients serum calcium levels should be followed and renal function should be monitored.

4.5 Interactions with other medicinal products and other forms of interaction

Thiazide diuretics reduce the urinary excretion of calcium. Due to increased risk of hypercalcaemia, serum calcium should be regularly monitored during concomitant use of thiazide diuretics.

Systemic corticosteroids reduce calcium absorption. During concomitant use, it may be necessary to increase the dose of Calcitugg (and associated names).

Calcium carbonate may interfere with the absorption of concomitantly administered tetracycline preparations. For this reason, tetracycline preparations should be administered at least two hours before or four to six hours after oral intake of calcium.

Hypercalcaemia may increase the toxicity of cardiac glycosides during treatment with calcium. Patients should be monitored with regard to electrocardiogram (ECG) and serum calcium levels.

If a bisphosphonate or sodium fluoride is used concomitantly, this preparation should be administered at least three hours before the intake of Calcitugg (and associated names) since gastrointestinal absorption may be reduced.

Oxalic acid (found in spinach and rhubarb) and phytic acid (found in whole cereals) may inhibit calcium absorption through formation of insoluble compounds with calcium ions. The patient should not take calcium products within two hours of eating foods high in oxalic acid and phytic acid.

4.6 Pregnancy and lactation

The adequate daily intake (including food and supplementation) for normal pregnant and lactating women is 1000-1300 mg calcium. During pregnancy, the daily intake of calcium should not exceed 1500 mg. Significant amounts of calcium are secreted in milk during lactation. Calcitugg can be used during pregnancy in case of a calcium deficiency.

4.7 Effects on ability to drive and use machines

There are no data about the effect of this product on driving capacity. An effect is, however, unlikely.

4.8 Undesirable effects

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: uncommon (>1/1,000, <1/100) or rare (>1/10,000, <1/1,000).
Metabolism and nutrition disorders
Uncommon: Hypercalcaemia and hypercalciuria.

Gastrointestinal disorders
Rare: Constipation, flatulence, nausea, abdominal pain, and diarrhoea.

Skin and subcutaneous disorders
Rare: Pruritus, rash and urticaria.

4.9 Overdose

Overdose can lead to hypervitaminosis and hypercalcaemia. Symptoms of hypercalcaemia may include anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, mental disturbances, polidipsia, polyuria, bone pain, nephrocalcinosis, renal calculi and in severe cases, cardiac arrhythmias. Extreme hypercalcaemia may result in coma and death. Persistently high calcium levels may lead to irreversible renal damage and soft tissue calcification.

Treatment of hypercalcaemia: The treatment with calcium must be discontinued. Treatment with thiazide diuretics, lithium, vitamin A, vitamin D and cardiac glycosides must also be discontinued. Emptying of the stomach in patients with impaired consciousness. Rehydration, and, according to severity, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin and corticosteroids. Serum electrolytes, renal function and diuresis must be monitored. In severe cases, ECG and CVP should be followed.

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcium
ATC-code: A12A A04
An adequate intake of calcium is of importance during growth, pregnancy and breastfeeding.

5.2 Pharmacokinetic properties

Calcium
Absorption: The amount of calcium absorbed through the gastrointestinal tract is approximately 30% of the swallowed dose.
Distribution and metabolism: 99% of the calcium in the body is concentrated in the hard structure of bones and teeth. The remaining 1% is present in the intra- and extracellular fluids. About 50% of the total blood-calcium content is in the physiologically active ionised form with approximately 10% being complexed to citrate, phosphate or other anions, the remaining 40% being bound to proteins, principally albumin.
Elimination: Calcium is eliminated through faeces, urine and sweat. Renal excretion depends on glomerular filtration and calcium tubular reabsorption.

5.3 Preclinical safety data

There is no information of relevance to the safety assessment in addition to what is stated in other parts of the SPC

6. Pharmaceutical Particulars

6.1 List of excipients

Sorbitol
Povidone
Isomalt
Flavouring (orange or spearmint)
Magnesium Stearate
Aspartame

Mono- and diglycerides of fatty acids

6.2 Incompatibilities

Not applicable

6.3 Shelf life

High Density Polyethylene tablet container: 3 years
Blister pack: 2 years

6.4 Special precautions for storage

High Density Polyethylene tablet container: Do not store above 30°C.
Keep the container tightly closed in order to protect from moisture.
Blister pack: Do not store above 25°C. Store in the original package.

6.5 Nature and content of container

The chewable tablets are packed in:
High Density Polyethylene tablet containers
Pack sizes: 20, 30, 50, 60, 90, 100, 120 and 180 tablets (500 mg)
60 tablets (1000 mg)
Blister pack (PVC/PE/PVdC/AI)
Package size: 50 x 1 tablets (unit dose)

Not all pack sizes may be marketed.

6.6 Instructions for use and handling

No special requirements

7. MARKETING AUTHORISATION HOLDER

(See Annex I – To be implemented nationally)

8. MARKETING AUTHORISATION NUMBERS

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF THE REVISION OF THE TEXT