Zorginstituut Nederland

Three wishes

Martin van der Graaff PhD
Zorginstituut Nederland

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EMA registration decisions increasingly tend to …..

Give broad (conceptual) indications, regardless of scope of supporting studies, e.g.

- diabetes drugs
- MS (2nd line reg. for 1st line studies)
- pirfenidone (80-100 % FEV much less studied)
- many orphans (hint of efficacy)

Include not-wholly proven indications in SmPC (e.g. rufinamide in children) creating a fuzzy boundary in the indication area

There are good reasons for doing this (e.g. protecting German GPs), the consequences however should be clear:

…leading to broad reimbursement, leading to….

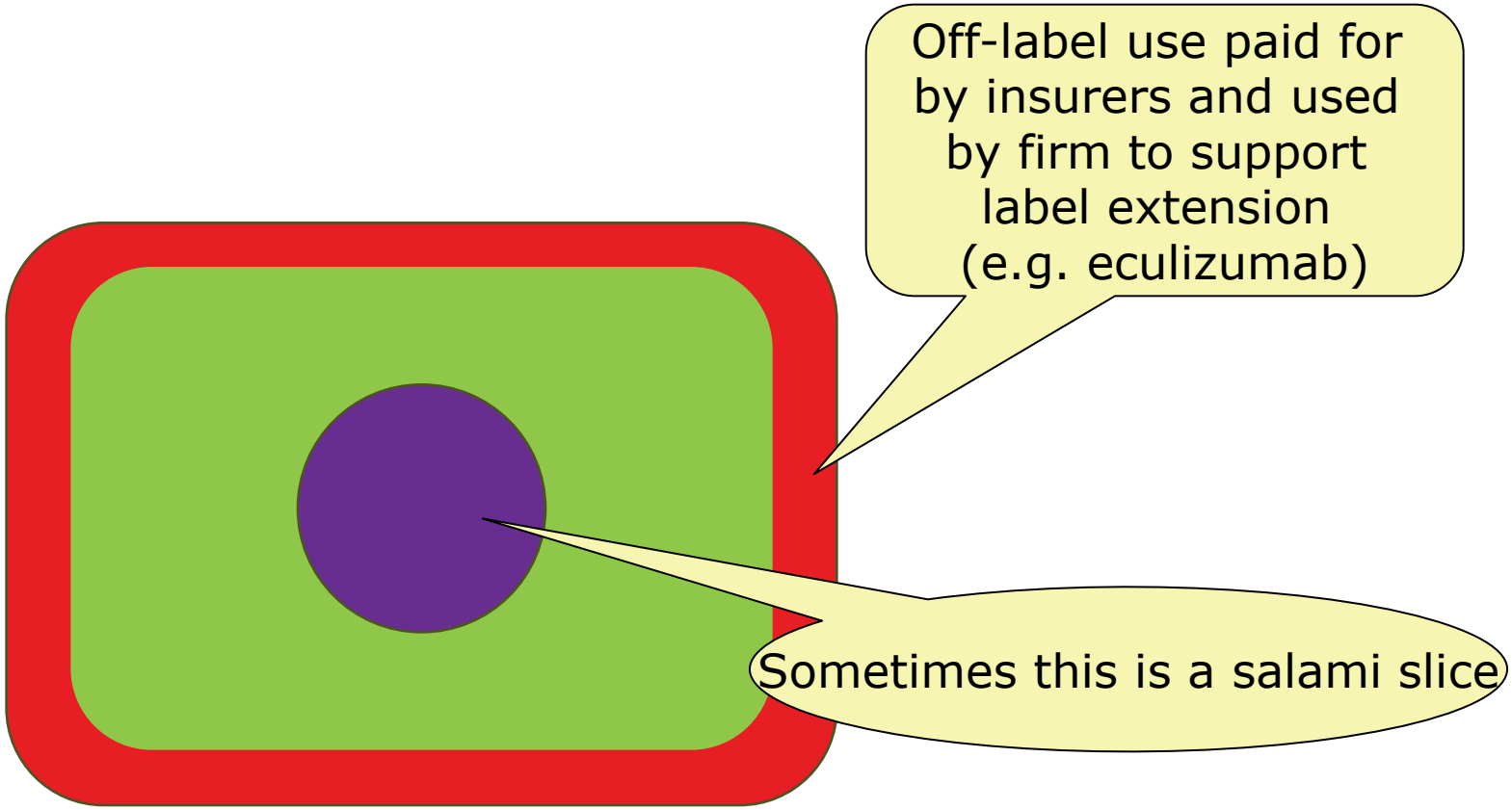
Drawn-out & complicated efforts to agree on reimbursed indications (e.g. Round Table Diabetes in NL)

Companies, learned bodies and patients present a registration as an indelible proof of excellence and demand full reimbursement at sometimes exagerrated price: “performance may not be spectacular, but all outcomes point in the same direction”

Discussions started by HTAs are sometimes bitterly resented: “institutionalized distrust”, say learned societies.

Lack of incentive to perform better or supplementary studies, since there is no additional reward for that

Possible discrepancies in reimbursement decisions, dependent on options payers have to set conditions



The Core		: population studied
The Full		: indication in EPAR
The Fringe		: potential for off-label use, use in slight disease, pre-emptive use, indication creep etc.

Pick & choose: SmPC or EPAR?

Sometimes EPAR nuances a product's performance, but that does not percolate into SmPC. Can payers motivate restrictions based on EPARs?

We sometimes have the impression that the EPAR and SmPC are edited post-positive opinion by stakeholders (including industry) to better support the decision, in the course of which doubts and reservations tend to be worded more friendly or even to disappear.

…and leading moreover to……

Early unrestricted registration by EMA can be killing for more in-depth research efforts. Therefore, MS require stand-alone or cooperative databasing, duplicating efforts that companies have to do for EMA but do not share with other stakeholders

Fall-out of unspecified registrations for pricing and negotiations:

- First indication sets price
- NL, FR, PL, NO, AT
- One weighted price for all indications
- FR, NO, BE, GE, AT
- Per indication a different price
- FR, LT, UK, IT

Example: Vimizim® (1/2)

Broad Indication: Vimizim® is indicated for the treatment of mucopolysaccharidosis, type IVA (Morquio A Syndrome, MPS IVA) in patients of all ages.

No “exceptional circumstances” nor “conditional registration”

▼This medicinal product is subject to additional monitoring. (However, no publicly accessible reports)

One study in 117 subjects older than 7

Example: Vimizim® (2/2)

Final report on monitoring required by 2025

No data segmentation by age

HTAs and payers left to themselves, but without resources to justify decision making.

MICD rarely named nor compared.

Plethora of outcomes measured rarely looked at critically for interdependence.

Risk: less central decision making leads to risk of more MS divergence in reimbursement decisions, or more MS with all-or-none decisions

Treatment to this community is so much more than just a therapy. It is hope for a future where their improved health allows them to reach their full potential."

The genie does not always grant wishes

They may not be appropriate

It may not be the remit or interest of the genie

Considerations:
“downstream organisations must solve their own problems”
“our remit is partly to promote innovation, not to stifle it”
“the product may still prove to be valuable”

Even so, it is time to formulate wishes:

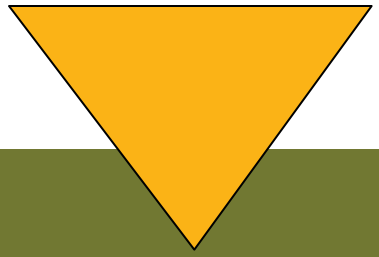
Wish one

EMA is a veritable powerhouse of pharmacotherapeutic knowledge, and yet:

Specificity of conclusions & warnings is unevenly divided

Preclinical & safety	: very cautious
Production & quality	: very extensive
Clinical assessment	: descriptive, not always firm conclusions

An orange triangle for non-definitive efficacy data (only to expire after better data have been submitted,not just after 5 years)



Wish two

EMA to demand and report in EPAR about patient stratification; would help HTAs enormously Instead of referring HTAs to CSRs to do their own computing (yes, we can sometimes do it ourselves, but)..

EMA to comment on sometimes seemingly inappropriate exclusion criteria e.g. no patients with brain metastases in melanoma studies even if these are the big killers

Wish three

Make some qualifying statements in the EPAR about:

stepped care (e.g. linaclotide)

Minimally Important Clinical Difference (MICD)

start-stop criteria (lack of those leads to e.g.: 'treatment should be continued as long as clinical benefit is observed’). Even statements
like: “patients who do not respond within 3 months are unlikely to ever respond” would help

possible interdepence of outcomes

A common interest

EMA rightly sees a role for itself in maintaining the momentum of innovation in medicinal products.

However if no restrictions are included in SmPCs or even strongly worded in EPARs, payers in extremis may have to resort to an overall “no” because they can not keep use of product in check

In that way, EMA’s purpose may defeat itself

Some sort of understanding is needed here

Even mutual understanding of dilemma’s may help

Will it cost? We don’t know

"If you could have three wishes, what would you pay for them?"

Will it work? You are never sure, but we hope

"These new regulations will fundamentally change the way we get around them."