EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

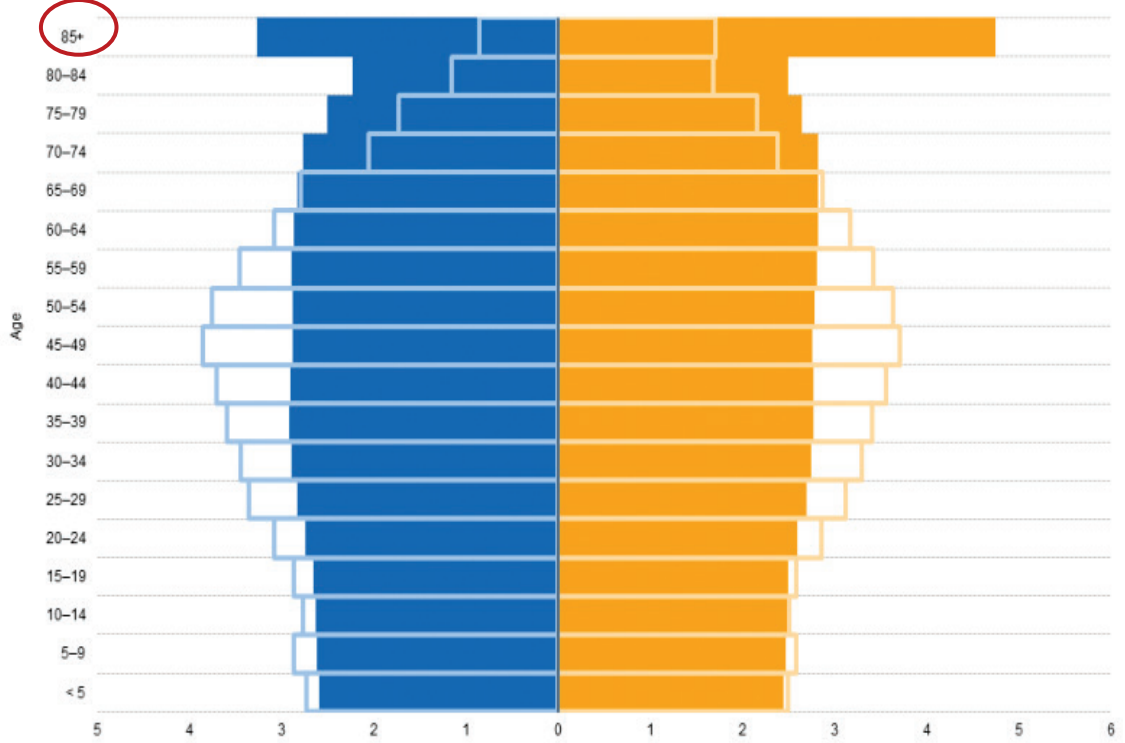
Information for the use of medicines in the elderly

Geriatric Medicines Strategy

EMA - Payer Community meeting

Presented by Francesca Cerreta

Population pyramid, EU-28, 2016 and 2080 (% of total population, Men , Women)



EMA Geriatric Medicines Strategy (2011):

Medicines used by geriatric patients must be of high quality, and appropriately researched and evaluated… **for use in this population**.

→ **Evidence based medicine**

Improve the availability of **information** on the use of medicines for older people.

→ **Informed prescription**

Study on off-label use of medicinal products in the EU (European Commission, 2017)

…"The efficacy and safety of medicines are hardly investigated in elder, multimorbid patients. The **lack of clinical data obtained in elderly** is (still) **a matter of concern.**

Elderly form a **grey area.**

One could argue that medicinal products authorized for adults and used in the elderly is **in principle not off-label unless the SmPC** mentions:

- **upper age ranges**
- special **warnings**
- other **restrictions** for use in the elderly"

CHMP D80 AR Pilot - Elderly population

EUROPEAN MEDICINES AGENCY

Clinical Trials Regulation (EU No 536/2014):

"justification for the age allocation of subjects if a specific age group is excluded from or underrepresented in the CTs".

ICH E7: Studies in Support of Special Populations: Geriatrics

- "population in the clinical development program is **representative** of the target patient population;
- in the MAA **data should be presented for various age groups (i.e. <65, 65-74, 75-84 and ≥85)** to assess the consistency of the treatment effect and safety profile".

CHMP initiated a pilot on 10 new Marketing Authorisations

Additional geriatric section to the ARs templates.

Day 80 and Day 210 → EPAR SmPC PIL

Information required for the EPAR

EUROPEAN MEDICINES AGENCY

Adequate data is available for age range?

Frail patients included?

eCTD Module	Age 65-74 number / total number (all ages)	Age 75-84 number / total number (all ages)	Age 85+ number / total number (all ages)
Efficacy and Safety Studies			
Human PK Studies			

Epidemiology

CT inclusion/exclusion criteria

Co-morbidities

Concomitant medication

Safety signals particularly relevant?
(e.g. dizziness, delirium, orthostatic effects, falls, sedation, bleeding, urinary retention, loss of appetite).

Appropriately grouped?

dizziness + falls + fractures + syncope reviewed together.

Anticholinergic effects?

MedDRA Terms	Age <65 number (percentage)	Age 65-74 number (percentage)	Age 75-84 number (percentage)	Age 85+ number (percentage)
Total ADRs				
Serious ADRs – Total				
- Fatal				
- Hospitalization/prolong existing hospitalization				
- Life-threatening				
- Disability/incapacity				
- Other (medically significant)				
AE leading to drop-out				
Psychiatric disorders				
Nervous system disorders				
Accidents and injuries				
Cardiac disorders				
Vascular disorders				
Cerebrovascular disorders				
Infections and infestations				
Quality of life decreased				
Sum of postural hypotension, falls, black outs, syncope, dizziness, ataxia, fractures				

What is the most frequent situation?

Geriatric population is the largest users of medicines, but …

Data are usually missing in patients over 75 and/or with comorbidities and co-medications.

The lack of data over a certain age is usually stated in **4.2 Posology**.

Reflection paper on the wording of therapeutic indication

Benefit-risk balance not established. Extrapolation possible?

Age limits in 4.1 indication ? (not in 4.2)

Warning in 4.4 ?

?

Specific sub-sections for the older patients in 4.8, 5.1?

SmPC guideline recommendation	Analysis of SmPC wording on older patients	Meaningful for payers?
4.1 Indication		
It should be stated in which age groups the product is indicated, **specifying age limits**	Very rarely specified (generic“adults” includes elderly) Not restricted indication	
4.2 Posology		
The safety and efficacy have not been established a) no data are available b) limited data are available	Sometimes, (with age limits >65, 75, 85)	
It **should not be used** because of efficacy or safety concerns.	**Other** commonly used: - the use is not recommended - should be initiated with caution	
4.3. Contraindications		
a) Safety data give rise to concerns b) Elderly patients have been **excluded** from studies on grounds of safety	Very rarely	
4.4 Warnings		
Patients populations **not studied** in clinical trials	Rarely	

SmPC guideline recommendation	Meaningful for payers?
4.1 Indication	**Very rarely specified**
It should be stated in which age groups the product is indicated, **specifying age limits**	**Age limits should be explicit -> defining target population important for economic analysis** **otherwise we pay for uncertainty** **..but: troublesome not to reimburse**
4.2 Posology	**Sometimes (with age limits >65, 75, 85). Other wordings.**
The safety and efficacy have not been established a) no data are available b) limited data are available	• **Age limits should be in 4.1.** • **CLEAR INFORMATION FOR PHYSICIANS:** **limited/no data, not established safety/efficacy.** • **Dose adjustment important for economic analysis -> PK/PD needed**
It **should not be used** because of efficacy or safety concerns.	• **"caution" is meaningless, uniform wording needed.** • **"not recommended" less strict than "should not be used", should be in 4.3 contraindication if safety concern.**

SmPC guideline recommendation	Meaningful for payers?
4.3. Contraindications	**Very rarely**
a) Safety data give rise to concerns b) Elderly patients have been **excluded** from studies on grounds of safety	**Off-label?** **If excluded from studies, for whatever reason, it should be CLEAR** ⇩ **important for physicians' proper treatment decision**
4.4 Warnings	**Rarely**
Patients populations **not studied** in clinical trials	**Off –label?** **If not studied it should be stated CLEAR** **+** **JUSTIFICATION of why POSITIVE BENEFIT/RISK balance is ASSUMED**