INTRON® A (Interferon alfa-2b, recombinant)

MEDICATION GUIDE

Including appendix with instructions for using INTRON® A Multidose Pen for Injection

Read this Medication Guide carefully before you start to take INTRON A (Intron aye) for Injection alone or INTRON A in combination with REBETOL® (REB-eh-tole) (ribavirin, USP) Capsules. Read the Medication Guide each time you refill your prescription because there may be new information. The information in this Medication Guide does not take the place of talking with your health care provider.

If you are taking INTRON A and REBETOL combination therapy, also read the Medication Guide for REBETOL (ribavirin, USP) Capsules.

What is the most important information I should know about INTRON® A?

INTRON A is a treatment for some people who have hairy cell leukemia, malignant melanoma, follicular lymphoma, AIDS-related Kaposi's sarcoma, chronic hepatitis B, chronic hepatitis C, and condylomata acuminata. If you have chronic hepatitis C, your health care provider may prescribe INTRON A in combination with REBETOL®. INTRON A used by itself or with REBETOL can help you, but can also have serious side effects and may cause death in rare cases. Before starting treatment, you should talk to your health care provider about the possible benefits and possible side effects of INTRON A alone or in combination with REBETOL, to decide if this treatment is right for you. While taking INTRON A alone or in combination with REBETOL, you need to see a health care provider regularly for medical examinations and lab tests to make sure the treatment is working and to check for side effects.

You should call your health care provider immediately if you develop any of these conditions while taking INTRON A:

- you become pregnant or if you are a male and your female partner becomes pregnant
- new or worsening mental health problems such as thoughts about hurting or killing yourself or others
- decreased vision
- trouble breathing or chest pain
- severe stomach or lower back pain
- bloody diarrhea or bloody bowel movements
- high fever
- easy bruising or bleeding

The most serious possible side effects of INTRON A include:

RISK TO PREGNANCY. Combination INTRON A and REBETOL therapy can cause death, serious birth defects or other harm to your unborn child. If you are pregnant, you or your male partner must not take INTRON A and REBETOL combination therapy. You must not become pregnant while either you or your partner are taking the combination of INTRON A and REBETOL and for 6 months after you stop taking the combination. If you are a woman of childbearing age you must have negative pregnancy tests immediately before starting treatment, during treatment, and for 6 months after you have stopped treatment. You should use two forms of birth control during and for 6 months after you have stopped treatment. If you are a man taking INTRON A/REBETOL combination therapy, one of the two forms of birth control should be a condom. You must use birth control even if you believe that you are not fertile or that your fertility is low. You should talk to your health care provider about birth control for you and your partner. If you or your partner becomes pregnant while either of you is being treated or within 6 months of stopping treatment, tell your health care provider right away. There is a Ribavirin Pregnancy Registry that collects information about pregnancy outcomes in female patients and female partners of male patients exposed to ribavirin. You or your health care provider are encouraged to contact the Registry at 1-800-593-2214.

Mental health problems and suicide. INTRON A may cause patients to develop mood or behavioral problems. These can include irritability (getting easily upset) and depression (feeling low, feeling bad about yourself, or feeling hopeless). Some patients may have aggressive behavior. Former drug addicts may fall back into drug addiction or overdose. Some patients think about hurting or killing themselves or other people. Some patients have killed themselves (suicide) or hurt themselves or others. You must tell your health care provider if you are being treated for a mental illness or had treatment in the past for any mental illness, including depression and suicidal behavior. You should also tell your health care provider if you have ever been addicted to drugs or alcohol.

Eye problems. If you notice any changes in your eyesight, such as difficulty seeing, it could mean that your eyes are being affected, so you should call your health care provider right away.

Heart problems. Some patients taking INTRON A may develop problems with their heart, including low blood pressure, fast heart rate, and very rarely, heart attacks. Tell your health care provider if you have had any heart problems in the past.

Blood problems. INTRON A commonly lowers two types of blood cells (white blood cells and platelets). In some patients, these blood counts may fall to dangerously low levels. If your blood cell counts become very low, you could get infections or have bleeding problems.

If you are taking INTRON A and REBETOL combination therapy, REBETOL can cause a drop in your number of red blood cells (anemia). A very low red blood cell count can be dangerous, especially if you have heart or breathing problems.

For other possible side effects of INTRON A, see *"What are the possible side effects of INTRON A?"* in this Medication Guide.

Body organ problems. Certain symptoms like severe stomach pain may mean that your internal organs are being damaged. Cases of weakness, loss of coordination, and numbness due to stroke have been reported in patients taking INTRON A, including patients with few or no reported risk factors for stroke.

What is INTRON® A?

The INTRON A product contains a man-made protein called interferon. Interferon is a protein that is part of the body's immune system that "interferes" with the growth of viruses or cancer cells.

It is not known if INTRON A or INTRON A/REBETOL® combination therapy can cure hepatitis B or C (permanently eliminate the virus) or if it can prevent liver failure or liver cancer that is caused by hepatitis B or C infection.

It is also not known if INTRON A or INTRON A/REBETOL combination therapy will prevent one infected person from infecting another person with hepatitis B or C.

Who should not take INTRON® A?

Do not take INTRON A alone or in combination with REBETOL® if you:

- are pregnant, planning to get pregnant, or breastfeeding
- are a male patient on combination therapy and have a female sexual partner who is pregnant or plans to become pregnant while you are being treated with REBETOL or during the 6 months after your treatment has ended

- have autoimmune hepatitis (hepatitis caused by your immune system attacking your liver) or unstable liver disease (yellowing of the skin and eyes, swelling of the abdomen)
- had an allergic reaction to another alpha interferon or ribavirin or are allergic to any of the ingredients in INTRON A or REBETOL

If you have any of the following conditions or serious medical problems, tell your health care provider before taking INTRON A alone or in combination with REBETOL:

- depression or anxiety
- eye problems
- sleep problems
- high blood pressure
- previous heart attack, or other heart problems
- liver problems (other than hepatitis B or C)
- any kind of autoimmune disease (where the body's immune system attacks the body's own cells), such as psoriasis, sarcoidosis, systemic lupus erythematosus, rheumatoid arthritis
- thyroid problems
- diabetes
- colitis (inflammation of the bowels)
- cancer
- hepatitis B or C infection
- HIV infection (the virus that causes AIDS)
- kidney problems
- bleeding problems
- alcoholism
- drug abuse or addiction
- body organ transplant and are taking medicine that keeps your body from rejecting your transplant (suppresses your immune system)
- high blood triglycerides (fat particles normally found in your blood)

How should I take INTRON® A?

To get the most benefit from this medicine, it is important that you take INTRON A exactly as your health care provider tells you. Your health care provider will decide your dose of INTRON A and how often you will take it. Do not take more than your prescribed dose. INTRON A is given as an injection either under the skin (subcutaneous) or into a muscle (intramuscular). You should be completely comfortable with how to prepare and measure your dose of INTRON A and how to inject yourself before you use INTRON A for the first time. Your health care provider will train you on how to use and inject INTRON A properly.

INTRON A comes in different strengths and different forms (a powder in a vial, a solution in a vial, and a multidose pen). Your health care provider will determine which form is best for you. The instructions for giving a dose of INTRON A are at the end of this leaflet.

If you miss a dose of INTRON A, take the missed dose as soon as possible during the same day or the next day, then continue on your regular dosing schedule. If several days go by after you miss a dose, check with your health care provider to see what to do. **Do not double your next dose** or take more than your prescribed dose without talking to your health care provider. Call your health care provider right away if you take more than your prescribed dose. Your health care provider may wish to examine you more closely and take blood for testing.

If you are taking INTRON A in combination with REBETOL®, you should also read the Medication Guide for REBETOL (ribavirin, USP) for more information about side effects and how to take REBETOL. **REBETOL capsules should be taken twice a day with food**. Taking REBETOL with food helps your body take up more of the medicine. Taking REBETOL at the same time of day every day will help keep the amount of medicine in your body at a steady level. This can help your health care provider decide how your treatment is working and how to change the number of REBETOL capsules you take if you have side effects. If you miss a dose of REBETOL, take the missed dose as soon as possible during the same day. If an entire day has passed, check with your health care provider about what to do. **Do not double your next dose**.

You must see your health care provider on a regular basis for blood tests so your health care provider can check how the treatment is working for you and to check for side effects.

Tell your health care provider if you are taking or planning to take other prescription or nonprescription medicines, including vitamin and mineral supplements and herbal medicines.

What should I avoid while taking INTRON® A?

- Avoid becoming pregnant while taking INTRON A. INTRON A alone and INTRON A taken in combination with REBETOL® may harm your unborn child or cause you to lose your baby (miscarry). If you or your partner becomes pregnant during treatment or during the 6 months after treatment with INTRON A/REBETOL combination therapy, immediately report the pregnancy to your health care provider. Your health care provider will make decisions about your treatment. Your health care provider should call 1-800-593-2214. Your health care provider will be asked to give follow-up information about the pregnancy.
- Do not breastfeed your baby while taking INTRON A.

What are the possible side effects of INTRON® A?

Possible, serious side effects include:

- **Risk to pregnancy; mental health problems, including suicide; blood problems; heart problems and eye problems,** see *"What is the most important information I should know about INTRON A?"*
- **Other body organ problems.** Certain symptoms like severe pain in the middle of your body, nausea, and vomiting may mean that your liver or pancreas is being damaged. A few patients have lung problems such as pneumonia (inflammation of the lung tissue), and inflammation of the kidney. If you are short of breath, coughing, or have severe stomach or back pains or a fever, you should call your health care provider right away.
- **Thyroid problems.** Some patients develop changes in the function of their thyroid. Symptoms of thyroid changes include the inability to concentrate, feeling cold or hot all the time, a change in your weight, and changes to your skin.
- **New or worsening autoimmune disease.** Some patients taking INTRON A develop autoimmune diseases (a condition where the body's immune cells attack other cells or organs in the body), including rheumatoid arthritis, systemic lupus erythematosus, sarcoidosis, and psoriasis. In some patients who already have an autoimmune disease, the disease may worsen while on INTRON A.

Common but less serious side effects include:

- **Flu-like symptoms.** Most patients who take INTRON A have flu-like symptoms (headache, muscle aches, tiredness, and fever) that usually lessen after the first few weeks of therapy. You can reduce some of these symptoms by injecting your INTRON A dose at bedtime. Over-the-counter pain and fever medications can be used to prevent or reduce the fever and headache. If your fever does not go away you should tell your health care provider.

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- **Extreme fatigue (tiredness).** Many patients become extremely tired while on INTRON A.
- **Appetite problems.** Nausea, loss of appetite, and weight loss occur commonly.
- **Blood sugar problems.** Some patients develop problems with the way their body controls their blood sugar and may develop high blood sugar or diabetes.
- **Skin reactions.** Redness, swelling, and itching are common at the site of injection. If after several days these symptoms do not disappear, contact your health care provider. You may get a rash during therapy. If this occurs, your health care provider may recommend medicine to treat the rash.
- **Hair thinning.** Hair thinning is common during INTRON A treatment. Hair loss stops and hair growth returns after therapy is stopped.

These are not all the side effects of INTRON A or INTRON A/REBETOL® combination therapy. Your health care provider can give you a more complete list.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1–800–FDA–1088.

General advice about prescription medicines

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. If you have any concerns about the INTRON® A product, ask your health care provider. Your health care provider can give you additional information about INTRON A. Do not use INTRON A for a condition for which it was not prescribed. Do not share this medication with other people.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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Instructional leaflet and video are available through your health care provider.

Schering-Plough
Kenilworth, NJ 07033 USA

 Rev. 6/08

Medication Guide Appendix: Instructions for Preparing and Giving a Dose of INTRON® A Multidose Pen

The INTRON A Solution for Injection Multidose Pen is a prefilled, Multidose Pen that contains six doses of either 3, 5, or 10 million international units (MIU) of INTRON A. The Multidose Pen can also be used for different doses if your health care provider wants you to increase or decrease your dose.

The Multidose Pen can provide between 3 to 12 doses depending upon the dose your health care provider tells you to use. The Multidose Pen prescribed for you by your health care provider will be one of the following:

- 3 Million International Units (MIU) with a brown push button and a brown color-coding strip. The different doses that it can deliver are 1.5 MIU, 3.0 MIU, 4.5 MIU, and 6.0 MIU. Six MIU is the maximum dose that this pen can deliver at one time.
- 5 Million International Units (MIU) with a light blue push button and a light blue color-coding strip. The different doses that it can deliver are 2.5 MIU, 5.0 MIU, 7.5 MIU, and 10.0 MIU. Ten MIU is the maximum dose that this pen can deliver at one time.

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- 10 Million International Units (MIU) with a pink push button and a pink color-coding strip. The different doses that it can deliver are 5.0 MIU, 10.0 MIU, 15.0 MIU, and 20.0 MIU. Twenty MIU is the maximum dose that this pen can deliver at one time.

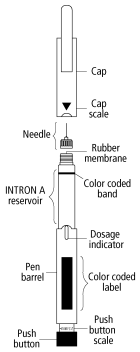
Make sure that you have the correct INTRON A Multidose Pen as prescribed by your health care provider.

Description of your INTRON® A Multidose Pen

- The INTRON A Multidose Pen should **ONLY** be used with **Novofine®** needles. These are the needles that come packaged with the pen. If you use other needles the pen may not work properly and you could get the wrong dose of INTRON A.

The two diagrams below show all the different parts of the INTRON A Multidose Pen and the Novofine needle. The parts of the pen you need to become familiar with are:

INTRON A Pen



Novofine Needle Assembly

- The **color-coded push button** and **push button scale**. These are located at the bottom of the pen when it is held with the cap side up. This tells you the dose that has been set.
- The **color-coding** band. This is located on the INTRON A reservoir. The band lets you know the dose that you are using. The 3 MIU INTRON A Multidose Pen has a brown push button, a brown color-coding band, and color-coded label. The 5 MIU INTRON A Multidose Pen has a light blue push button, a light blue color-coding band, and color-coded label. The 10 MIU INTRON A Multidose Pen has a pink push button, a pink color-coding band, and color-coded label.
- The **cap**. The cap is used for setting the dose and storing the pen. You will not be able to set the dose or completely close the pen unless you line up the **triangle** on the **cap scale** with the **dosage indicator** on the barrel.

To avoid the possible transmission of disease, do not allow anyone else to use your Multidose Pen.

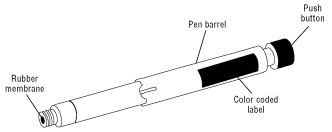
Storing INTRON® A Solution Multidose Pen for Injection

INTRON A Solution Multidose Pen for Injection should be stored in the refrigerator between 2° and 8°C (36° and 46°F). Discard any unused INTRON A pen remaining after 4 weeks. **DO NOT FREEZE**.

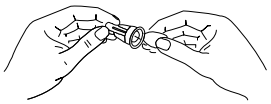
How do I prepare for an injection using the INTRON® A Multidose Pen?

1. Find a well-lit, clean, flat working surface such as a table. Collect the supplies you will need for an injection:
   - the INTRON A Multidose Pen
   - two alcohol swabs
   - a cotton ball or gauze
   - a puncture-proof disposable container
2. Before removing the Multidose Pen from the carton, check the date printed on the carton to make sure that the expiration date has not passed. Do not use if the expiration date has passed.

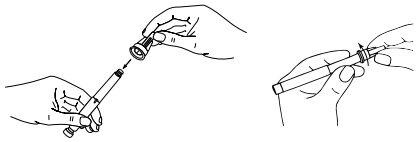
3. Wash your hands with soap and warm water. It is important to keep your work area, your hands, and injection site clean to minimize the risk of infection.
4. Remove the Multidose Pen from the carton. Pull the cap off the pen and wipe the rubber membrane with one alcohol swab.



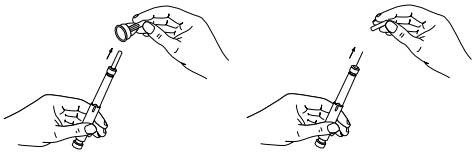
5. Check the solution inside the pen. The solution should be clear and colorless, without particles. Do not use the INTRON A if the medicine is cloudy, has particles, or is any color besides clear and colorless.
6. Remove the paper backing from the Novofine® needle by pulling the paper tab. You will see the back of the needle once the paper tab is removed.



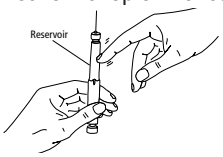
7. Keep the needle in its outer clear needle cap and gently push the Novofine needle straight into the pen's rubber membrane you just cleaned. Screw the needle onto the INTRON A Multidose Pen by turning it clockwise.



8. With the needle facing up, pull off the outer clear needle cap and set the outer needle cap down on your flat work surface for later use. Next, carefully pull off the white inner needle cap. The needle will now be exposed.

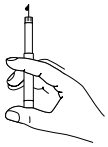


9. Keep the needle facing up and remove any air bubbles that may be in the reservoir by tapping the reservoir with your finger. If you have any air bubbles, they will rise to the top of the reservoir.



10. Hold the pen by the barrel and turn the INTRON A reservoir clockwise until you feel it click into place.

11. Keep the needle facing up and press the push button all the way up. A drop of INTRON A solution should come out of the tip of the needle.



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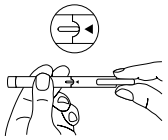
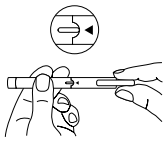
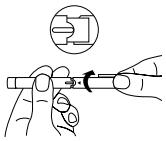
12. Place the cap back on the INTRON A Multidose Pen. Make sure you line up the black triangle on the pen cap with the dosage indicator on the pen barrel. The pen is now ready to set the dose.



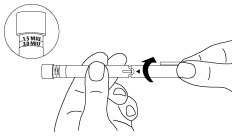
Setting the dose prescribed by your health care provider

13. Hold the pen horizontally in the middle of the pen barrel so the push button can move freely. With the other hand, hold the Multidose Pen cap.

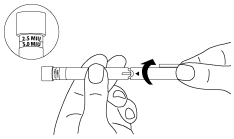




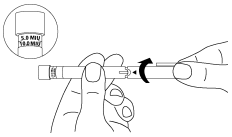
14. Set the dose prescribed by your health care provider by turning the cap clockwise. With each clockwise turn, the push button will start to rise and you will see the push button scale. Do not use force to turn the pen cap or you may damage the pen.
    - To set a 3.0 MIU dose using the 3 MIU Multidose Pen, turn the cap 2 full turns (10 clicks) = 3.0 MIU.



    - To set a 5 MIU dose using the 5 MIU Multidose Pen, turn the cap 2 full turns (10 clicks) = 5.0 MIU.



    - To set a 10 MIU dose using the 10 MIU Multidose Pen, turn the cap 2 full turns (10 clicks) = 10.0 MIU.



15. After each complete turn, make sure the triangle on the cap is lined up with the dosage indicator on the pen barrel.

IF YOUR HEALTH CARE PROVIDER HAS PRESCRIBED A DOSE OTHER THAN 3.0, 5.0, OR 10.0 MIU, THE DOSE CAN BE SET BY TURNING THE CAP AS MANY TIMES AS SHOWN BELOW:

A dose prescribed other than 3.0 MIU from the 3 MIU Multidose Pen

1 full turn (5 clicks) = 1.5 MIU
3 full turns (15 clicks) = 4.5 MIU
4 full turns (20 clicks) = 6.0 MIU

A dose prescribed other than 5.0 MIU from the 5 MIU Multidose Pen

1 full turn (5 clicks) = 2.5 MIU
3 full turns (15 clicks) = 7.5 MIU
4 full turns (20 clicks) = 10.0 MIU

A dose prescribed other than 10.0 MIU from the 10 MIU Multidose Pen

1 full turn (5 clicks) = 5.0 MIU
3 full turns (15 clicks) = 15.0 MIU
4 full turns (20 clicks) = 20.0 MIU

16. Check the push button scale to make sure you have set the correct dose.
17. If you have set a wrong dose, turn the cap back (counterclockwise) as far as you can until the push button is all the way in and the push button scale is completely covered, then begin at step 13 again.

18. Gently warm the INTRON® A Solution for Injection by slowly rolling the capped Multidose Pen in the palms of your hands for about 1 minute. DO NOT SHAKE.
19. Place the Multidose Pen on your flat work surface until you are ready to inject INTRON A.

Choosing an injection site

You should inject a dose of INTRON® A subcutaneously (under the skin). If it is too difficult for you to inject, ask someone who has been trained to give injections to help you.

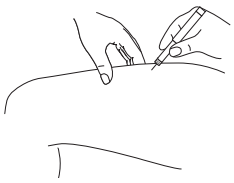
The best sites for injection are areas on your body with a layer of fat between skin and muscle such as:

- the front of the middle thighs
- the outer area of the upper arms
- the abdomen, except around the navel

You should use a different site each time you inject INTRON A to avoid soreness at any one site. Do not inject INTRON A into an area where the skin is irritated, red, bruised, infected or has scars, stretch marks, or lumps.

Injecting your dose of INTRON® A

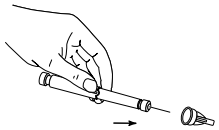
1. Clean the injection site with a new alcohol swab.
2. Pick up the Multidose Pen from your flat work surface and remove the cap from the needle.
3. With one hand, pinch a fold of the skin at the cleaned injection site.
4. With the other hand, hold the Multidose Pen (like a pencil) at a **45-degree angle** to the skin. With a quick "dart-like" motion, push the needle into the skin.



5. After the needle is in, remove the hand used to pinch the skin and use it to hold the pen barrel. If blood comes into the pen reservoir, the needle has entered a blood vessel. **Do not inject INTRON A**. Withdraw the needle and discard the used Multidose Pen in the puncture-proof container. Contact your health care provider. Repeat the steps to prepare for an injection.
6. If no blood is present in the pen reservoir, inject the medicine by gently pressing the push button all the way down.
7. Leave the needle in place for a few seconds while holding down the push button.
8. Slowly release the push button and pull the needle out of the skin.
9. Place a cotton ball or gauze over the injection site and press for several seconds. Do not massage the injection site. If there is bleeding, cover the injection site with a bandage.
10. It is important to check your injection site approximately 2 hours after your injection for redness, swelling, or tenderness. These are signs of inflammation that you may need to talk to your health care provider about if they do not go away.

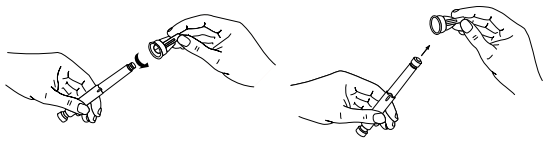
Removing the needle from the Multidose Pen

11. Using a scooping motion, **carefully** replace the outer clear needle cap (like capping a pen).

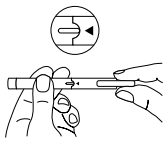


INTRON® A (Interferon alfa-2b, recombinant) Multidose Pen for Injection

12. Once capped, remove the needle by holding the clear outer needle cap with one hand and holding the pen barrel with the other hand, turning counterclockwise.



13. Carefully lift the needle off the pen and discard the capped needle. See *"How should I dispose of materials used to inject INTRON® A?"*
14. Replace the pen cap over the pen reservoir so that the black triangle is lined up with the dosage indicator.



Storing INTRON® A Solution Multidose Pen for Injection

INTRON A Solution Multidose Pen for Injection should be stored in the refrigerator between 2° and 8°C (36° and 46°F). Discard any unused INTRON A pen remaining after 4 weeks. **DO NOT FREEZE.**

How should I dispose of material used to inject INTRON® A?

There may be special state and local laws for disposal of used needles and Multidose Pens. Your health care provider should provide you with instructions on how to properly dispose of your used needles and Multidose Pens. Always follow those instructions. The instructions below should be used as a general guide for proper disposal.

- The needles should never be reused.
- Place all used needles and Multidose Pens in a puncture-proof disposable container that is available through your pharmacy or health care provider. You may use a hard plastic container with a screw-on cap (like a laundry detergent container). DO NOT use glass or clear plastic containers for disposal of needles.
- The container should be clearly labeled as "USED NEEDLES AND MULTIDOSE PENS." When the container is about two-thirds full, dispose of the container as instructed by your health care provider. DO NOT throw the container in your household trash. DO NOT recycle.
- **Always keep the container out of the reach of children.**

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