

Accesso ai farmaci per il diabete: quali principi

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10 Ottobre 2020

BARRIERS PERSIST IN MANY DEVELOPING COUNTRIES

90%

of the population pays for medicines out-of-pocket

100
million

people are driven into poverty every year



Medicines represent the **LARGEST** family expenditure after food



On average, a family in Tanzania spends **53%** of family income to treat a child with type-1 diabetes

EFFECTIVENESS



“SOME MEDICINES ARE MORE IMPORTANT THAN OTHERS”

No public sector or health insurance system can afford to supply or reimburse every available medicine or health technology

- Need for systems to facilitate selection - improve supply and access, rational prescribing and control costs

WHO Essential Medicines List (EML) - selection of medicines that offer the best payback in terms of benefits to patients – since 1977

Essential Diagnostics List - 2018

Accesso ai farmaci: il ruolo di AIFA

Valore terapeutico – usi ottimali – rimborsabilità SSN e prezzi

- Approvazione e sintesi critica evidenze
- Prezzi e sostenibilità SSN
- Raccomandazioni usi ottimali – Note AIFA, schede, altro
- Ricerca indipendente e gaps – ruolo SSN (priorità)
- Informazione pubblica - SSN
- Drug utilization, OsMED, monitoraggio – SSN/SSR
- Coinvolgimento pz, cittadini

Quali professionalità per un *continuum*

- Approvazione e sintesi critica evidenze
- Raccomandazioni usi ottimali – Note AIFA, schede, altro
- Informazione pubblica SSN
- Drug utilization, OsMED, monitoraggio
- Coinvolgimento pazienti e cittadini
- Prezzi e sostenibilità SSN/SSR
- Ricerca indipendente e gaps – ruolo SSN

Approvazione SSN e ruolo AIFA

- Le nuove terapie avanzate hanno importanti spazi di ricerca clinica al momento della registrazione
- Occorre abbinare approvazione e sviluppo clinico
- Ruolo attivo di AIFA su:
 - Definizione strategia complessiva usi ottimali, ricerca e rimborso/usu SSN
 - Legame più coordinato approvazione EMA – CTS-CPR – SSN/SSR
 - Ricerca indipendente SSN
 - Coinvolgimento pazienti, associazioni e cittadini

Farmaci antidiabetici: WHO EML 2017

➤ **The Selection and Use of Essential Medicines** Report of the 21st WHO Expert Committee

*Second-line treatments for type 2 diabetes – comprehensive review –
EML and EMLc*

Second-line treatments for type 2 diabetes:

**Sulfonylureas, meglitinides, alpha-glucosidase inhibitors,
thiazolidinediones, dipeptidyl peptidase-4 inhibitors,
sodium-glucose co-transporter-2 inhibitors**

**Glucagon-like peptide-1 agonists, basal insulins, bolus insulins
and biphasic insulins**

ATC Code: see supplementary tables

Proposal

The application proposed updating of section 18.5 Insulins and other medicines used for diabetes of the EML and EMLc with a comprehensive and comparative assessment of all available second-line therapies (to be used in combination with metformin) for treatment of type 2 diabetes in adults, adolescents and children: sulfonylureas, meglitinides, alpha-glucosidase inhibitors, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, sodium-glucose co-transporter-2 inhibitors, glucagon-like peptide-1 agonists, basal insulins, bolus insulins, and biphasic insulins, including analogues.

Applicant(s)

George A. Wells, Shannon Kelly, Amy Johnston, Shuching Hsieh, Jesse Elliott, Zemin Bai, Li Chen, Alomgir Hossain, Becky Skidmore, Methods and Applications Group for Indirect Treatment Comparisons (MAGIC), Ottawa, Canada; Cardiovascular Research Methods Centre, University of Ottawa Heart Institute, Ottawa, Ontario.

Farmaci antidiabetici: WHO EML 2017

1. For adults with type 2 diabetes on metformin monotherapy with inadequate glycaemic control, what is the comparative efficacy and safety of using a drug from one of the following classes as second-line agent:
 - sulfonylurea
 - insulin
 - DPP-4 inhibitor
 - GLP-1 agonist
 - SGLT-2 inhibitor?
2. For adults with type 2 diabetes, what are the comparative cardiovascular effects of drugs belonging to one of the following classes
 - insulin
 - DPP-4 inhibitor
 - GLP-1 agonist
 - SGLT-2 inhibitor?

Question 1: Patients inadequately controlled on metformin

For the first research question, 175 unique RCTs and 78 companion publications were

Farmaci antidiabetici: WHO EML 2017

Table C. All-cause mortality – hazard ratios (HR) for all class comparisons

<i>Treatment</i>	<i>Reference</i>	<i>HR (95% CrI)</i>
DPP-4	Placebo	1.02 (0.83, 1.20)
SGLT-2		0.67 (0.47, 0.95)
GLP-1		0.89 (0.71, 1.12)
TZD		0.91 (0.71, 1.16)
SGLT-2	DPP-4	0.66 (0.45, 0.99)
GLP-1		0.87 (0.67, 1.19)
TZD		0.90 (0.67, 1.24)
GLP-1	SGLT-2	1.32 (0.89, 2.03)
TZD		1.36 (0.90, 2.09)
TZD	GLP-1	1.03 (0.74, 1.42)
Random-effect model		Total residual deviance 7.678 vs 8 data points Deviance information criteria –10.022

DPP-4 = dipeptidyl peptidase 4 inhibitor, SGLT-2 = sodium-glucose co-transporter 2 inhibitor, GLP-1 = glucagon-like peptide-1 agonist, TZD = thiazolidinediones

Statistically significant differences are shown in bold.

Farmaci antidiabetici: WHO EML 2017

t Series No.1006 , 2017

In synthesis, based on network meta-analyses, adjunctive second-line therapies were associated with possible reductions in glycaemic control when compared with metformin monotherapy, with few differences between any of the active treatments. Sulfonylurea and GLP-1 agonists reduced glycated haemoglobin when compared with DPP-4 inhibitors; GLP-1 agonists and sulfonylurea reduced weight when compared with metformin monotherapy, while insulin and sulfonylurea increased weight when compared with the other classes. GLP-1 agonists and insulins increased the number of adverse events and withdrawals. In high-risk patients, SGLT-2 inhibitors were possibly associated with a reduction in all-cause mortality when compared with placebo and with DPP-4 agonists and SGLT-2 inhibitors were not associated with severe hypoglycaemia events.

Sulfonylurea and insulins increased non-severe hypoglycaemia when compared with metformin monotherapy and other classes. However, basal insulin was associated with fewer non-severe hypoglycaemia events when compared with sulfonylurea.

Farmaci antidiabetici: WHO EML 2017

Committee recommendations

The Expert Committee acknowledged the wide coverage of the application, which compared all second-line therapies used in the intensification phase of therapy (i.e. between the initial therapy with metformin and any treatment combination containing insulin) in patients with type 2 diabetes.

The Committee noted that the application represents an advanced version of a report commissioned by the Canadian Agency for Drugs and Technologies in Health (CADTH). The Committee considered that data on the effectiveness of and harms caused by some of the medicines covered in the application will be supplemented in the coming years as new trials and longer follow-up are completed. The Committee considered the evidence provided was insufficient to propose changes to the EML, which thus far includes only sulfonylurea as intensification therapy.

The Committee confirmed the role of sulfonylureas as (one of) the most cost-effective treatment options for intensification therapy of type 2 diabetes.

The Committee noted that SGLT-2 inhibitors have been reported to be associated with a relevant clinical benefit as intensification therapy in patients at high risk of cardiovascular events, leading to a relevant reduction in overall mortality. This finding needs to be confirmed in other trials, before this class of medicines can be selectively supported for patients with type 2 diabetes.

On the basis of the evaluation, the Expert Committee did not recommend the inclusion of any additional medicines for second-line therapy of type 2 diabetes.

- Si è avviata una discussione approfondita (da Giugno 2020)
- Idee guida: nuova Nota nell'ambito della **Cronicità e prossimità**
- Complessità e rapidità (– relazione LG e tempi)
- Istituzione **tavolo AIFA** e Conflitti di interessi: **fine Ottobre**
- Necessità di un **confronto** privilegiando la **rapidità**
- Pubblicazione **nuova Nota AIFA** – privilegiando **l'efficacia**

A soft touch final

Thoughts for new medical students at a new medical school

Richard Smith

Giving advice to medical students makes doctors think about what is important in what they do

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BMJ 2003;327:1430-3

Earlier this year I had the privilege of speaking to new medical students at a new medical school—the Hull York Medical School. What should I say? I felt almost overawed. It seemed a major responsibility, although I knew that most of what I said would—thankfully—be forgotten or ignored as the ramblings of yet another “old fart.” Needing help and a method, I started by asking members of our editorial board, doctors from all over the world, what I should say. They responded with enthusiasm, giving me the thought that it might be a good idea to broaden the debate. That’s the main reason for this article: it’s a preliminary statement in what I hope might be a rich debate. In thinking what we want to say to new entrants to the profession we have to think of what is important about what we do.

What follows is a mixture of my own ideas and those I selected from the responses of the members of the edi-

I asked the students when I spoke to them, “What was the greatest invention of the 20th century?” Was it quantum mechanics, aircraft, penicillin, the atomic bomb, the double helix, the randomised controlled trial? I suggested (slightly tongue in cheek) that it was D W Winnicott’s “the good enough mother.” (Actually, it was jazz.) The attempt to be the best mother in the world, the best neurosurgeon, or the best medical editor will end in tears. Being a good enough mother is to be a good mother, whereas the attempt to be the best will guarantee that you won’t be (indeed, you may be a highly damaging mother). Similarly, you should aim to be a good enough medical student and doctor.

One of the curses of doctors is that they have such strong stereotypes. Doctors are upstanding, trustworthy, clever, straitlaced, conservative, authoritarian,

R Smith ... Riflessioni per i giovani medici

Box 6: As the world changes, what should persist?

- Clear ethical values
- Being clear about the purpose of your organisation
- Putting patients first
- Constantly trying to improve
- Basing what we do on evidence
- Leadership
- Education and learning

Medicina e' un'arte al
crocevia di varie scienze

G. Canguilhem