

elis

Pharmaceuticals

Elis is the license holder of Vitaros for the Middle East

The logo for Vitaros features the word "vitaros" in a blue, lowercase, sans-serif font. The letter "o" is replaced by a stylized yellow and blue water drop icon. Below the brand name, the text "(alprostadiil cream)" is written in a smaller, grey, lowercase font.

vitarosTM
(alprostadiil cream)



Topical Treatment for Erectile Dysfunction

Health Canada & European Health Authorities granted marketing approval for **Vitaros**[®] as a

FIRST-LINE THERAPY FOR ERECTILE DYSFUNCTION

for entire patient population including non-PDE5 patients



vitaros™

(alprostadil cream)

**FIRST-IN-CLASS TOPICAL CREAM TREATMENT
FOR ERECTILE DYSFUNCTION**

Vitaros Marketed in the following countries

- By Takeda in the United Kingdom - June 2014
- By Novartis-S/ Hexal in Germany, Sweden & Belgium in 2014
- By Majorelle Laboratory in France in 2015
- By BRACCO in Italy in 2015

Vitaros® is the right treatment for the ED Unmet Needs



VITAROS®

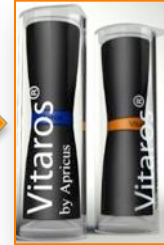
Topical alprostadil/DDAIP for the Treatment of Erectile Dysfunction

Vitaros is the first approved topical prescription drug for impotence



- Cold Chain (2°C -8°)
- 7 Days Room Temp
- Shelf Life 18 Month

Second Generation
Room Temperature
Available in 2016



- Room Temperature
- Expected 24-36 month shelf life
- **Key driver of market growth and expansion**

- Topical cream, high viscosity
- Prostaglandin E1, potent vasodilator
- Rapid onset (generally 5-30 minutes)
- Significant efficacy, including difficult to treat populations

- **Diabetic patients**
- **Hypertensive patients**
- **Patients with cardiac issues**
- **Patients on nitrates and alpha blockers**
- **Prostatectomy patients**
- **Sildenafil (Viagra®) failures**

- Side effects are generally mild, transient and topically related
- Studied in over 3,300 patients
- Offers first choice/ first line option in discussion of alternatives with ED patients

Strong IP Estate:

Issued patents through 2026 and patent applications filed for extended protection through 2032

Award Winner ESSM 2011



ESSM Career Award-Winner **VITAROS®**
Jacques Buvant

AWARD WINNER

VITAROS® Podium Presentation Named **Best Clinical Presentation Award** 2011 (Male Sexual Disorder) by the Scientific Committee of the Congress for the **ESSM** European Society of Sexual Medicine Meeting in Milan.

Efficacy and Safety of topical alprostadil Cream (**Vitaros®**) in hypertensive, diabetic and cardiac patients with male erectile dysfunction (ED)

VITAROS®

World's Approvals



Canada Approval

HEALTH CANADA

Nov. 2010



European Decentralized
Approval (10 Countries)



EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

June 2013

European National Phase Approvals in



United Kingdom



Aug. 2013



Spain

MINISTERIO
DE SANIDAD, SERVICIOS SOCIALES
E IGUALDAD

April 2014



Germany



Oct. 2013



Sweden



Aug. 2013



Netherlands



Ministry of Health,
Welfare and Sport

Aug. 2013



France

Dec. 2013



Ireland



Aug. 2013



Italy

Nov. 2013



Luxembourg

April 2014



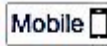
Belgium

Jan. 2014

Also approved in August in Austria, Cyprus, the Czech Republic, Denmark, Finland, Greece, Iceland, Norway, Poland, Portugal, Romania and the Slovak Republic

Partnerships throughout the world of **Vitaros®**





1519 VITAROS® EFFICACY AND SAFETY IN VIAGRA® NON-RESPONDERS WITH LONGER TERM USE

John Mulhall, Jacques Buvat, Irwin Goldstein, Bassam Damaj, Daniel Frank, Ysabella Fernando

DOI: <http://dx.doi.org/10.1016/j.juro.2013.02.2997>

Article Info

Abstract

Full Text

Vitaros® (alprostadil topical cream) is a novel erectogenic therapy, applied topically to the urethral meatus. The efficacy and safety of Vitaros®, was tested in erectile dysfunction (ED) patients in Phase 3 clinical trials including men who had previously taken the phosphodiesterase type 5 (PDE-5) inhibitor, Viagra®. Efficacy after twelve weeks and longer term use was evaluated to determine whether Vitaros® may sustain erectile function in men previously unresponsive to PDE-5 inhibitors.

CONCLUSIONS

In general, Vitaros® 200 and 300 mcg doses showed improved erections in this population and adverse events were limited, decreasing with repeated exposure. Therefore, Vitaros® may be a viable treatment option for those patients previously unresponsive to PDE-5 inhibitors.

Jump to Section

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PGE1s Drugs; side effects comparison

THE CANADIAN JOURNAL OF UROLOGY™

Urology Update for Primary Care Physicians for 2013

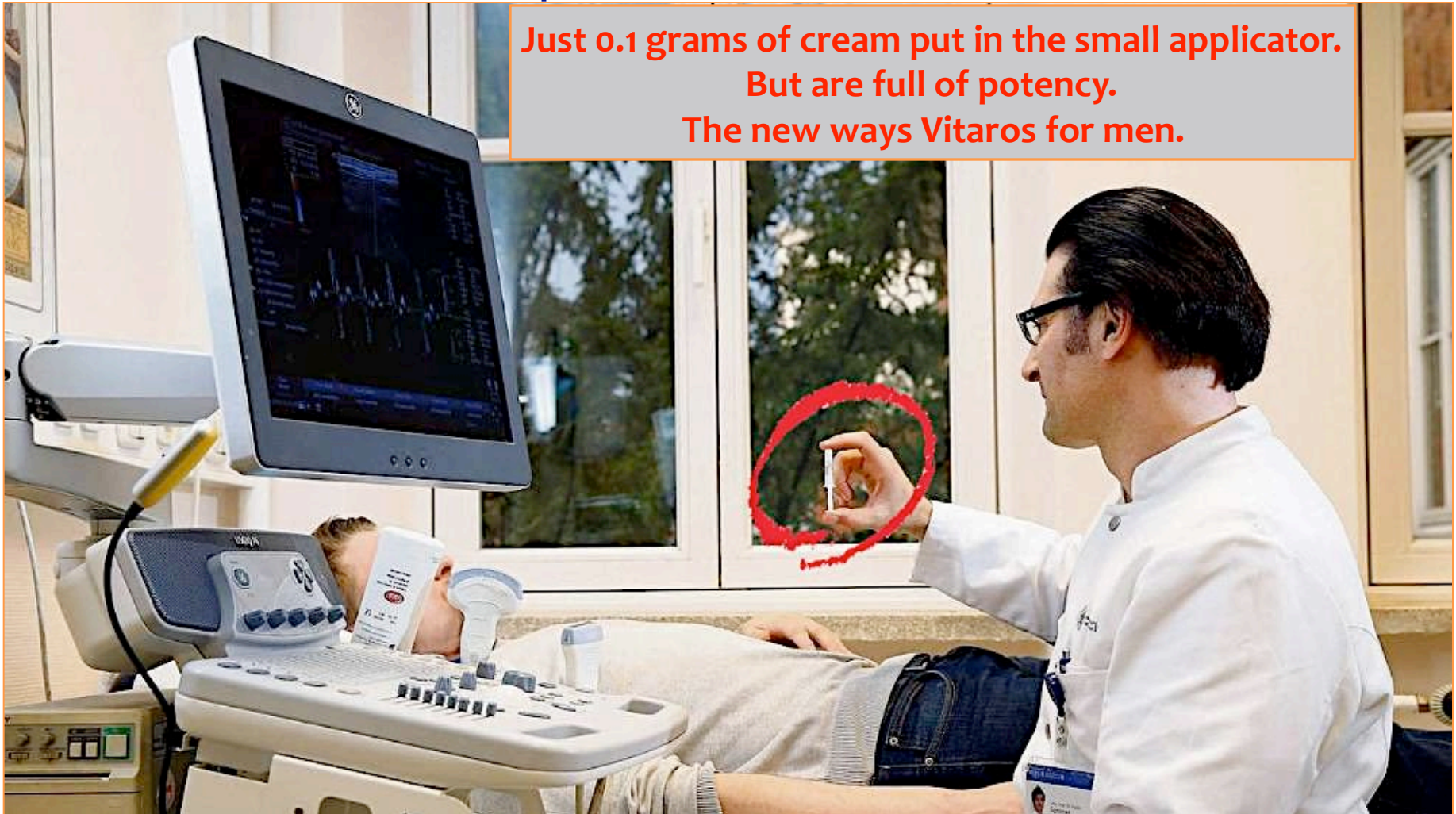
TABLE 2. Transurethral (TU) and intracavernosal (IC) therapy for erectile dysfunction (ED)

Name (Brand name)	Dosage	Mechanism of action	Side effects/Notes
Alprostadil TU (MUSE)	250 mcg-1000 mcg Max 2 administrations per 24 hrs	Synthetic PGE1 stimulates increased levels of cAMP	Painful erection; urethral pain; bleeding; priapism (rare)
Alprostadil cream (Vitaros [approved in Canada])		Synthetic PGE1 stimulates increased levels of cAMP	Penile burning sensation
Alprostadil IC (Caverject, Edex 1)	2.5 mcg-20 mcg* Max 1x daily and 3x weekly	Same as above	Penile pain, fibrosis hematoma; priapism (rare)



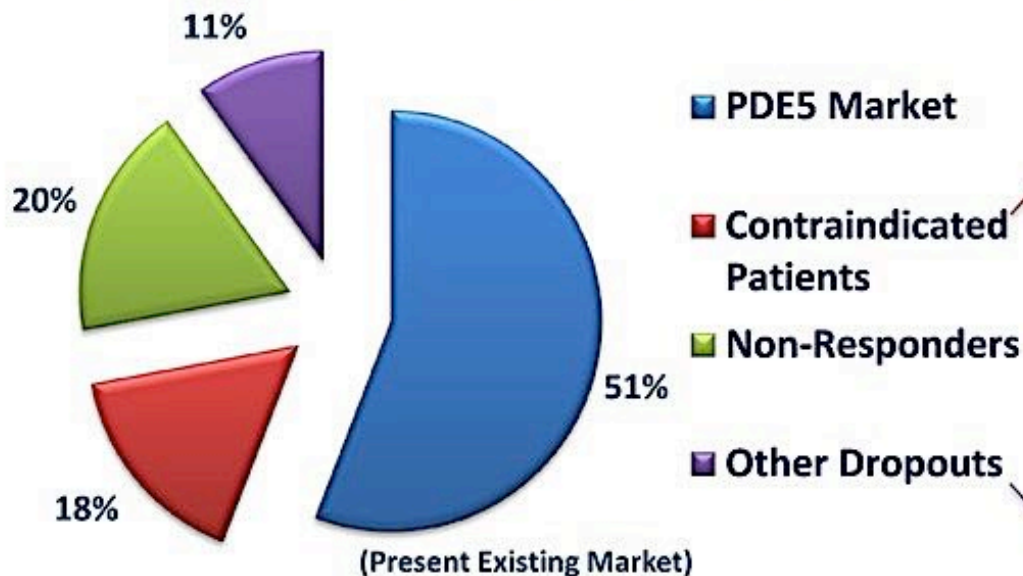
**UKE - University Medical Center Hamburg-Eppendorf
Professor treated impotent men with sex cream FROM THE TUBE**

**Just 0.1 grams of cream put in the small applicator.
But are full of potency.
The new ways Vitaros for men.**

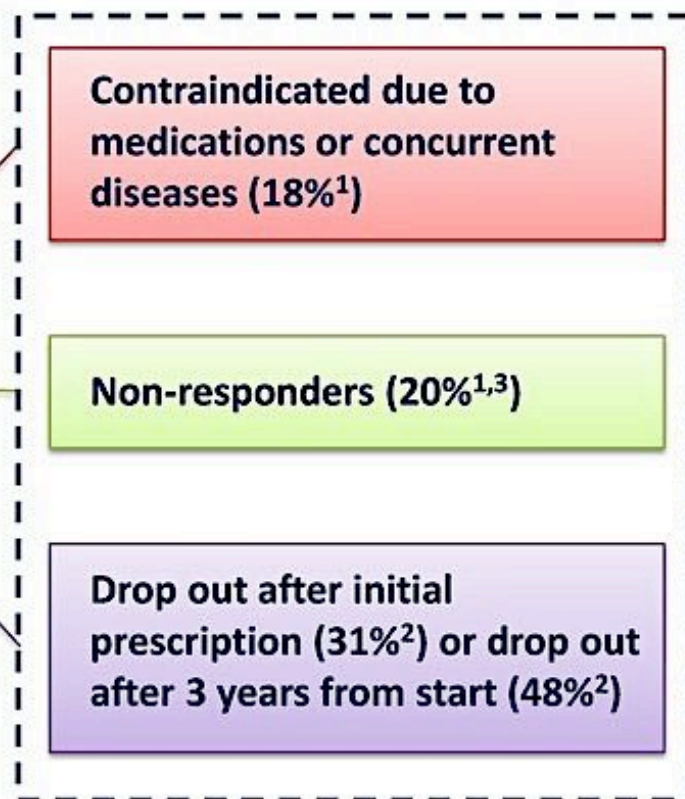


Vitaros®: Targeting the Untreated

ED Market Segmentation



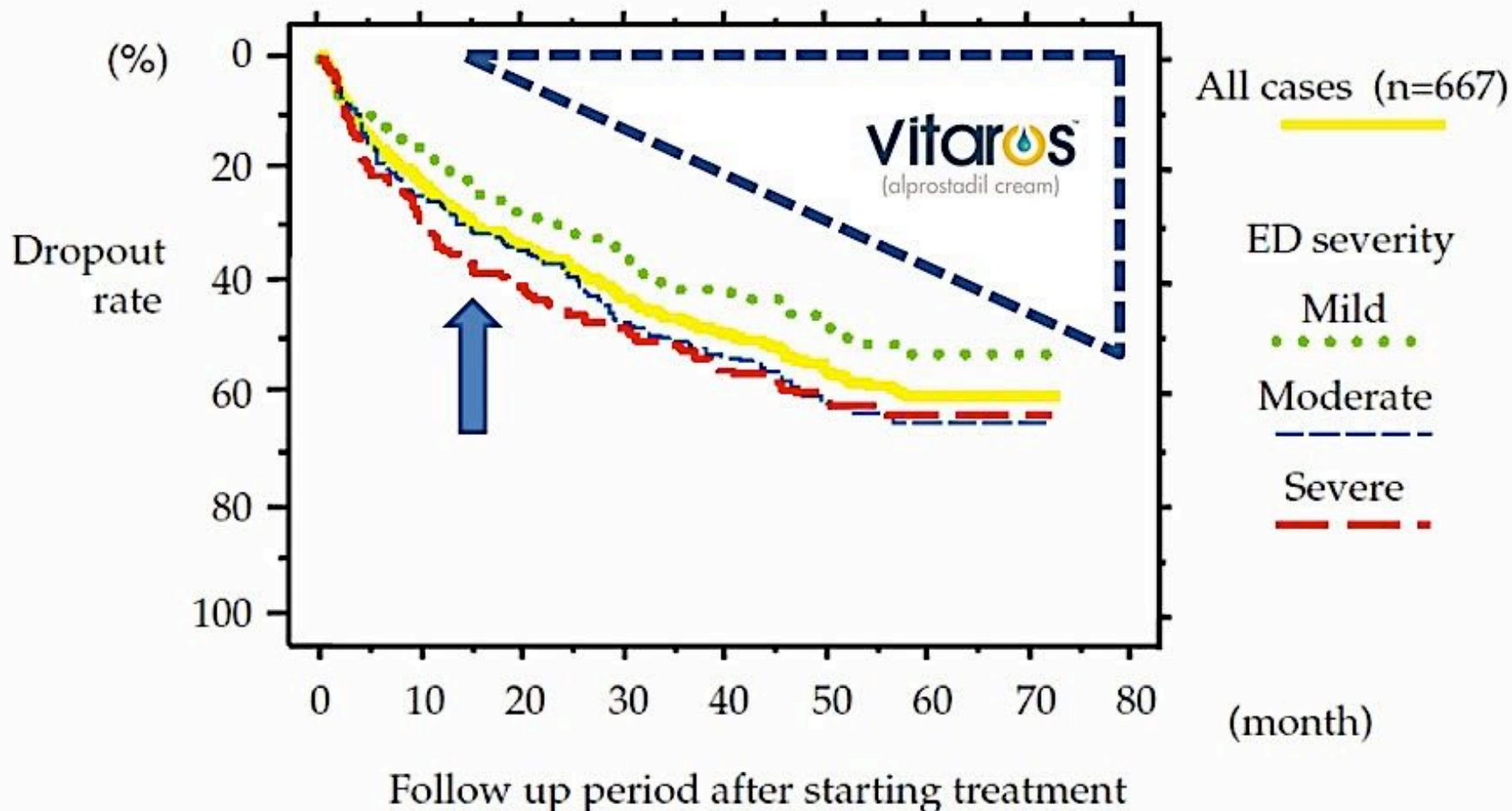
There is a significant ED patient population with an unmet need



49% of ED patients cannot be treated with PDE5

1. D2 Market Research, June 2007
2. Sato Y et al, How long do patients with erectile dysfunction continue to use sildenafil citrate? *International Journal of Urology*. (2007) 14, 339-342
3. Carvalheira AA, Pereira NM, Maroco J, and Forjaz V. Dropout in the treatment of erectile dysfunction with PDE5: A study on predictors and a qualitative analysis of reasons for discontinuation. *J Sex Med* 2012;9:2361-2369

ED: Significant Market of Untreated Patients: Sildenafil Drop-out Rate



Kaplan-Meier dropout rate in all successful sildenafil treatment cases and dependence on severity of erectile dysfunction (ED); significant differences in ED severity by the log-rank test ($P = 0.029$)¹²

Global ED market estimated at \$5.5 billion

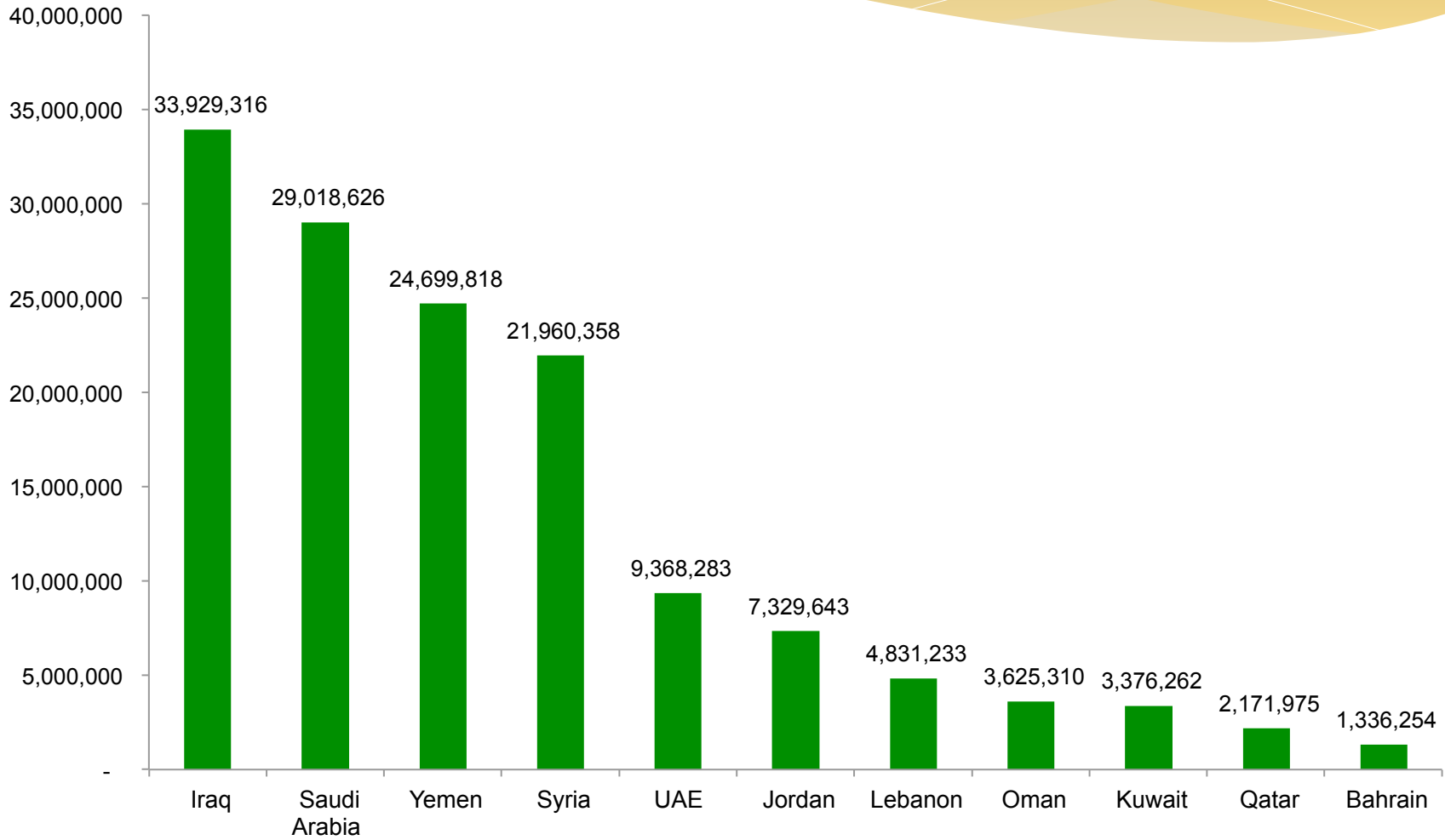
IMS Health 2013

Middle East

The current Middle Eastern ED market exceed **10,000,000 unit** sold per year from the PDE5 drugs including Viagra, Levitra, Cialis, Snafi as well as generic to serve the PDE5 inhibitors responders, patients represent 51% of the total ED patients; **the unmet need counter-indicated and non responders to PDE5 medicines represent 49% still need to be served.**

Several local studies showed that the prevalence of ED was >60% among Arab men. Risk factors and medical comorbidities that negatively affect the cardiovascular system, endothelial function and ultimately erectile function were common in men in Arab countries. For instance, at least five Arab countries are included in the top 10 countries worldwide with a high prevalence of diabetes mellitus. The global statistics showed that other risk factors such as obesity, smoking, hypertension and dyslipidaemia are also very prevalent in Arab countries. This fact can explain the high incidence of both cardiovascular disease and ED among Arab men.

Markets Demographics



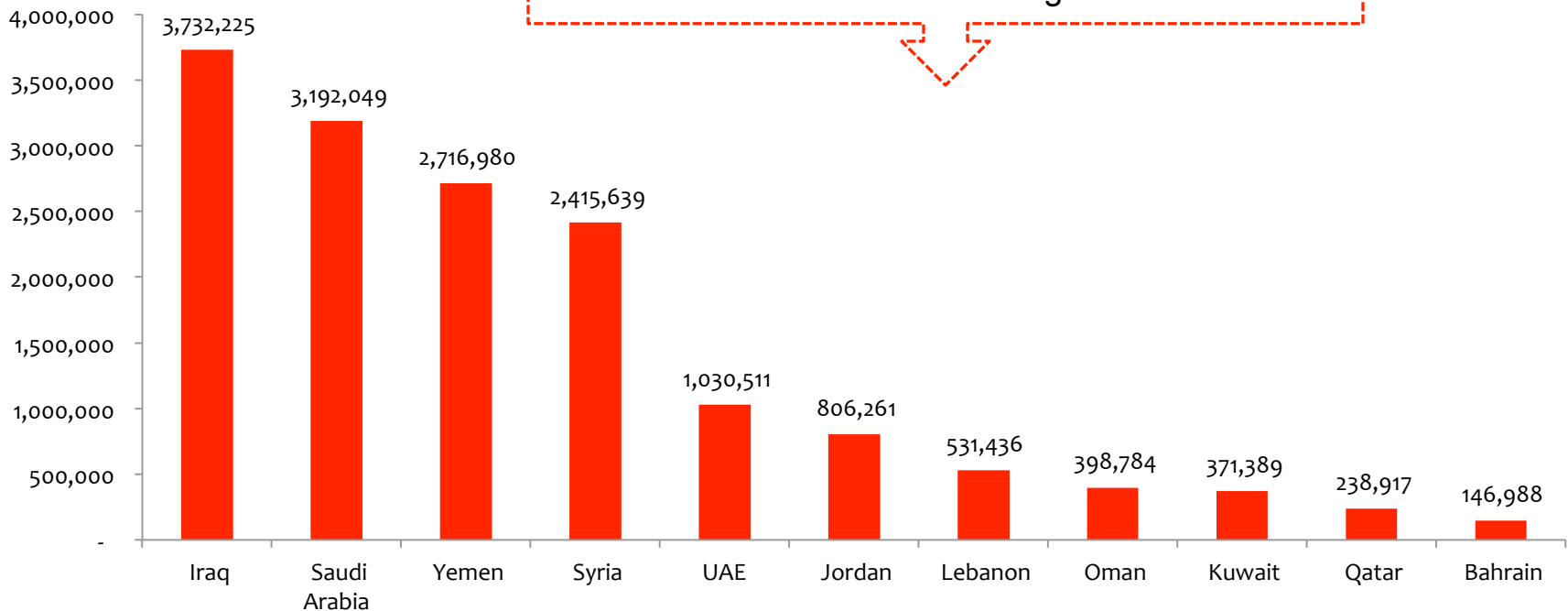
Total population in the Concerned Countries
141,647,078 people

Markets Demographics

Market Demand

ED prevalence rate is growing based on demographic trends

The prevalence of ED in the world; Men-Age over 40 is 50% and >60% among Arab men

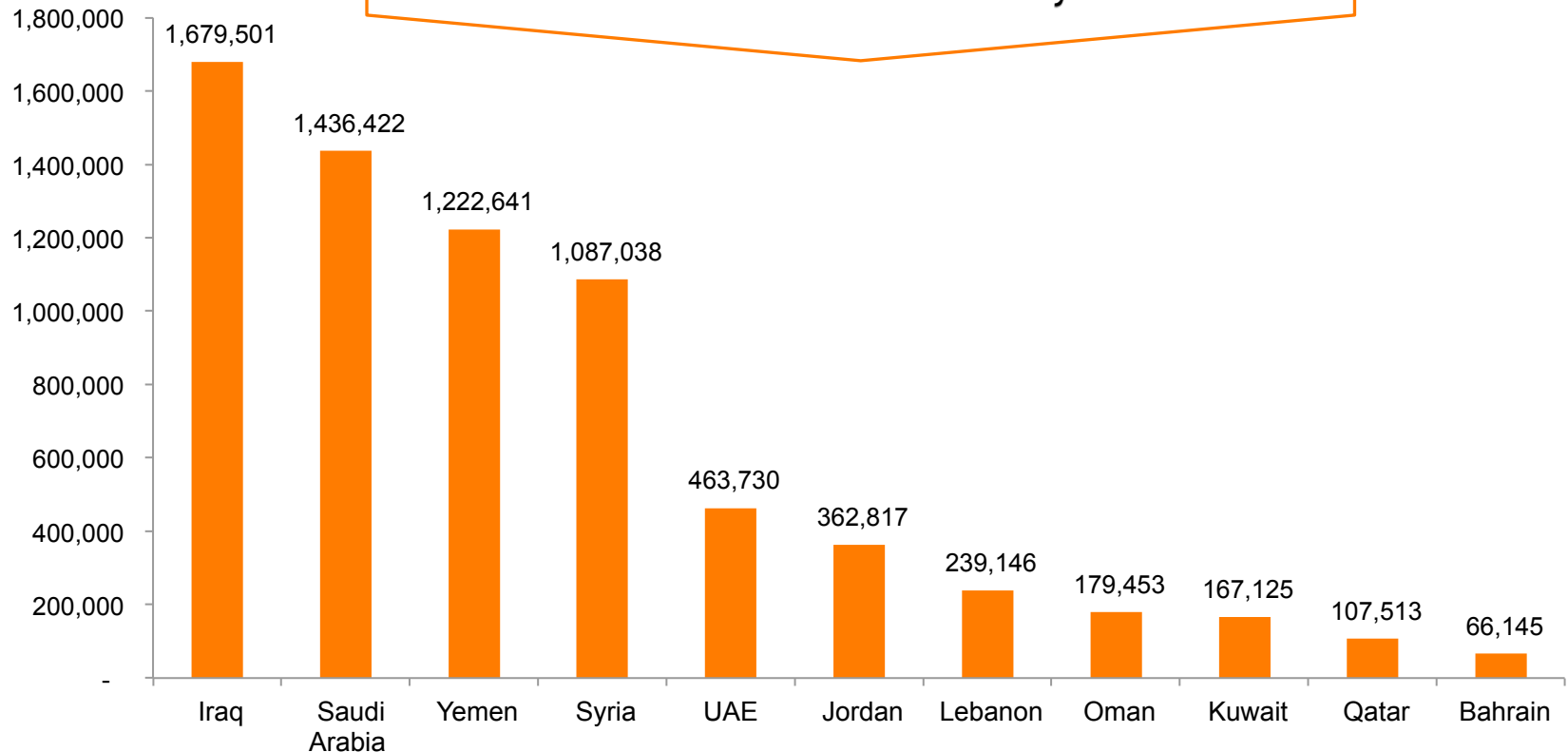


15,581,179 Men suffering from ED

Markets Demographics

ED Untreated Market

49% of the total ED patients still need to be treated; over 7 million men will benefit from Vitaros in Elis territory



Over 7 million men are the direct potential clients for Vitaros

Core market

Considering the following:

- Vitaros is a new dosage form
- Vitaros is a topical treatment with high safety profile
- Vitaros application offers better patient convenience
- ED market is lacking new innovations
- ED market is lacking new launch since 10 years
- Vitaros pricing related to topical ED treatment products
- New innovation is the price driver

VITAROS®

Provides Significant Value to Untreated Population

Ideal 1st Choice Option for Patients

- * who want on-demand fast action with minimal side effects
- * who don't want to worry about food effect
- * who can't or prefer not to take PDE₅ Inhibitors
- * who don't respond satisfactorily to PDE₅ inhibitors
- * who have had a prostatectomy
- * who have diabetes and prefer an on-demand topical to lessen systemic exposure to a drug



Vitaros® is an easily administered

Topical First-line Treatment for all ED Patients

patients and has demonstrated **Efficacy and Safety** in large clinical trials.

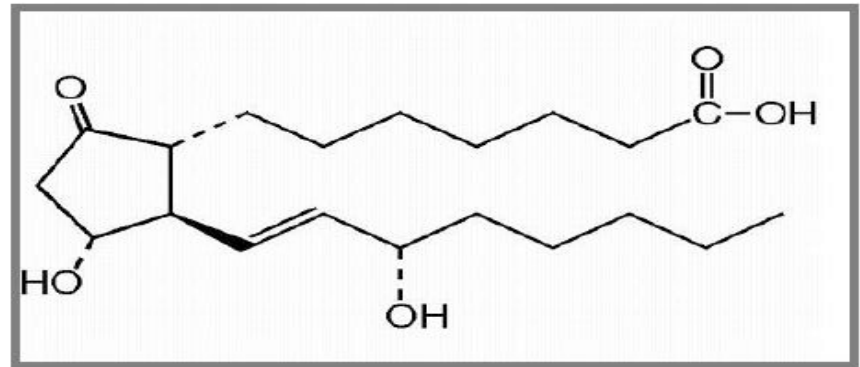
- * **Vitaros®** is a topically delivered formulation (cream) of alprostadil (a vasodilator) supplied in a single dose dispenser (AccuDose™), for the treatment of erectile dysfunction (ED). It is delivered with Dodecyl 2-N, N-(dimethylamino)-propionate hydrochloride (DDAIP HCl), Apricus' proprietary NexACT® delivery technology.
- * **Vitaros®** is applied directly to the penis and absorbed locally, instead of being administered orally. This topical application provides men who are unable to take existing oral medication with a patient-friendly alternative. Vitaros® has been studied in over 3,300 patients³ including difficult to treat populations (diabetes, cardiac issues, sildenafil failures, prostatectomies, patients on nitrates and alpha blockers).¹ Vitaros® demonstrates clinical efficacy and a favorable safety profile versus currently approved oral medication.

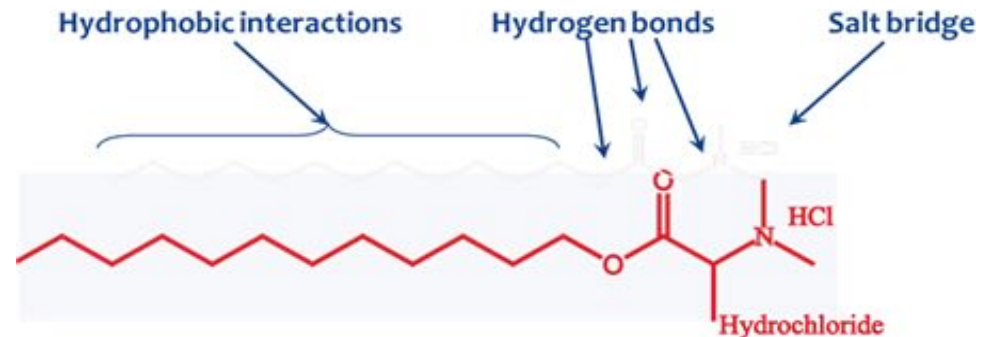
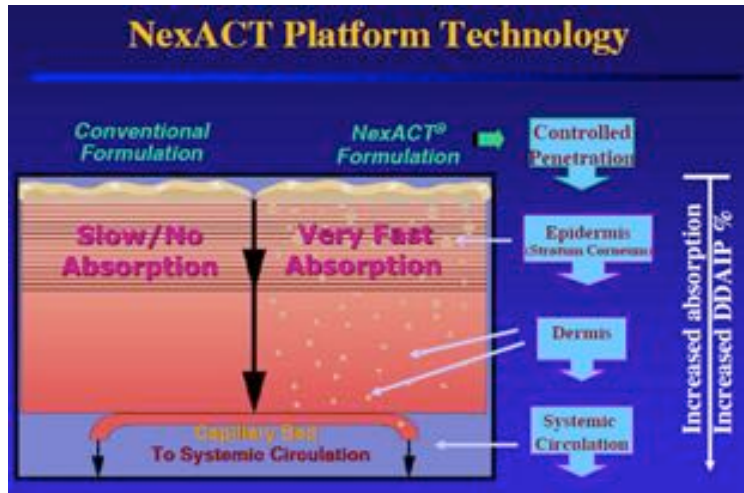
Vitaros® Rapid onset (generally 5-30 minutes)

Mechanism of Action

- ★ Synthetic form of naturally occurring PGE₁
- ★ Released from penile neurons
- ★ Mediates generation of cyclic adenosine monophosphate (cAMP)
- ★ Causes smooth muscle relaxation
- ★ Allowing blood to enter the penis

Alprostadil
(Prostaglandin E₁)





Chemical structure of DDAIP HCl (Dodecyl 2-(N, N dimethylamino)-propionate)

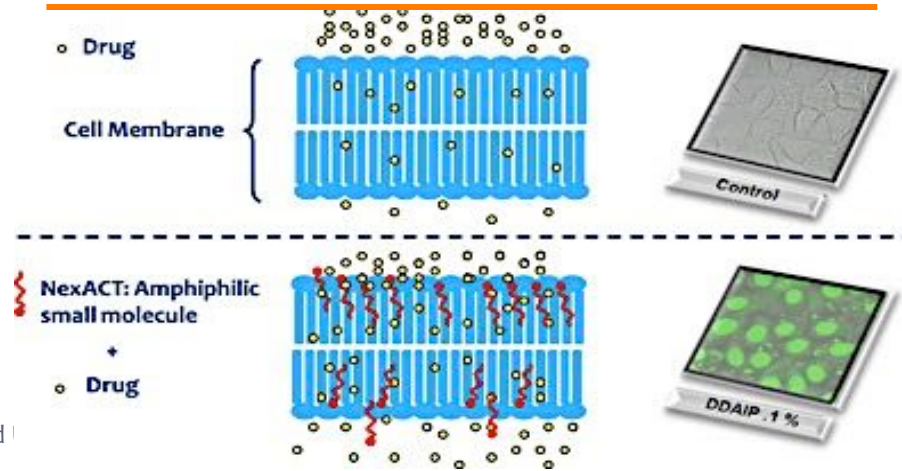
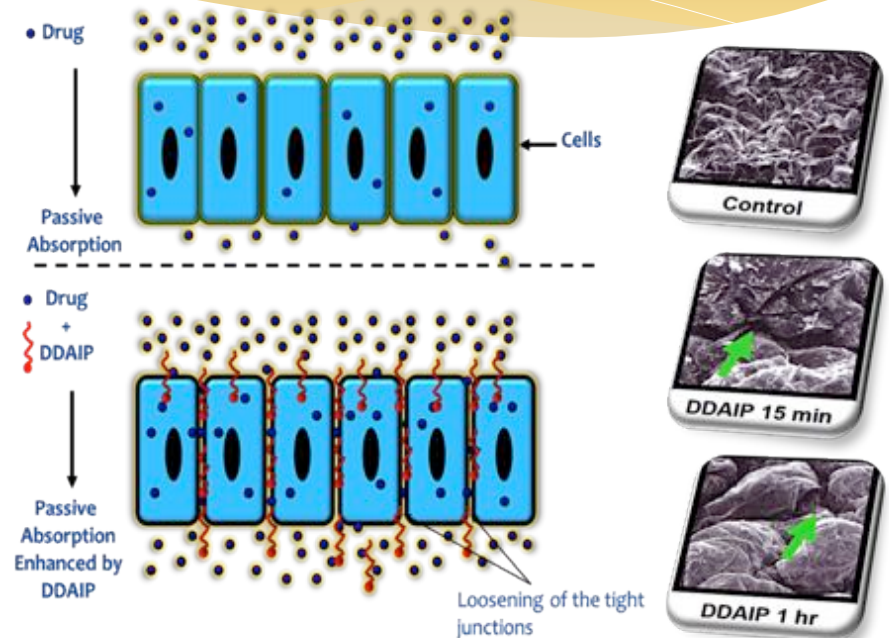
The NexACT multi-route drug delivery platform consists of more than 100 different skin permeation enhancer molecules that could be used in drug formulation to increase permeation and achieve higher bioavailability.

- ★ **Patented** NCE patents based on proprietary permeation enhancers that are biodegradable, biocompatible, safe excipients
- ★ **Effective** Enables rapid absorption of high concentrations of drug directly to target site or systemically into blood stream
- ★ **Safe** Excellent pre-clinical and clinical safety dossiers through thousands of patient exposures
- ★ **Versatile** Effective with wide range of drugs classes and different routes
 - Small molecules, peptides, proteins, SiRNA, anti-sense, and antibodies
 - Transdermal, Oral, Sub-Q, Buccal, Rectal, Nasal, Ophthalmic

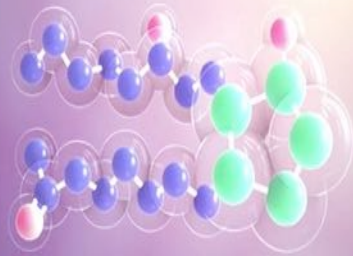
NexACT is a multi-route drug delivery technology that has been confirmed in clinical studies. It makes use of patented highly effective, novel excipients or "penetration enhancers" to radically improve a drug's absorption and bioavailability.

Schematic representation of how permeation enhancers can temporarily change the permeation dynamics of the lipid bilayer and loosen the tight junctions between the cells, which enables an increased absorption of drug into the systemic circulation or an increase in local absorption. Scanning electron micrographs of human skin.

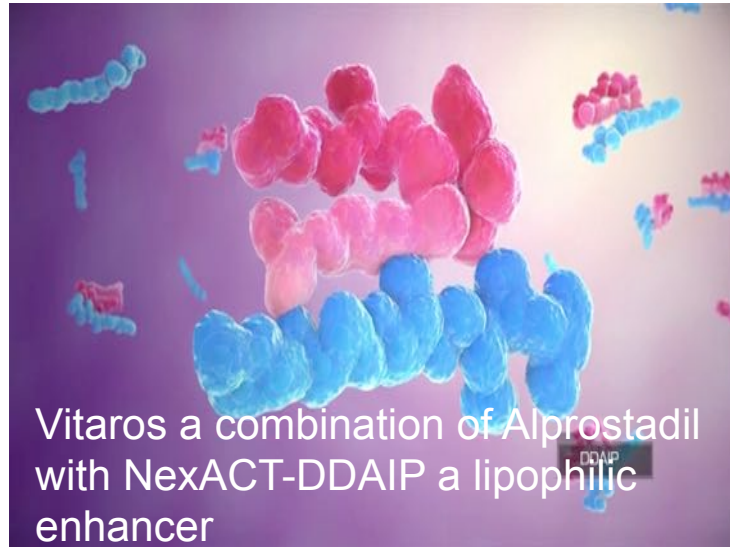
Mechanism of enhanced permeation. Real-time confocal microscopy of the DDAPI on uptake of Green Nucleic Acid Stain compared with control



Demonstration of Alprostadil-NexAct Penetration to the penis blood flow



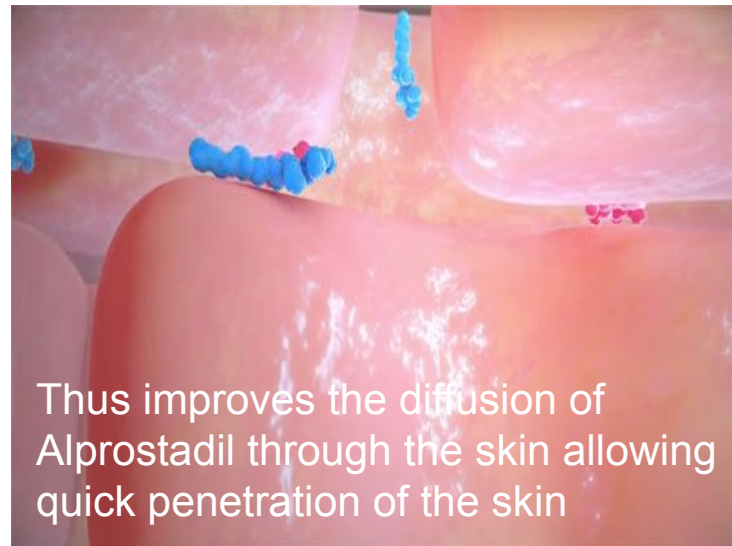
Alprostadil Prostaglandin



Vitaros a combination of Alprostadil with NexACT-DDAIP a lipophilic enhancer

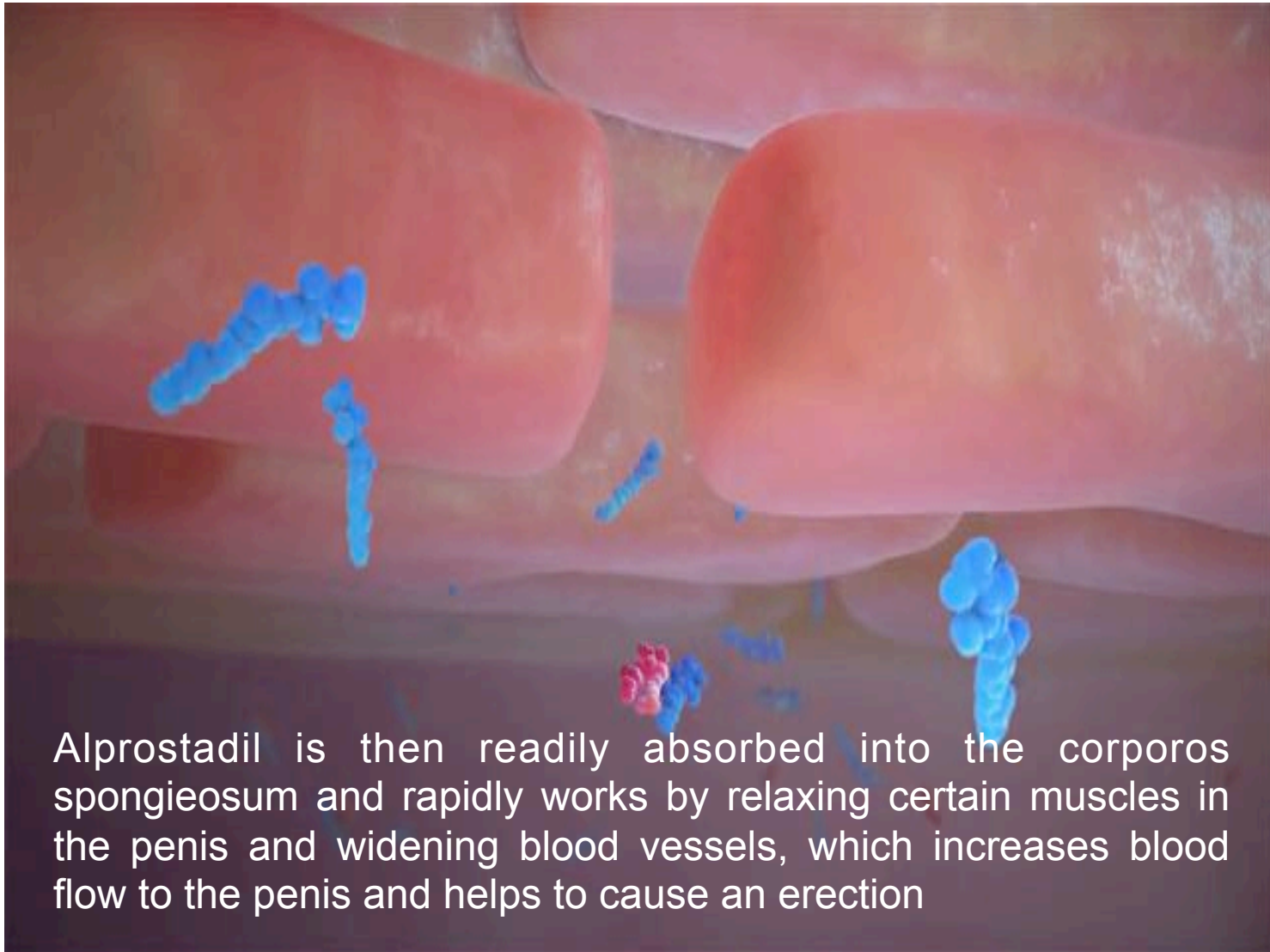


DDAIP temporarily loosens tight junctions present in skin epithelial cells



Thus improves the diffusion of Alprostadil through the skin allowing quick penetration of the skin

Demonstration of Alprostadil-NexAct Penetration to the penis blood flow



Alprostadil is then readily absorbed into the corporos spongiosum and rapidly works by relaxing certain muscles in the penis and widening blood vessels, which increases blood flow to the penis and helps to cause an erection

Demonstration of Alprostadil-NexAct Penetration to the penis blood flow

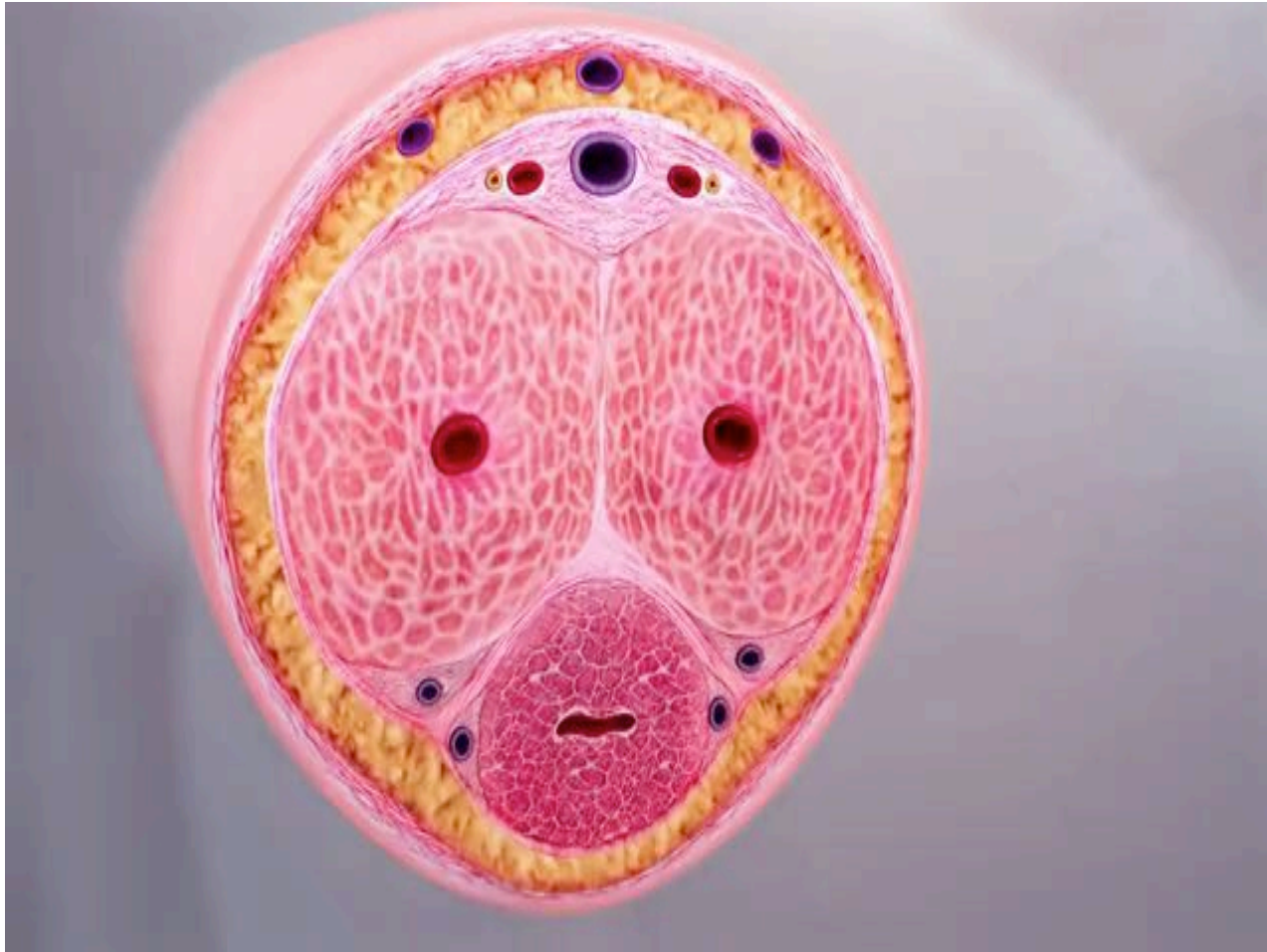


More erectile tissue



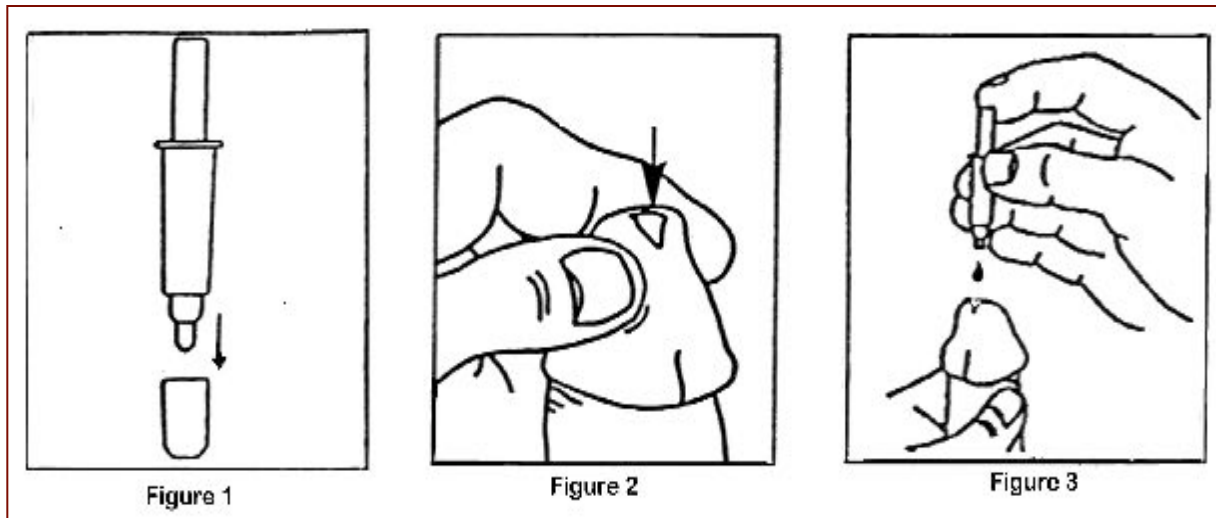
**Allow more blood to enter the penis and
enlarge the spaces in the erectile tissue**

Demonstration of Alprostadil-NexAct Penetration to the penis blood flow



Alprostadil is delivered to the penis blood capillaries and causing vasodilation, blood flow and erection

Dosing Instructions
Single Dose (0.1ml cream) Dispenser

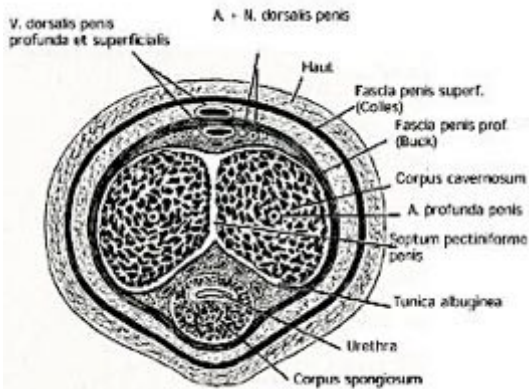
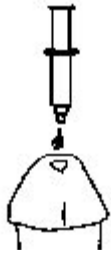


To be dispensed to tip of penis in drop-wise manner,

Not inserted



Induced Erection



- ★ Easy application to the urethral meatal region

- ★ PGE₁ unlike MUSE® penetrates rapidly through the communicating veins into the corpus cavernosum **does not need to be instilled in the urethra.**

- ★ Tumescence of the entire penis and full erection with sexual stimulation



Conclusions

- * VITAROS[®] demonstrated significant efficacy across a broad range of ED severities and co-morbidities
- * VITAROS[®] presents an excellent safety profile
 - No serious side effects
 - Most adverse events were localized to the site of application but were mild, short in duration and well tolerated
- * VITAROS[®] shows the potential for **treating difficult to treat ED** patients such as those with diabetes, cardiac comorbidity, hypertension, prostatectomies or who were non responsive to Viagra[®]
 - Effective from first dose
 - Fast onset on demand
 - Non-invasive
 - No food effect
 - Systemically and locally well tolerated
 - Effective and safe in difficult to treat patients
 - No interference with sexual spontaneity

SUMMARY OF PRODUCT CHARACTERISTICS

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single use container contains 300 micrograms of alprostadil in 100 mg of cream (3 mg/g).

PHARMACEUTICAL FORM

Cream

Vitaros is a white to off-white cream supplied in AccuDose, a single dose container. AccuDose is a container consisting of a plunger, barrel, and protective cap provided in a protective sachet.

Therapeutic indications

Treatment of men ≥ 18 years of age with erectile dysfunction, which is the inability to achieve or maintain a penile erection sufficient for satisfactory sexual performance.

Posology and method of administration

Vitaros is applied to the tip of the penis. Vitaros is available in two dosage strengths of 200 and 300 mcg alprostadil in 100 mg of cream. Vitaros should be used as needed to achieve an erection. Each Vitaros AccuDose container is for single use only and should be properly discarded after use.

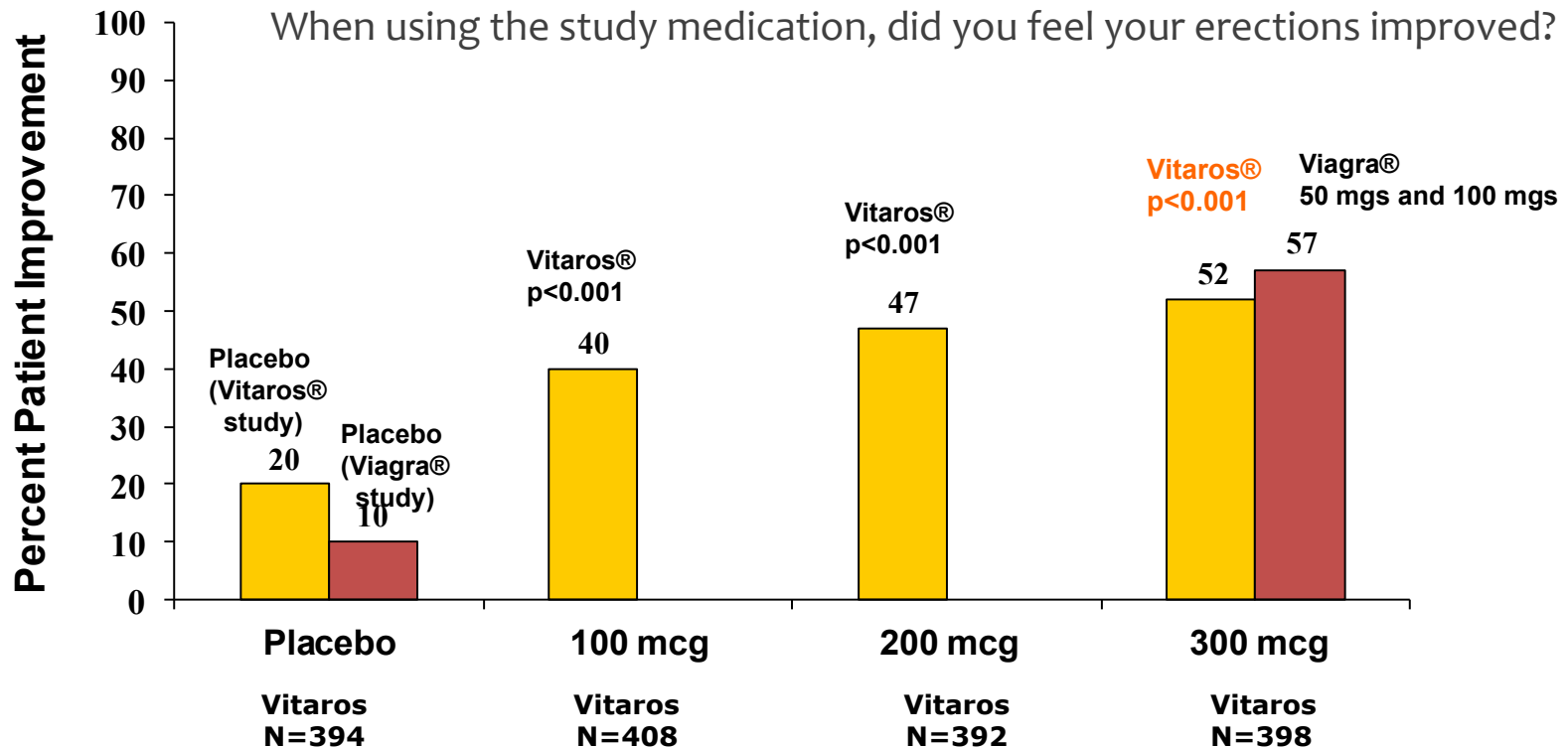
The onset of effect is within 5 to 30 minutes after administration. The duration of effect is approximately 1 to 2 hours. The maximum frequency of use is no more than 2-3 times per week and only once per 24- hour period.

Vitaros® 300 mcgs/100 ml dose strength is comparable to Viagra® 50 mgs dose strength

Phase 3 Pivotal Clinical Studies Integrated Efficacy Analysis – Intent to Treat Population

Global Assessment Question

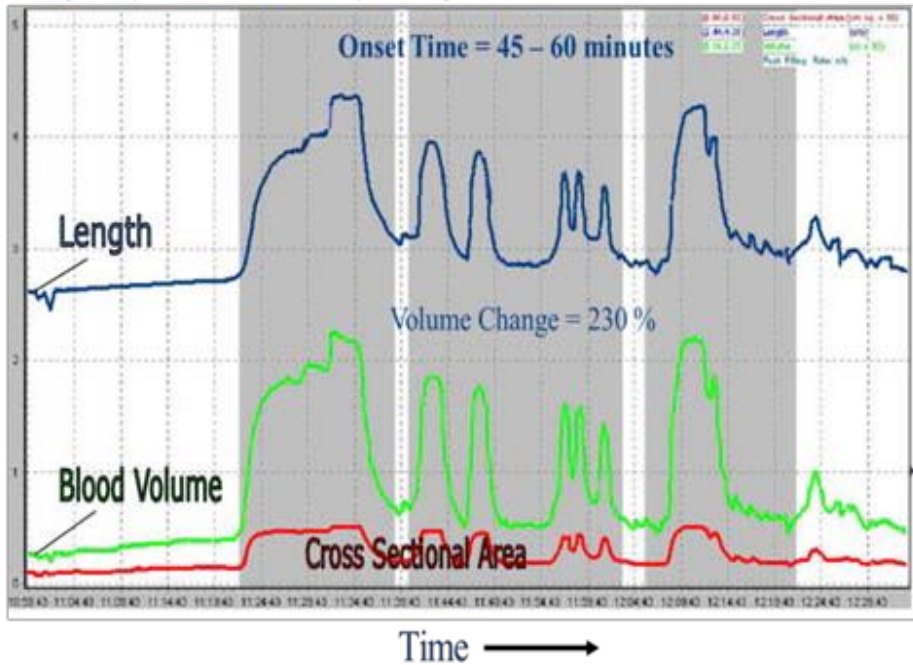
When using the study medication, did you feel your erections improved?



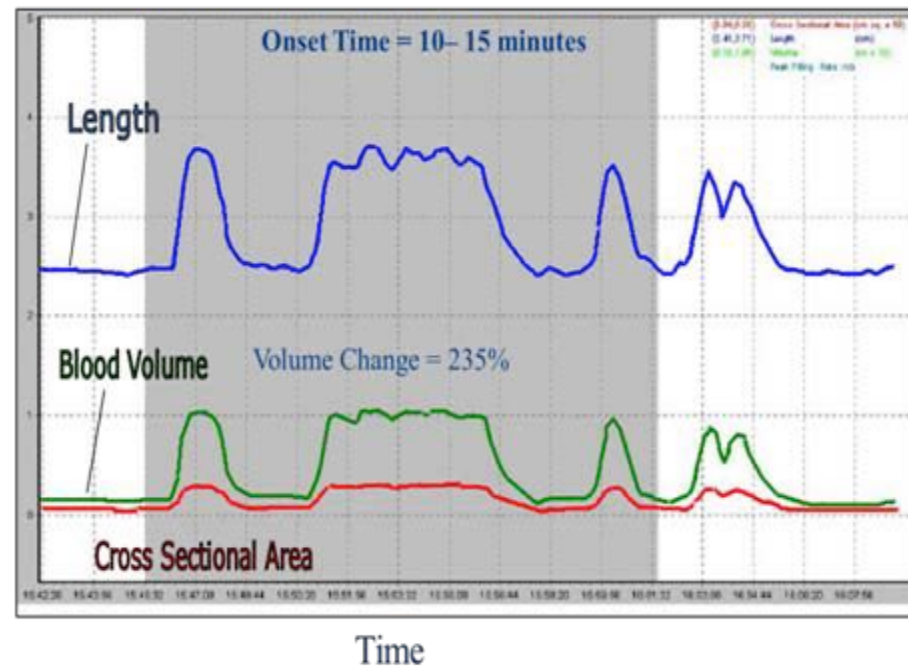
Source: Viagra PI; Patients were started on 50 mg and allowed to adjust the dose up to 100 mg or down to 25 mg of VIAGRA; all patients, however, were receiving 50 mg or 100 mg at the end of the study. On a global improvement question, 57% of VIAGRA patients reported improved erections versus 10% on placebo.

(alprostadil/DDAIP)
For the Treatment of Erectile Dysfunction

Viagra® (Sildenafil Citrate) 50 mg Tablet



Vitaros (Alprostadil) 300 mcg Topical Cream



Comparison of Vitaros and the leading PDE5s

Key Conclusion:

Vitaros® demonstrated significant efficacy across a broad range of ED severities and co-morbidities

Brand (molecule)	Company	Form (doses available)	Strengths	Weaknesses
Vitaros® (alprostadil)	NexMed USA	Topical (200 mcgs/ 100 ml and 300 mcgs/ 100 ml)	No food effect Quick onset of action: 10-30 minutes Efficacy demonstrated in patient types, that are either contraindicated for PDE5s, or do not show efficacy: <ul style="list-style-type: none"> ○ Diabetes, ○ Prostatectomy, ○ Cardiac History, ○ Viagra History and ○ Hypertension 	
Viagra® (sildenafil)	Pfizer	Oral (25mg, 50mg and 100mg)	Effective 30–60 minutes after administration and maintained for up to 12 hours	Efficacy reduced after large fatty meals. Contraindicated for patients on nitrate therapy. 50mg or 100mg of <i>sildenafil</i> should not be taken within 4 hours following treatment with an alpha-blocker.
Cialis® (tadalafil)	Eli Lilly	Oral (10mg and 20mg)	Effective from 30 minutes after administration, with peak efficacy after about 2 hours. Efficacy is maintained for up to 36 hours and is not affected by food intake.	Contraindicated for patients on nitrate therapy and in patients taking alphasblockers.
Levitra® (vardenafil)	Bayer Schering/ GlaxoSmith Kline	Oral (5, 10 and 20mg)	Effective from 30 minutes after administration. Coadministration of <i>vardenafil</i> with <i>tamsulosin</i> is not associated with clinically significant hypotension.	Efficacy is reduced after large fatty meals. Contraindicated for patients on nitrate therapy

Comparison of Vitaros® and the leading PDE5s
Discontinuation Due to Serious Adverse Events: Orals vs. Vitaros®

Drug	Discontinuation Rate	% of Patients					
		Headaches	Flushing	Rhinitis/Nasal Congestions	Back Pain	Dyspepsia	Abnormal Vision
Vitaros®	0	0	0	0	0	0	0
Viagra®	2	16	10	7	>2	7	11
Cialis®	3.1	15	3	3	6	10	
Levitra®	3.4	15	11	3	2	5	

Key Conclusions:

- ◆ **Vitaros®** presents an excellent safety profile
 - ◆ No serious side effects
 - ◆ Most adverse events were localized to the site of application but were mild, short in duration and well tolerated
 - ◆ Rate of patient discontinuation from the Phase III Integrated Safety Analysis :
 - Penile burning (1.2%)
 - Genital pain (0.9%)
 - Penile erythema (0.2%)
 - Vaginal burning (0.2%)
 - Other (0.5%)

Vitaros®

*topical treatment
for erectile dysfunction*

vitaros®
(alprostadil cream)



VITAROS®

Thank You

elis
Pharmaceuticals

For the following countries:

United Arab Emirates, Oman, Bahrain, Qatar, Saudi Arabia, Kuwait, Lebanon, Syria,
Jordan, Iraq and Yemen

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