WHITE PAPER

LOOKING PAST THE WINDOW DRESSING:

UNDERSTANDING BLOOD GLUCOSE TESTING STRIPS IN A FORMULARY ENVIRONMENT

March 2013

PURPOSE

This paper explores the science behind glucose test strips and proposes the format by which insurers can implement a reference based, interchangeability formulary.

HISTORY

In 1962, Leland Clark and Champ Lyons at the Medical College of Alabama developed the first glucose enzyme electrode. The enzyme in the electrode functioned in the presence of glucose to decrease the amount of oxygen available to the oxygen electrode, thereby relating oxygen levels to glucose concentration.

Home glucose monitoring was demonstrated to improve glycemic control of type 1 diabetes in the late 1970s, and the first meters were marketed for home use around 1981. The two models initially dominant in North America in the 1980s were the Glucometer, introduced on November 1981 whose trademark is owned by Bayer and the Accu-chek meter (by Roche). Consequently, these brand names have become synonymous with the generic product to many health care professionals.

Over the last 30+ years, the features of glucose testing machines and strips have improved, but pricing has not properly reflected the competition in the marketplace.

MARKET SIZE AND GROWTH

Self-monitoring of blood glucose (SMBG) is big business and is getting bigger every year. Since 1980, the market for blood glucose monitoring products has undergone phenomenal growth. While the United States is the single largest market for SMBG, with about 40% of the global market, there has been dramatic growth in demand for these products across the globe. To provide some perspective, Enterprise Analysis Corporation estimates that the world market for SMBG testing supplies was $1.7 billion in 1994. By 2000, the market had reached approximately $3.8 billion, and by 2008, worldwide sales of these products climbed to an astonishing $8.8 billion. This represents an approximate 12.5% compound annual growth rate since 1994. In fact, the SMBG testing market, which barely existed in 1980, now accounts for approximately 22% of the entire $39 billion IN VITRO diagnostics industry.[1] In 2011, Visiongain reported global sales of $9.7 billion and predicted that the market would be worth 27.42 billion by 2022.

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[1] The Business of Self Monitoring of Blood Glucose: A market profile; Mark D Hughes B.S. M.B.A
J Diabetes Sci Technol. 2009 September; 3(5): 1219–1223.

DEFINING THE DIFFERENCES

ACCURACY – A KEY DIFFERENTIATOR?

Health Canada has adopted the standard ISO 15197:2003 for accuracy. Health Canada will only license products that meet this standard. Proof of a products' acceptable level of accuracy? Licensure.

Health Canada Therapeutic Products Directorate's (TPD) Recognized Standard for medical devices: ISO 15197:2003: In Vitro diagnostic test systems – Requirements for blood-glucose monitoring systems for self testing in managing diabetes mellitus.

Accuracy Parameter Current EN ISO 15197

Accuracy Parameter	ISO 15197:2003	Draft ISO 15197 (new standard contemplated by ISO)
Target blood glucose level from which to base mmol/L bias or % bias	4.2 mmol/L	5.6 mmol/L
Acceptable bias from reference value for lower target glucose levels	+/- .8 mmol/L	+/- .8 mmol/L
Acceptable bias from reference value for higher target glucose levels	+/- 20%	+/- 15%
Acceptable % of all results within bias limits	95%	95%
Parks Error Grid	Not required	99% of results within Zones A and B

Many meters already meet new standard including value priced strips. Those that do not are already working towards meeting the draft new standard.

REAGENTS DEFINE THE METER

re·a·gent
/rēˈājənt/

Noun
A substance or mixture for use in chemical analysis or other reactions.

Synonyms
test

Reagent type is an important clinical consideration when selecting the most appropriate meter and strip type due to possible interactions associated with each strip type.

One of the best kept secrets in the category is that of the 25 meters in the marketplace,

48% use a GOD reagent strip,

30% use at GDH-FAD or NAD strip

12% use GDH PQQ, or its mutated version MUT Q-GDH.

THE SCIENCE OF STRIPS

A key component to understanding the SMBG marketplace is to understand the difference and classification of glucose testing strips

There are three common Reagent Types. They are based on the following action: Electrons from the glucose oxidation reaction are first taken up by the enzyme's cofactor (primary electron acceptor) and transferred to either oxygen (first generation), an electron mediator (second generation), or directly to the electrode (third generation).[2]

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[2] Review of Glucose Oxidases and Glucose Dehydrogenases: A Bird's Eye View of Glucose Sensing Enzymes Stefano Ferri, Ph.D., Katsuhiro Kojima, Ph.D., and Koji Sode, Ph.D.

Strip reagent type and potential interactions			
	GDH PQQ + (MUT)	**GDH-FAD and NAD**	**GOD**
	3rd generation	**2nd generation**	**1st generation**
Definition	**GDH-PQQ**= glucose dehydrogenase-pyrroloquinolinequinone; **MUT Q-GDH =** glucose dehydrogenase-with pyrroloquinolinequinone modified to eliminate maltose interference	**GDH-FAD**= glucose dehydrogenase-flavin adenine dinucleotide **GDH-NAD**=glucose dehydrogenase with nicotinamide-adenine dinucleotide	**GOD**= glucose oxidase
FDA/HC Warnings	PQQ subject of FDA and Health Canada warnings. 12,672 AE's reported between 2004-2008. Some manufacturers have modified their meter technology but strips are interchangeable in PQQ reading meter therefore not recommended for use by Baxter for peritoneal dialysis patients[3]	No warnings associated with technology	No warnings associated with technology
Detects glucose &	Maltose, xylose, galactose.	Some but not all strips detect sugars other than glucose[4]	Not affected by non-glucose sugars
Cautions	Do not rely on strip readings in the presence of: Icodextrin (used in peritoneal dialysis); some IV immunoglobulins (Octagam 5%);, Gamimune N 5%; WinRho SDF liquid; Vaccinia Immune Globulin Intravenous (Human); HepaGamB; Orencia (abetacept); Adept adhesion reduction solution (4% icodextrin); BEXXAR radioimmunotherapy agent; Any product containing or metabolized into maltose, galactose or xylose.[5]	Xylose: Xylose is present in some fruits and vegetables, aloe vera gel, kelp, echinacea, *Boswellia*, and psyllium. Xylose 0.5 mg/kg is orally administered (to a maximum of 25 g) to determine if intestinal malabsorption is present. Xylose is also available as a dietary supplement in some health food stores. When used clinically, the doses of xylose may be sufficient to interfere with some blood glucose monitoring systems.[6]	High doses of acetaminophen – "At certain concentration levels, acetaminophen may begin to impact and cause inaccurately high results. Because all patients may metabolize drugs differently, it is important to understand that abnormally high concentration levels in blood may affect blood glucose testing accuracy."[7]
Mechanism of action	Employ direct electron transfer to the electrode, thus eliminating toxic artificial electron mediators and avoiding errors due to variations in the concentration of oxygen in blood samples.	enzymes transfer electrons to artificial electron acceptors (also referred to as electron mediators or redox dyes) instead of oxygen to avoid interference from other redox species. The reacted (reduced) artificial electron acceptors are monitored colorimetrically or electrochemically.	Systems employ oxygen as the electron acceptor, determining glucose concentration by following either the consumption of oxygen or the liberation of hydrogen peroxide.

[3] http://www.glucosesafety.com/ca/en/downloads/canada_specific_glucose_monitor_list.pdf
[4] http://www.glucosesafety.com/my/pdf/health%20letters.pdf
[5] http://www.patientsafety.gov/alerts/GlucoseMonitoringTestStripAlertAL10-01WWW.pdf
[6] Interference of Maltose, Icodextrin, Galactose, or Xylose with Some Blood Glucose Monitoring Systems Thomas G. Schleis, M.S. Pharmacotherapy. 2007;27(9):1313-132
[7] http://www.bernardfarrell.com/blog/uploaded_docs/RocheSystemLimitationsWhitePaper.pdf

THE TRUE COST OF TEST STRIPS

Test Strips can run from 40 cents to well over $1 apiece, and people often question why they cost so much. Beyond the enzymes, precious metals, chemicals, and other materials that make up test strips, manufacturers must design and build plants to produce the strips. Once those upfront costs have been paid, the everyday cost of making strips goes down. Strip makers are "buying this material in huge quantities and spreading this cost over a billion pieces," says diabetes business expert David Kliff, founder of DiabeticInvestor.com

Kliff estimates that manufacturers reap a 70 to 80 percent profit on strips. "This is America; you are allowed to make money," he says, adding that a part of the profits is plowed back into strip-making to "make better systems." Investment in new technology over the past couple of decades has made blood glucose testing faster, easier, and less painful for people with diabetes.

Health insurers can also affect the price of strips. "Ninety percent [of test strips] are paid for with insurance," says Kliff. This gives insurance companies negotiating power over the price they pay for strips—as well as the ability to specify which brands they'll cover.[8]

THE NEED TO RE-EVALUATE COSTS

The benefits of well managed blood sugar are well known. However, leading authorities agree:

From the Canadian Diabetes Association (CDA)

Cost of Diabetes Medication, Supplies and Medical Devices

Position Statement:

Federal, provincial and territorial governments should commit to a strategy such that the cost to the individual of diabetes medication, supplies and medical devices, as well as the costs associated with diabetes-related complications, are not a barrier or a burden to managing the disease.[9]

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[8] *American Diabetes Association, Diabetes Forecast – the Health Living Magazine July 2012*

[9] http://www.diabetes.ca/about-us/what/position-statements/medications/cost/

From the Canadian Agency for Drugs and Technology in Health (CADTH)

Cost-Effectiveness of Blood Glucose Test Strips in the Management of Adult Patients with Diabetes Mellitus

A reduction in the price of blood glucose test strips would improve the cost-effectiveness of SMBG. For patients with insulin-treated type 2 diabetes, SMBG testing frequencies beyond 21 test strips per week require unrealistically large A1C estimates of effect to achieve favourable incremental cost per QALY estimates.

And patients have spoken:

57% of Canadians with diabetes say they do not comply with their prescribed therapy because they cannot afford their medications, devices and supplies, thus potentially compromising their diabetes management.

September 12, 2011

Report: Government Coverage of Diabetes Medications, Devices and Supplies Canadian Diabetes Association

FORMULARY MANAGEMENT: A TWO-FOLD PROCESS

USAGE MANAGEMENT

Strip use limitations have long been eyed by public and private insurers as a method of gaining control over spiraling costs; however concerns regarding the many variables associated with patient need has many insurers cautious in this approach.

The Institute for clinical Evaluative Sciences in their report "Blood Glucose Test Strip Use – Patterns, Costs and potential cost reductions[10] identified four diabetes therapy groups:

Exhibit 1 Description of the four diabetes therapy groups used to stratify study patients

Diabetes Therapy Group	Description
1. Insulin	At least one prescription for insulin regardless of other diabetes drug therapy
2. Hypoglycemia-inducing oral glucose-lowering drugs	At least one prescription for an oral glucose-lowering drug that can cause hypoglycemia (sulfonylureas, repaglinide), but no insulin treatment
3. Non-hypoglycemia-inducing oral glucose-lowering drugs	At least one prescription for an oral glucose-lowering drug not generally associated with hypoglycemia (metformin, thiazolidinediones, acarbose), but no treatment with insulin or the other oral glucose-lowering drugs described above
4. No glucose-lowering drug therapy	Diabetes controlled through diet and exercise

Further they offered 5 scenarios for strip usage restrictions within these groups

Exhibit 2 Description of the five scenarios related to testing frequency, based on diabetes therapy group

Scenario	Description
1	Unlimited use in Group 1; no SMBG use in Groups 2, 3 and 4
2	Unlimited use in Group 1; a maximum of 100 strips per person per year in Groups 2 and 3; no SMBG use in Group 4
3	Unlimited use in Groups 1 and 2; a maximum of 100 strips per person per year in Groups 3 and 4
4	Unlimited use in Groups 1 and 2; a maximum of 200 strips per person per year in Groups 3 and 4
5	Unlimited use in Groups 1 and 2; a maximum of 400 strips per person per year in Groups 3 and 4

PRICE MANAGEMENT

[10] Gomes T, Juurlink DN, Shah BR, Paterson JM, Mamdani MM. *Blood Glucose Test Strip Use: Patterns, Costs and Potential Cost Reduction Associated with Reduced Testing. ICES Investigative Report.* Toronto: Institute for Clinical Evaluative Sciences; 2009.

By reference pricing the blood glucose testing strip category by reagent group, not only does the formulary offer the choice required by clinicians and addresses all possible interactions, but limits pricing to lowest cost product in that category while not restricting strip utilization requirements.

Sample formulary:

mck number	description	manuf.	price/100	reagent type	comments
GDH-PQQ= glucose dehydrogenase-pyrroloquinolinequinone					
99796	ACCU-CHEK COMPACT TEST FASTER STRIP 102	RDH	75.96	GDH PQQ	PQQ: Due to the risks associated with this category (including MUT Q-GDH), could be considered for delisting.
291591	ACCU-CHEK ADV COMF STRIP 100	RDH	74.46	GDH PQQ	
803262	TRUETEST TEST STRIPS 100	NDC	56.43	GDH PQQ	
MUT Q-GDH =glucose dehydrogenase with pyrroloquinolinequinone modified to eliminate maltose interference					
492249	ACCU-CHEK AVIVA STRIP 100	RDH	74.46	MUT Q-GDH	
2297	ACCU-CHEK MOBILE CASETTE 100	RDH	74.46	MUT Q-GDH	
GDH-FAD= glucose dehydrogenase-flavin adenine dinucleotide					FAD: Second most common strip type. GLUCODR is the value priced entry in this reagent category. Health Canada approval is expected in the first half of 2013.
25758	BAY CONTOUR NEXT STRIP 100	BAH	73.04	GDH-FAD	
272229	BAY CONTOUR STRIP 100	BAH	73.04	GDH-FAD	
550962	FREESTYLE LITE ZIPWIK TEST STRIP 100	ADC	72.11	GDH-FAD	
706622	FREESTYLE TEST STRIPS 100	ADC	72.11	GDH-FAD	
TBA	GLUCODR *****AWAITING LICENSURE****	MDH	49.00	GDH-FAD	
GDH-NAD=glucose dehydrogenase with nicotinamide-adenine dinucleotide					NAD: This category could be considered for grouping with GDH FAD as its cautions are similar.
946442	STRIPS TESTS PRECISION XTRA 100/BOX	ADC	72.01	GDH-NAD	
GOD= glucose oxidase					
142653	NOVAMAX GLUC STRP 100	NBC	73.05	GOD	
361444	BAY BREEZE 2 TEST STRIP 100	BAH	73.04	GOD	GOD: Most common strip type. Medisure currently lowest price offering.
989665	ONE TOUCH ULTRA GLUC TEST STRIPS BLUE 100	LIF	72.56	GOD	
14146	ONE TOUCH VERIO STRIP 100	LIF	72.56	GOD	
38000	ORACLE T/STRP 100	WMN	72.56	GOD	
22118	BG STAR TEST STRIPS 2X50	SAC	70.54	GOD	
9668	ACCUTREND GLUC STRIP 25 ($/25's= 17.63)	RDH	70.52	GOD	
553891	ITEST TEST STRIPS 100	AUM	65.84	GOD	
7560	BIONIME GS100 BLD T/STRP 100	BMC	58.32	GOD	
LISTED	MEDISURE STRIPS 100	MSL	49.00	GOD	

****Note: GlucoDr (pronounced "Glucodoctor") is a value priced GDH-FAD strip currently being evaluated by Health Canada. Licensure is expected in the first half of 2013. It will be offered at a 0 .49 cent strip.***

CONCLUSION

Value priced glucose testing systems using recognized reagent systems offer price savings while not impeding clinical choice or patient care. Using the science of reagents helps to clearly categorize the marketplace thus creating the potential framework for interchangeability and reference based pricing.

Medi+Sure offers a value priced competative product that can offer immediate savings to patients as well as formulary budgets in a referenced pricing/ interchangeability environment. For more information on Medi+Sure's visit http://www.medisure.ca/