HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

OPINION

04 February 2009

AXELER 20 mg/5 mg, film-coated tablets
B/30 (CIP: 388 538-7)
B/50 (CIP: 573 840-8)
B/90 (CIP: 388 540-1)

AXELER 40 mg/5 mg, film-coated tablets
B/30 (CIP: 388 544-7)
B/50 (CIP: 573 537-7)
B/90 (CIP: 388 547-6)

AXELER 40 mg/10 mg, film-coated tablets
B/30 (CIP: 388 541-8)
B/50 (CIP: 573 838-3)
B/90 (CIP: 388 543-0)

Applicant: A. MENARINI FARMACEUTICA INTERNAZIONALE Srl

Olmesartan medoxomil/amlodipine besilate

ATC Code: C09DB02

List I

Date of Marketing Authorisation: 03/10/2008

Reason for request: Inclusion on the list of medicines reimbursed by National Insurance (boxes of 30 and 90) and approved for use by hospitals (boxes of 30, 50 and 90).

Medical, Economic and Public Health Assessment Division

1 CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

Olmesartan medoxomil
Amlodipine besilate

1.2. Indication

"Treatment of essential hypertension.
AXELER is indicated in patients whose blood pressure is not adequately controlled on olmesartan medoxomil or amlodipine monotherapy."

1.3. Dosage

"Adults:
The recommended dosage of AXELER is 1 tablet per day.

AXELER 20 mg/5 mg may be administered in patients whose blood pressure is not adequately controlled by 20 mg olmesartan medoxomil or 5 mg amlodipine alone.
AXELER 40 mg/5 mg may be administered in patients whose blood pressure is not adequately controlled by AXELER 20 mg/5 mg.
AXELER 40 mg/10 mg may be administered in patients whose blood pressure is not adequately controlled by AXELER 40 mg/5 mg.

A step-wise titration of the dosage of the individual components is recommended before changing to the fixed combination. When clinically appropriate, direct change from monotherapy to the fixed combination may be considered.

For convenience, patients receiving olmesartan medoxomil and amlodipine from separate tablets may be switched to AXELER tablets containing the same component doses.

Method of administration:
The tablet should be swallowed with a sufficient amount of fluid (e.g. one glass of water). The tablet should not be chewed and should be taken at the same time each day. AXELER can be taken with or without food.

Elderly (age 65 years or over):
No adjustment of the recommended dose is generally required for elderly patients. If up-titration to the maximum dose of 40 mg olmesartan medoxomil daily is required, blood pressure should be closely monitored.

Renal impairment:
The maximum dose of olmesartan medoxomil in patients with mild to moderate renal impairment (creatinine clearance of 20 – 60 mL/min) is 20 mg olmesartan medoxomil once daily, owing to limited experience of higher dosages in this patient group.
The use of AXELER in patients with severe renal impairment (creatinine clearance < 20 mL/min) is not recommended.
Monitoring of potassium levels and creatinine is advised in patients with moderate renal impairment.

Hepatic impairment:
AXELER should be used with caution in patients with mild to moderate hepatic impairment. In patients with moderate hepatic impairment, an initial dose of 10 mg olmesartan medoxomil once daily is recommended and the maximum dose should not exceed 20 mg once daily. Close monitoring of blood pressure and renal function is advised in hepatically-impaired patients who are already receiving diuretics and/or other antihypertensive agents. There is no experience of olmesartan medoxomil in patients with severe hepatic impairment.
As with all calcium antagonists, amlodipine's half-life is prolonged in patients with impaired liver function and dosage recommendations have not been established. AXELER should therefore be administered with caution in these patients.

Children and adolescents:
AXELER is not recommended for use in children and adolescents below 18 years of age due to a lack of data on safety and efficacy. "

2 SIMILAR MEDICINAL PRODUCTS

2.1 ATC Classification (2008)

C: Cardiovascular system
C09: Agents acting on the renin-angiotensin system
C09D: Angiotensin II antagonists, combinations
C09DB: Angiotensin II antagonists and calcium channel blockers
C09DB02: olmesartan medoxomil and amlodipine besilate

2.2 Medicines in the same therapeutic category

- Separate treatment with olmesartan 20 mg/day or 40 mg/day (ALTEIS, OLMETEC, tablets) and 5 mg/day or 10 mg/day amlodipine (AMLOR tablets).

- Fixed-dose combination of an ARA II and a calcium channel inhibitor:
  Valsartan 80 mg/160 mg + amlodipine 5 mg/10 mg: EXFORGE

2.3 Medicines with a similar therapeutic aim

All medicinal products indicated in the treatment of essential hypertension: other antihypertensives that are prescribed as monotherapy or in combinations.

Other products based on fixed combinations with an ACE inhibitor, a calcium channel inhibitor or a sartan:

a). Angiotensin II receptor antagonist (ARA II) + diuretic:
candesartan 8 mg or 16 mg + HCTZ 12.5 mg: COKENZEN, HYTACAND
eprosartan 600 mg + HCTZ 12.5 mg: COTEVETEN
irbesartan 150 mg (or 300 mg) + HCTZ 12.5 mg (or 25 mg): COAPROVEL
losartan 50 mg (or 100 mg) + HCTZ 12.5 mg (or 25 mg): FORTZAAR, HYZAAR
olmesartan medoximil 20 mg + HCTZ 12.5 mg (or 25 mg): ALTEISDUO, COOLMETEC
telmisartan 40 mg or 80 mg + HCTZ 12.5 mg (or 25 mg): MICARDISPLUS, PRITORPLUS
valsartan 80 mg or 160 mg + HCTZ 12.5 mg (or 25 mg): COTAREG, NISISCO

b). CEI + calcium channel inhibitor:
trandolapril 2 mg + verapamil 180 mg:TARKA SR; OKADRIK SR.

c). CEI + diuretic:
benazepril 10mg + HCTZ1 12.5mg: BRIAZIDE, CIBADREX
captopril 50 mg + HCTZ 25.0 mg: CAPTEA, ECAZIDE, and G2
enalapril 20 mg + HCTZ 12.5 mg: CO-RENITEC, and G
fosinopril 20 mg + HCTZ 12.5 mg: FOZIRETIC
lisinopril 20 mg + diHCTZ 12.5 mg: PRINZIDE, ZESTORETIC, and G
perindopril 2 mg (4 mg) + indapamide 0.625 mg (1.25 mg): PRETERAX, BIPRETERAX
quinapril 20 mg + HCTZ 12.5 mg: ACUILIX, KORETIC, and G
ramipril 5 mg + HCTZ 12.5 mg: COTRIATEC
zofenopril 30 mg + HCTZ 12.5 mg: ZOFENILDUO

d). calcium channel inhibitor + beta-blocker:
nifedipine 20 mg + atenolol 50 mg: BETA-ADALATE, TENORDATE, and generics

2. ANALYSIS OF AVAILABLE DATA

3.1. Efficacy

Efficacy and safety have been assessed in three randomised double-blind phase III studies involving patients with arterial hypertension.
The aim of these studies was to determine the efficacy in terms of reduction in diastolic blood pressure (DBP) of combination treatments with olmesartan + amlodipine in comparison with baseline or with a monotherapy:

- Study 301: 12-arm factorial study (placebo, olmesartan 10, 20 and 40 mg, amlodipine 5 and 10 mg, olmesartan + amlodipine 10 mg/5 mg, 20mg/5 mg, 40 mg/5 mg, 10 mg/10 mg, 20 mg/10 mg, 40 mg/10 mg) involving 1689 patients who were followed up for 8 weeks.
- Study 302: comparative study of olmesartan 20 mg + amlodipine 5 mg and olmesartan 20 mg + amlodipine 10 mg versus olmesartan 20 mg alone, involving 538 patients who had not responded to an 8-week course of treatment with olmesartan 20 mg. These patients were followed up for 8 weeks.
- Study 303: comparative study of amlodipine 5 mg + olmesartan 5 mg, amlodipine 5 mg + olmesartan 20 mg, amlodipine 5 mg + olmesartan 40 mg versus amlodipine 5 mg alone, involving 746 patients who had not responded to an 8-week course of treatment with amlodipine 5 mg. These patients were followed up for 8 weeks.

3.1.1. Study 301
Inclusion criteria: adult patients with DBP of between 95 mmHg and 120 mmHg

Treatments:
- Placebo, n=160,
- olmesartan 10 mg, n=160
- olmesartan 20 mg, n=159
- olmesartan 40 mg, n=160
- amlodipine 5 mg, n=161,
- amlodipine 10 mg, n=163,
- olmesartan + amlodipine 10 mg/5 mg, n=163
- olmesartan + amlodipine 20 mg/5 mg, n=160

1 Hydrochlorothiazide, thiazide diuretic: “HCTZ”.
2 "G": generic products. See Afssaps Generics Register.

- olmesartan + amlodipine 40 mg/5 mg, n=157
- olmesartan + amlodipine 10 mg/10 mg, n=161
- olmesartan + amlodipine 20 mg/10 mg, n=158
- olmesartan + amlodipine 40 mg/10 mg, n=161

Note: in this study, the choice of treatment and dosage did not take into account patients' "blood pressure profiles", which is not in line with the dosage instructions in the marketing authorisation, which states that dosages may be increased and that combination treatments may be offered to patients whose blood pressure is "inadequately controlled".

Primary endpoint: mean change (reduction) in DBP (in mmHg) after 8 weeks in comparison with baseline. Combination treatments were compared with the respective monotherapies involving each active substance.

RESULTS: ITT analysis (see Tables 1 and 2)

Table 1: Mean variation in DBP (in mmHg) at 8 weeks

Treatments	N	Inclusion Mean ± SD	8 weeks Mean ± SD	Change from baseline Mean ± SD	p
Placebo	160	102.4 ± 4.79	99.3 ± 11.18	-3.1 ± 10.67	<0.0001
OLM10	160	101.8 ± 5.93	93.5 ± 10.45	-8.3 ± 9.28	<0.0001
OLM20	159	101.5 ± 4.59	92.3 ± 10.77	-9.2 ± 9.73	<0.0001
OLM40	160	101.2 ± 5.02	91.0 ± 12.23	-10.2 ± 10.69	<0.0001
AML5	161	101.5 ± 5.15	92.1 ± 8.94	-9.4 ± 8.25	<0.0001
AML10	163	101.6 ± 4.84	88.8 ± 7.80	-12.7 ± 8.25	<0.0001
OLM10/AML5	163	102.1 ± 5.36	88.3 ± 9.06	-13.8 ± 7.48	<0.0001
OLM20/AML5	160	101.7 ± 5.06	87.7 ± 9.51	-14.0 ± 9.07	<0.0001
OLM40/AML5	157	100.9 ± 4.74	85.4 ± 9.69	-15.5 ± 8.15	<0.0001
OLM10/AML10	161	101.4 ± 5.50	85.4 ± 9.56	-16.0 ± 8.62	<0.0001
OLM20/AML10	158	101.1 ± 4.67	84.1 ± 8.41	-17.0 ± 8.04	<0.0001
OLM40/AML10	161	102.3 ± 5.80	83.3 ± 9.77	-19.0 ± 8.90	<0.0001

OLM: olmesartan, AML: amlodipine

After 8 weeks of treatment, a reduction in DBP from baseline was observed in all treatment groups.

Table 2: Comparison of mean DBP values (in mmHg) at 8 weeks

Treatments compared	**Mean (SD)**	**Difference (tx 1 - tx 2)**		
Tx 1 vs Tx 2	Tx 1 Tx 2	Mean (SD)	95% CI	p
OLM10/AML5 vs. OLM10	-14.3 (0.74) -8.8 (0.75)	-5.5 (0.99)	(-7.4, -3.5)	<0.0001
OLM10/AML5 vs. AML5	-14.3 (0.74) -10.0 (0.75)	-4.3 (0.99)	(-6.3, -2.4)	<0.0001
OLM20/AML5 vs. OLM20	-14.6 (0.75) -9.9 (0.75)	-4.7 (1.00)	(-6.6, -2.7)	<0.0001
OLM20/AML5 vs. AML5	-14.6 (0.75) -10.0 (0.75)	- 4.6 (0.99)	(-6.5, -2.6)	<0.0001
OLM40/AML5 vs. OLM40	-16.3 (0.76) -10.9 (0.75)	-5.4 (1.00)	(-7.3, -3.4)	<0.0001
OLM40/AML5 vs. AML5	-16.3 (0.76) -10.0 (0.75)	-6.3 (1.00)	(-8.2, -4.3)	<0.0001
OLM10/AML10 vs. OLM10	-16.7 (0.75) -8.8 (0.75)	-7.8 (0.99)	(-9.8, -5.9)	<0.0001
OLM10/AML10 vs. AML10	-16.7 (0.75) -13.3 (0.74)	-3.3 (0.99)	(-5.3, -1.4)	=0.0004
OLM20/AML10 vs. OLM20	-17.7 (0.75) -9.9 (0.75)	-7.8 (1.00)	(-9.8, -5.9)	<0.0001
OLM20/AML10 vs. AML10	-17.7 (0.75) -13.3 (0.74)	-4.4 (0.99)	(-6.3, -2.4)	<0.0001
OLM40/AML10 vs. OLM40	-19.4 (0.74) -10.9 (0.75)	-8.5 (0.99)	(-10.5, -6.6)	<0.0001
OLM40/AML10 vs. AML10	-19.4 (0.74) -13.3 (0.74)	-6.1 (0.99)	(-8.0, -4.2)	<0.0001

OLM: olmesartan, AML: amlodipine, Tx: treatment

After 8 weeks of treatment, a significant reduction in DBP was observed in the groups treated with combinations involving olmesartan/amlodipine in comparison with those receiving monotherapy with one of the components.

3.1.2. Study 302

Inclusion criteria:
- adult patients with untreated hypertension with DBP ≥ 100 mmHg and SBP ≥ 160 mmHg, or
- adult patients with hypertension previously treated with olmesartan with DBP ≥ 90 mmHg and SBP ≥ 140 mmHg, or
- patients with hypertension previously treated with antihypertensive drugs, regardless of DBP and SBP values.

Treatments:
After a 2-week wash-out period, all patients were treated with olmesartan 20 mg as an open-label treatment for 8 weeks. All patients were then included in the double-blind randomised phase, and were distributed into the following three treatment groups:
- olmesartan 20 mg, n=179
- olmesartan + amlodipine 20 mg/5 mg, n=182
- olmesartan + amlodipine 20 mg/10 mg, n=177

Primary endpoint: mean change (reduction) in DBP (in mmHg) after 16 weeks in comparison with values measured at 8 weeks.

RESULTS: ITT analysis

Table 3: Mean variation in DBP (in mmHg) at 16 weeks

Treatments	N	8 weeks Mean ± SD	16 weeks Mean ± SD	Variation (adjusted mean)	Difference with respect to olmesartan 20 mg	
					Mean ± SD	p
OLM 20	179	97.2 ± 4.89	89.4 ± 8.54	- 7,6 ± 0,55		-
OLM 20 / AML 5	182	97.5 ± 4.34	86.9 ± 7.39	- 10,4 ± 0,55	-2.7 ± 0.75	0.0006
OLM 20 / AML 10	177	97.1 ± 4.22	86.0 ± 7.59	- 10,9 ± 0,56	-3.2 ± 0.76	<0.0001

After 8 weeks of treatment, a significant reduction in DBP was observed in those on olmesartan + amlodipine 20 mg/5 mg in comparison with olmesartan 20 mg given as monotherapy: -10.4 mmHg (± 0.55) versus -7.6 mmHg (± 0.55), difference -2,7 mmHg ± 0.75, p=0.0006.

3.1.3. Study 303

Inclusion criteria:
- adult patients with untreated hypertension with DBP ≥ 100 mmHg and SBP ≥ 160 mmHg, or
- patients with hypertension previously treated with amlodipine with DBP ≥ 90 mmHg and SBP ≥ 140 mmHg, or
- patients with hypertension previously treated with antihypertensive drugs, regardless of DBP and SBP values.

Treatments:
The study protocol planned for 4 distinct treatment periods.

After a 2-week wash-out period (with the exception of non-pretreated patients), all patients were treated with amlodipine 5 mg as an open-label treatment for 8 weeks (period I).

After the 8-week treatment period, patients whose hypertension was not controlled on amlodipine 5 mg were included in an 8-week double-blind phase (period II, weeks 8 to 16), and were randomised into the following four treatment groups:
- amlodipine 5 mg + placebo, n=184,
- amlodipine 5 mg + olmesartan 10 mg, n=189
- amlodipine 5 mg + olmesartan 20 mg, n=187
- amlodipine 5 mg + olmesartan 40 mg, n=186.

The primary endpoint was assessed for this population.
Note: Only the 20 mg/5 mg combination was administered to patients whose blood pressure was inadequately controlled on 5 mg amlodipine, as recommended in the marketing authorisation. In addition, the olmesartan 10 mg/amlodipine 5 mg combination is not part of the AXELER range of products.

After 16 weeks of treatment, in patients whose hypertension was uncontrolled, the olmesartan dose was increased (period III, weeks 16 to 24). Finally, the study was concluded by an open-label follow-up period to 52 weeks (period IV, weeks 24 to 52).

Primary endpoint: mean change (reduction) in DBP (in mmHg) after 16 weeks (period II) in comparison with values measured at 8 weeks.

RESULTS: ITT analysis

Table 2: Mean variation in DBP (in mmHg) at 16 weeks

Treatments	N	8 weeks Mean ± SD	16 weeks Mean ± SD	Variation Adjusted mean	Difference with respect to olmesartan 20 mg	
					Mean ± SD	p
AML 5	184	97.2 ± 5.03	91.5 ± 8.39	- 5,7 ± 0,53		-
AML 5 / OLM 10	189	96.9 ± 5.37	89.5 ± 7.58	-7.7 ± 0.52	-2.0 ± 0.73	0.02
AML 5 / OLM 20	187	96.9 ± 5.10	87.6 ± 8.63	-9.5 ± 0.52	-3.7 ± 0.73	<0.0001
AML 5 / OLM 40	186	97.0 ± 4.96	87.5 ± 7.22	-9.6 ± 0.52	-3.8 ± 0.73	<0.0001

After 8 weeks of treatment, a significant reduction in DBP was observed for those on olmesartan + amlodipine 20 mg/5 mg in comparison with amlodipine 5 mg given as monotherapy: -9.5 mmHg (± 0.52) versus -5.7 mmHg (± 0.53), difference -3.7 mmHg (± 0.73), p<0.0001.

3.2. Adverse effects

The study data have shown that the combination of these two active substances did not give rise to any new adverse effects.

In the three studies cited above, the most commonly observed adverse effects (> 10%) were: headache, dizziness, oedema and fatigue.

3.3. Conclusion

AXELER is a fixed-dose combination of olmesartan (angiotensin II antagonist) and amlodipine (calcium channel inhibitor) which is available in three dosage forms: 20 mg / 5 mg, 40 mg / 5 mg and 40 mg / 10 mg.

Efficacy and safety of these products has been assessed using three randomised controlled double-blind comparative studies (studies 301, 302 and 303).

In study 301, after 8 weeks of treatment, a reduction in DBP from baseline was observed in all treatment groups.
In addition, a significant reduction in DBP was observed in the groups treated with combinations involving olmesartan/amlodipine in comparison with those receiving monotherapy with one of the components.

In study 302, after 8 weeks of treatment, a significant reduction in DBP was observed in those on olmesartan + amlodipine 20 mg/5 mg in comparison with olmesartan 20 mg given as monotherapy: -10.4 mmHg (± 0.55) versus -7.6 mmHg (± 0.55), difference -2.7 mmHg ± 0.75, p=0.0006.

In study 303, after 8 weeks of treatment, a significant reduction in DBP was observed in those on olmesartan + amlodipine 20 mg/5 mg in comparison with amlodipine 5 mg given as monotherapy: -9.5 mmHg (± 0.52) versus -5.7 mmHg (± 0.53), difference -3.7 mmHg (± 0.73), p<0.0001.

These studies assessed olmesartan and amlodipine taken separately; no studies on the fixed-dose combination (AXELER) are available. The usefulness of administering two antihypertensive drugs as a fixed-dose combination rather than separately has not been established.

In addition, it has not been established that the combination of 20 or 40 mg of olmesartan and 5 or 10 mg of amlodipine has any effect on morbidity and mortality.

The usefulness of this combination in comparison with other combination antihypertensive treatments (whether of the same class or not) has not been documented.

The safety profile of olmesartan/amlodipine combinations (20 mg/5 mg, 40 mg/5 mg and 40 mg/10 mg) did not differ, in these studies, from the known safety profiles of the two active substances. The most commonly observed adverse effects (> 10%) were: headache, dizziness, oedema and fatigue.

3. TRANSPARENCY COMMITTEE CONCLUSIONS

3.1. Actual benefit

Essential hypertension can be life-threatening, because of its complications.
These products come within the scope of preventive treatment.

The efficacy/adverse effect ratio, assessed by measuring reduction in blood pressure on treatment with fixed-dose AXELER combinations, is high.These fixed-dose combinations have not been shown to have an effect in terms of reduction in morbidity and mortality.

These products are second-line treatments for patients whose blood pressure is inadequately controlled by:

- 20 mg olmesartan medoxomil alone or 5 mg amlodipine alone for AXELER 20 mg/5 mg.
- AXELER 20 mg/5 mg for AXELER 40 mg/5 mg.
- AXELER 40 mg/5 mg for AXELER 40 mg/10 mg.

Public Health Benefit:

Essential hypertension and cardiovascular disease (for which hypertension is a significant risk factor) represent a significant public health burden.
Reducing the morbidity and mortality attributed to hypertension is a public health need (a priority identified in the GTNDO* and the Public Health Act).
However, existing treatments (including flexible combinations of olmesartan and amlodipine) already help to meet this need.
There is no indication that these fixed-dose combinations have any added benefit (even in terms of increased observance) over flexible combinations of the two active substances.
As a result, AXELER is not expected to benefit public health.
* GTNDO: National Technical Group for Defining Objectives (DGS-2003)

There are many other alternative products, which have been shown to have an impact in terms of reduction in morbidity and mortality.

The actual benefit of AXELER products is substantial.

3.2. Improvement in actual benefit

AXELER 20 mg/5 mg, 40 mg/5 mg and 40 mg/10 mg fixed-dose combinations of olmesartan medoxomil 20 or 40 mg and amlodipine besilate 5 or 10 mg provide no improvement in actual benefit (IAB V) in comparison with concurrent use of the two active substances taken separately.

3.3. Therapeutic use

Antihypertensive treatment aims to prevent cardiovascular and renal complications of hypertension. The goal should be to normalise blood pressure. Diuretics, beta-blockers, calcium channel antagonists and renin-angiotensin system antagonists have been shown to reduce the occurrence of cardiovascular complications. For these reasons, national and international guidelines suggest that one of these treatments should be used in initial treatment for hypertension.

AXELER 20 mg/5 mg is a second-line treatment, and would only be prescribed for patients whose blood pressure is inadequately controlled on 20 mg olmesartan medoxomil alone or 5 mg amlodipine alone or whose disease is already treated with and controlled by 20 mg/day olmesartan and 5 mg/day amlodipine.

AXELER 40 mg/5 mg is a second-line treatment, and would only be prescribed for patients whose blood pressure is inadequately controlled on AXELER 20 mg/5 mg or whose disease is already treated with and controlled by 40 mg/day olmesartan and 5 mg/day amlodipine.

AXELER 40 mg/10 mg is a second-line treatment, and would only be prescribed for patients whose blood pressure is inadequately controlled on AXELER 40 mg/5 mg or whose disease is already treated with and controlled by 40 mg/day olmesartan and 10 mg/day amlodipine.

Moreover, the Committee notes that the usefulness of a fixed-dose combination in the management of patients with hypertension, in comparison with separate doses of both drugs, has not been established. In addition, this product is not suitable for all patients.

3.4. Target Population

The prevalence of diagnosed and/or treated hypertension in France appears to be between 6.5 and 7.4 million patients (HCSP data 2002 and CREDES 1999, extrapolated to the French population in 2003, THALES, CEMKA 2001).
However, the current prevalence of hypertension could be higher than the prevalence of diagnosed and/or treated hypertension. The MONICA survey showed that only 52.2% of people with hypertension aged between 35 and 64 were aware of their hypertension.
If the MONICA data are extrapolated, and if we assume that only 52.2% of patients with hypertension are diagnosed and/or treated, the real prevalence of hypertension could be of the order of 12.5-14.2 million people in France.

For information, a study on treatment methods for hypertension in general practice (THALES/CEMKA 2001) showed that 49% of patients were treated with a monotherapy, 34% with a dual therapy, 13% with triple therapy and 4% with four or more agents.

No data are available concerning the percentage of patients in France who are treated with 20 or 40 mg olmesartan and 5 or 10 mg of amlodipine and whose blood pressure is stable. The target population for AXELER (20 mg/5 mg, 40 mg/5 mg et 40 mg/10 mg) cannot be calculated.

According to a study conducted using data from RSI reimbursement data for the whole of France (3,347,332 people covered) between September and November 2008 (3 months):
45, 528 patients were treated with amlodipine (14,113 at a dose of 10 mg and 32,750 at a dose of 5 mg),
10,290 patients were treated with olmesartan (8049 at a dose of 20 mg and 2410 at a dose of 40mg).
In this study, only 447 patients were treated with a combination of both active substances, in the following distribution:
olmesartan 20 mg + amlodipine 10 mg, n=119
olmesartan 20 mg + amlodipine 5 mg, n=174
olmesartan 40 mg + amlodipine 10 mg, n=75
olmesartan 40 mg + amlodipine 5 mg, n=79
After these three months, patients were able to change treatment.

3.5. Transparency Committee recommendations

The Transparency Committee recommends inclusion on the list of medicines reimbursed by National Insurance (boxes of 30 and 90) and on the list of medicinal products approved for use by hospitals and various public services (boxes of 30, 50 and 90) for the indication and at the dosage given in the marketing authorisation.

Packaging: appropriate for the prescription conditions.

Reimbursement rate: 65%

ANNEX

Posology of olmesartan (OLMETEC/ALTEIS) in the treatment of hypertension (from SPC):

The recommended starting dose of olmesartan medoxomil is 10 mg once daily. In patients whose blood pressure is not adequately controlled at this dose, the dose of olmesartan medoxomil may be increased to 20 mg once daily as the optimal dose.

If additional blood pressure reduction is required, olmesartan medoxomil dose may be increased to a maximum of 40 mg daily or hydrochlorothiazide (diuretic) therapy may be added.

Posology of amlodipine (AMLOR) in the treatment of hypertension (from SPC):

The usual initial dose is one capsule (5 mg) once daily which may be increased to a maximum dose of 10 mg once daily depending on the individual patient's response.