LET'S TALK ABOUT ED™

A Pharmacological Guide to Switching Intracavernosal Injection Medications that may be Prescribed for Erectile Dysfunction (ED)

Why and when do I switch medications?

In 2011 and 2012, over 60% of customers ordered or were prescribed Tri-Mix Standard (PGE1/Papaverine HCl/Phentolamine Mesylate 5.88ug/18mg/0.6mg/ml) as the initial intracavernosal injection medication for ED. Of those patients who started on Tri-Mix Standard, only 15% switched to another preparation during that time period.

However, during a recent series of prescriber interviews, the same question was asked time and time again,"I've started my patient *on Tri-Mix Standard. When needed,where do I go from there?"*

Here is an attempt to give some guidance on that question from a pharmacological perspective. Active ingredients, usage, dosing ranges and mono vs.combination therapies have been charted to provide some guidance regarding switching intracavernosal injection therapies for patients with ED.

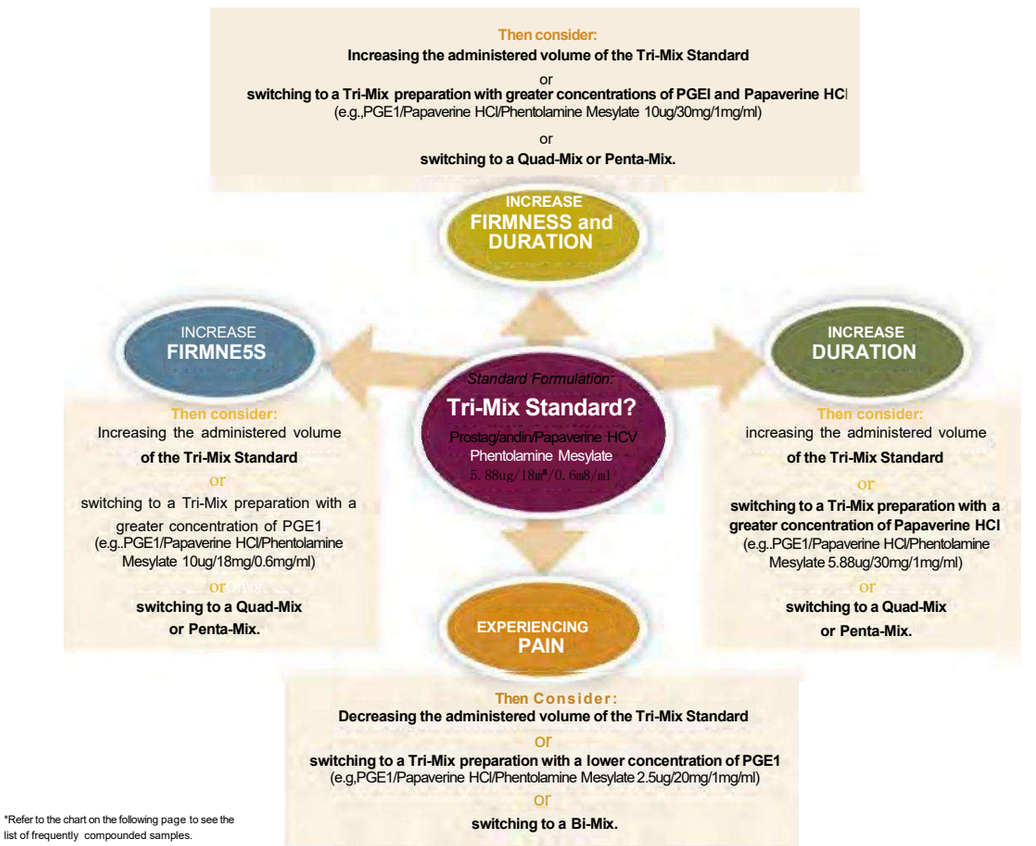
This content is for informational/educational purposes only and is not intended to treat or diagnose any disease or person. No claims are made as to the safety or efficacy of the mentioned preparations.

The compounded medications featured in this piece are prescribed and administered by physicians who helped write this article. This guide is not a substitute for your medical judgment. This guide compiles referenced study/research material, contemporary clinical practice measures, as well as prescription volume history specific to the company who wrote this artiicle in order to assist you in navigating complex alternatives.

This is an effort to better serve you and your concerns. If you have any questions or comments, we encourage you to reach out to your physician.

Mono Therapies:

Prostaglandin (PGE1) is the only FDA-approved option for intracavernosal injection. Research has shown that PGEI has the potential to be a less effective option than Tri-Mix and that some patients may experience a higher occurrence of pain. Studies have also shown Papaverine HCl as being effective in some men at higher dosages. The reported increased incidence of fibrosis, however, may make this a less desirable option than Tri-Mix.



*Refer to the chart on the following page to see the list of frequently compounded samples.

Pain:

If pain with any of these injection medications is reported, the first concern of the physician needs to be the patient's self-injection technique, especially if pain was not an issue during in-office titration.

If the patient is injecting correctly, then the culprit is most likely PGEl. Incidence of pain is most widely reported with PGE1 compared to any of the other mono or adjunct therapies. Decreasing the strength of PGE1 to a point where a satisfactory erection takes place but pain is reduced is key. If a non-therapeutic level of PGEl is reached, Bi-Mix may be considered. Bi-Mix contains Papaverine and Phentolamine only, and as reported, some men can receive satisfactory erections with very limited incidence of pain.

Formulary ranges of strengths:

The company who wrote this original article compounded more than 560 different injectable preparations that may be prescribed for erectile dysfunction-all prepared to your exact specifications to meet your patient's needs. The table below illustrates the scope of their formulary by indicating the ranges of strengths available for those preparations.

Chemical	**Mono**	Bi-Mix	Tri-Mix	Quad-Mix	**Penta-Mix**
Prostaglandin	1-500ug/ml	N/A	1-120ug/ml	5.88-100ug/ml	4.08ug-100ug/ml
Papaverine Hc	20-30mg/ml	5-30mg/ml	1-30mg/ml	9-30mg/ml	18-30mg/ml
Phentolamine Mesylate	1-10mg/ml	0.1-5mg/ml	0.1-5mg/ml	0.6-5mg/ml	0.6-5mg/ml
Forskolin	1-200ug/ml	N/A	N/A	67.5-100ug/m	63.3-100ug/ml
VIP	30-200ug/ml	N/A	N/A	20,8-30ug/ml	18.9 • 30ug/ml
Atropine	N/A	N/A	0.04-0.2mg/ml	0.01-1.5mg/ml	0,1-1.5mg/ml

Examples of frequently compounded preparations:

PGE1	10ug,20ug,40ug/ml
Bi-Mix	Papaverine HCl/Phentolamine Mesylate 30mg/1mg/ml
Tri-Mix "2.5-20-1"	PGE1/Papaverine HCl/Phentolamine Mesylate 2.5ug/20mg/1mg/ml
Tri-Mix "Standard"	PGE1/Papaverine HCl/Phentolamine Mesylate 5.88ug/18mg/0.6mg/ml
Tri-Mix"5.88-30-1"	PGE1/Papaverine HCl/Phentolamine Mesylate 5.88ug/30mg/1mg/ml
Tri-Mix "10-18-0.6"	PGE1/Papaverine HCl/Phentolamine Mesylate 10ug/18mg/0.6mg/ml
Tri-Mix"10-30-1"	PGE1/Papaverine HCl/Phentolamine Mesylate 10ug/30mg/1mg/ml
Tri-Mix "Double Strength"	PGE1/Papaverine HCl/Phentolamine Mesylate 11.8ug/18mg/0.6mg/ml
Tri-Mix"50-30-1"	PGE1/Papaverine HCl/Phentolamine Mesylate 50ug/30mg/1mg/ml
Quad-Mix "Standard"	PGE1/Papaverine HCl/Phentolamine Mesylate/Forskolin 20ug/30mg/2mg/100ug/ml
Penta-Mix"Standard"	PGE1/Papaverine HCl/Phentolamine Mesylate/Forskolin/VIP 5.88ug/30mg/4mg/100ug/30ug/ml

"Double Strength" refers to the doubling in strength of the PGE1 only from the Tri-Mix Standard formulation.

Volume:

In finding the right dose of intracavernosal injection medication for your patient, it is worth mentioning that along with changing the preparation's strength, adjusting the preparation's administered volume is an equally important tactic. There are a number of patient-specific variables and comorbidities to take into account. No one starting point is definitive for everyone. Patient-specific considerations include but are not limited to: diabetes, hypertension, obesity, prostate health (e.g. hormone ablation, removal, radiation, etc.), as well as predisposition to priapism due to hematologic issues (e.g.Sickle Cell Anemia, Multiple Myeloma, Leukemia, etc.)

General/titration parameters have been reported as follows:

▶0.1-0.2ml for patients less than 60 years old with no history of ED.
▶0.3ml for patients 55 or older with a history of ED.

It has been reported that the dose can be "titrated up" by 0.1-0.2ml increments until the patient experiences an erection that is satisfactory for sexual activity. "It **is not recommended that the dose exceed 1ml in** volume." Again, the guidelines referenced above should not be taken as a recommendation for therapy or as being appropriate for every patient. Use your best clinical judgment in treating each patient on an individual basis. Take their unique circumstances into account when prescribing an intracavernosal injection compounded medication.

Glossary

To better understand the options available, you need to know about the Active Pharmaceutical ingredients (APIs) that are used in the compounding of intracavernosal injection medications.The glossary below represents API used in intracavernosal injection therapy and their physiologic use/result as defined in a number of referenced external sources, including urology-specific publications, peer-reviewed journals and clinical education materials.

Prostaglandin (PGE1):
Directly stimulates the cAMP (cyclic Adenosine Mono-Phosphate) pathway to decrease intracellular calcium concentrations, allowing for relaxation of arterial and smooth muscle tissue that may result in and has been reported to increase firmness.

Papaverine HCl:
Blocks the breakdown of cAMP and cGMP (cyclic Guanosine Mono-Phosphate), leading to a decrease in intracellular calcium and the relaxation of smooth muscle that may result in and has been reported to increase duration of erection.

Phentolamine Mesylate:
A non-selective Alpha Blocker adjunct therapy that inhibits smooth muscle contraction and has a direct effect on smooth muscle activity. Phentolamine has been reported to provide a synergistic effect when combined with PGE1 and Phentolamine,

Forskolin:
Increases concentrations of cAMP by directly activating adenylate cyclase leading to relaxation of smooth muscle tissue that may result in and has been reported to increase firmness when used as adjunct therapy.

VIP(Vasoactive Intestinal Peptide):
A neuropeptide that facilitates an increase in concentrations of cAMP resulting in smooth muscle relaxation that may result in and has been reported to increase firmness when used as an adjunct therapy.

Atropine:
A parasympatholytic drug that enables the relaxation of smooth muscle tissue that is derived from the release of endothelium. This may result in and has been reported to increase firmness when used as an adjunct therapy.

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