

Tambahan Indikasi yang diluluskan dalam Mesyuarat PBKD 408, 29 April 2025

*Products approved for additional indication (DCA 408 – 29 April 2025)*

No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
1.	BRUKINSA 80 mg capsules  [Zanubrutinib 80mg]	<b>INDICATION :</b>  BRUKINSA as monotherapy is indicated for the treatment of adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based therapy.	<b>BEIGENE MALAYSIA SDN. BHD.</b> Suite 33-34, Lot 4-401 & 4-402, Level 4, The Starling Mall, No. 6, Jalan SS 21/37, Damansara Uptown, 47400 Petaling Jaya, Selangor.

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2.	RAVIDA TABLET 200MG  [Ravidasvir Hydrochloride 200mg]	<p><b>POSOLOGY :</b></p> <p>Treatment with Ravida should be initiated and monitored by a physician experienced in the management of patients with chronic hepatitis C.</p> <p><u>Posology</u></p> <p>Adults</p> <p>The recommended dose of Ravida is 200 mg once daily, to be taken orally with or without food.</p> <p>Ravida must be used in combination with other medicinal products indicated for the treatment of chronic hepatitis C. The package insert for the co-administered medicinal products should be referred to before initiation of therapy with Ravida.</p> <p>Table 1: Recommended treatment for Ravida combination therapy in patients with compensated cirrhosis and without cirrhosis</p> <table border="1" data-bbox="539 919 1727 1038"> <thead> <tr> <th data-bbox="539 919 1106 959">Patient Population</th> <th data-bbox="1106 919 1727 959">Regimen and duration</th> </tr> </thead> <tbody> <tr> <td data-bbox="539 959 1106 999">Patients without cirrhosis</td> <td data-bbox="1106 959 1727 999">Ravida + sofosbuvir for 8 weeks</td> </tr> <tr> <td data-bbox="539 999 1106 1038">Patients with compensated cirrhosis</td> <td data-bbox="1106 999 1727 1038">Ravida + sofosbuvir for 24 weeks</td> </tr> </tbody> </table> <p>For HCV genotype information, see section Warnings and Precautions.</p> <p>Dose interruption and discontinuation If treatment interruption or discontinuation of the other medicinal products in the regimen is necessary, Ravida must not be given as monotherapy.</p> <p>Vomiting and missed doses Patients should be instructed that if vomiting occurs within 2 hours of dosing, an additional</p>	Patient Population	Regimen and duration	Patients without cirrhosis	Ravida + sofosbuvir for 8 weeks	Patients with compensated cirrhosis	Ravida + sofosbuvir for 24 weeks	<p><b>PHARMANIAGA MANUFACTURING BERHAD</b> 11A, Jalan P/1, Kawasan Perusahaan Bangi, 43650 Bandar Baru Bangi, Selangor.</p>
Patient Population	Regimen and duration								
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Patients with compensated cirrhosis	Ravida + sofosbuvir for 24 weeks								

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		<p>tablet should be taken. If vomiting occurs more than 2 hours after dosing, no additional dose for the day is needed. These recommendations are based on the absorption kinetics of ravidasvir, which are suggestive that the majority of the dose is absorbed within 2 hours after dosing.</p> <p>Patients should be instructed that, if they miss a dose of Ravida, the dose should be taken as soon as possible if remembered within 18 hours of the scheduled dose time. However, if the missed dose is remembered more than 18 hours after the scheduled dose, the dose should be skipped and the next dose taken at the appropriate time.</p>	

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3.	<p>Symvenu 1.5mg Hard Capsules</p> <p>[Cariprazine Hydrochloride 1.635mg (equivalent to 1.5mg Cariprazine)]</p> <p>Symvenu 3mg Hard Capsules</p> <p>[Cariprazine Hydrochloride 3.270mg (equivalent to 3mg Cariprazine)]</p>	<p><b>INDICATION :</b></p> <p>Symvenu® is indicated for</p> <ul style="list-style-type: none"> <li>• adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD) in adult patients (1.5mg and 3mg only). The long-term efficacy of Symvenu® as an adjunctive therapy to antidepressant has not been systematically evaluated in controlled studies (see Clinical efficacy and safety).</li> </ul> <p><b>POSODOLOGY :</b></p> <p>Adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD)</p> <p>The starting dose of cariprazine is 1.5 mg once daily. Depending upon clinical response and tolerability, the dosage can be increased to 3 mg once daily on Day 15. In clinical studies dosage titration at intervals of less than 14 days resulted in a higher incidence of adverse reactions. Maximum recommended dosage is 3 mg once daily. The physician who elects to use cariprazine for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.</p>	<p><b>mitsubishi tanabe pharma malaysia sdn. bhd.</b></p> <p>Suite 8-3, Level 8, Wisma UOA Damansara II, No. 6, Changkat Semantan, Damansara Heights, 50490 Kuala Lumpur, Wilayah Persekutuan Kuala Lumpur.</p>



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		<p><b>Table 1: Ravulizumab weight-based dosing regimen for adult patients with body weight greater than or equal to 40 kg</b></p> <table border="1" data-bbox="526 411 1704 703"> <thead> <tr> <th>Body weight range (kg)</th> <th>Loading dose (mg)</th> <th>Maintenance dose (mg)*</th> <th>Dosing interval</th> </tr> </thead> <tbody> <tr> <td>≥ 40 to &lt; 60</td> <td>2,400</td> <td>3,000</td> <td>Every 8 weeks</td> </tr> <tr> <td>≥ 60 to &lt; 100</td> <td>2,700</td> <td>3,300</td> <td>Every 8 weeks</td> </tr> <tr> <td>≥ 100</td> <td>3,000</td> <td>3,600</td> <td>Every 8 weeks</td> </tr> </tbody> </table> <p>* First maintenance dose is administered 2 weeks after loading dose</p> <p>Supplemental dosing following treatment with plasma exchange (PE), plasmapheresis (PP), or intravenous immunoglobulin (IVIg) Plasma exchange (PE), plasmapheresis (PP) and intravenous immunoglobulin (IVIg) have been shown to reduce ravulizumab serum levels. A supplemental dose of ravulizumab is required in the setting of PE, PP or IVIg (Table 2).</p> <p><b>Table 2: Supplemental dose of ravulizumab after PP, PE, or IVIg</b></p> <table border="1" data-bbox="526 1045 1720 1412"> <thead> <tr> <th>Body weight range (kg)</th> <th>Most recent ravulizumab dose (mg)</th> <th>Supplemental dose (mg) following each PE or PP intervention</th> <th>Supplemental dose (mg) following completion of an IVIg cycle</th> </tr> </thead> <tbody> <tr> <td rowspan="2">≥ 40 to &lt; 60</td> <td>2,400</td> <td>1,200</td> <td rowspan="2">600</td> </tr> <tr> <td>3,000</td> <td>1,500</td> </tr> <tr> <td>≥ 60 to &lt; 100</td> <td>2,700</td> <td>1,500</td> <td>600</td> </tr> </tbody> </table>	Body weight range (kg)	Loading dose (mg)	Maintenance dose (mg)*	Dosing interval	≥ 40 to < 60	2,400	3,000	Every 8 weeks	≥ 60 to < 100	2,700	3,300	Every 8 weeks	≥ 100	3,000	3,600	Every 8 weeks	Body weight range (kg)	Most recent ravulizumab dose (mg)	Supplemental dose (mg) following each PE or PP intervention	Supplemental dose (mg) following completion of an IVIg cycle	≥ 40 to < 60	2,400	1,200	600	3,000	1,500	≥ 60 to < 100	2,700	1,500	600	
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			3,300	1,800			
		≥ 100	3,000	1,500	600		
			3,600	1,800			
		<b>Timing of ravulizumab supplemental dose</b>		Within 4 hours following each PE or PP intervention	Within 4 hours following completion of an IVIg cycle		
		<p>Abbreviations: IVIg = intravenous immunoglobulin, kg = kilogram, PE = plasma exchange, PP = plasmapheresis</p> <p>PNH is a chronic disease and treatment with ravulizumab is recommended to continue for the patient's lifetime, unless the discontinuation of ravulizumab is clinically indicated (see section 4.4).</p> <p>In aHUS, ravulizumab treatment to resolve thrombotic microangiopathy (TMA) manifestations should be for a minimum duration of 6 months, beyond which length of treatment needs to be considered for each patient individually. Patients who are at higher risk for TMA recurrence, as determined by the treating healthcare provider (or clinically indicated), may require chronic therapy (see section 4.4).</p> <p>In patients with gMG or NMOSD, treatment with ravulizumab has only been studied in the setting of chronic administration (see section 4.4).</p> <p>Ravulizumab has not been studied in gMG patients with an MGFA Class V.</p>					

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		<p><u>Special populations</u></p> <p><b>Elderly</b> No dose adjustment is required for patients with PNH, aHUS, gMG, or NMOSD aged 65 years and over. There is no evidence indicating any special precautions are required for treating a geriatric population – although experience with ravulizumab in elderly patients with PNH, aHUS, or NMOSD in clinical studies is limited.</p> <p><b>Renal impairment</b> No dose adjustment is required for patients with renal impairment (see section 5.2).</p> <p><b>Hepatic impairment</b> The safety and efficacy of ravulizumab have not been studied in patients with hepatic impairment; however pharmacokinetic data suggest that no dose adjustment is required in patients with hepatic impairment.</p> <p><b>Paediatric population</b> Paediatric patients with PNH and aHUS with body weight <math>\geq 40</math> kg are treated in accordance with the adult dosing recommendations (Table 1). The weight-based doses and dosing intervals for paediatric patients <math>\geq 10</math> kg to <math>&lt; 40</math> kg are shown in Table 3.</p> <p>For patients switching from eculizumab to ravulizumab, the loading dose of ravulizumab should be administered 2 weeks after the last eculizumab infusion, and then maintenance doses should be administered per weight-based dosing regimen shown in Table 3, starting 2</p>	

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		<p>weeks after loading dose administration.</p> <p><b>Table 3: Ravulizumab weight-based dosing regimen for paediatric patients with PNH or aHUS below 40 kg</b></p> <table border="1" data-bbox="526 512 1709 804"> <thead> <tr> <th data-bbox="526 512 846 616">Body weight range (kg)</th> <th data-bbox="846 512 1111 616">Loading dose (mg)</th> <th data-bbox="1111 512 1395 616">Maintenance dose (mg)*</th> <th data-bbox="1395 512 1709 616">Dosing interval</th> </tr> </thead> <tbody> <tr> <td data-bbox="526 616 846 676">≥ 10 to &lt; 20</td> <td data-bbox="846 616 1111 676">600</td> <td data-bbox="1111 616 1395 676">600</td> <td data-bbox="1395 616 1709 676">Every 4 weeks</td> </tr> <tr> <td data-bbox="526 676 846 737">≥ 20 to &lt; 30</td> <td data-bbox="846 676 1111 737">900</td> <td data-bbox="1111 676 1395 737">2,100</td> <td data-bbox="1395 676 1709 737">Every 8 weeks</td> </tr> <tr> <td data-bbox="526 737 846 804">≥ 30 to &lt; 40</td> <td data-bbox="846 737 1111 804">1,200</td> <td data-bbox="1111 737 1395 804">2,700</td> <td data-bbox="1395 737 1709 804">Every 8 weeks</td> </tr> </tbody> </table> <p data-bbox="504 807 1395 839">* First maintenance dose is administered 2 weeks after loading dose</p> <p data-bbox="504 911 1720 1018">Data to support safety and efficacy of ravulizumab for patients with body weight below 10 kg are limited. Currently available data are described in section 4.8 but no recommendation on a posology can be made for patients below 10 kg body weight.</p> <p data-bbox="504 1066 1720 1249">Ravulizumab has not been studied in paediatric patients with PNH who weigh less than 30 kg. The posology of ravulizumab for paediatric patients less than 30 kg is based on the posology used for paediatric patients with aHUS, on the basis of the pharmacokinetic/pharmacodynamic (PK/PD) data available in aHUS and PNH patients treated with ravulizumab.</p> <p data-bbox="504 1297 1720 1369">The safety and efficacy of ravulizumab in children with gMG or NMOSD have not been established. No data are available.</p>	Body weight range (kg)	Loading dose (mg)	Maintenance dose (mg)*	Dosing interval	≥ 10 to < 20	600	600	Every 4 weeks	≥ 20 to < 30	900	2,100	Every 8 weeks	≥ 30 to < 40	1,200	2,700	Every 8 weeks	
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6.	<p>Opdivo 10mg/ml, Concentrate for solution for infusion</p> <p>[Nivolumab 10mg/ml]</p>	<p><b>INDICATION :</b></p> <p><u>Urothelial carcinoma</u></p> <p>OPDIVO in combination with cisplatin and gemcitabine is indicated for the first-line treatment of adult patients with unresectable or metastatic urothelial carcinoma.</p> <p><b>POSODOLOGY:</b></p> <p><u>First-line treatment of unresectable or metastatic urothelial carcinoma</u></p> <p>The recommended dose is 360 mg nivolumab administered intravenously over 30 minutes in combination with cisplatin and gemcitabine every 3 weeks for up to 6 cycles followed by nivolumab monotherapy administered intravenously at either 240 mg every 2 weeks over 30 minutes or at 480 mg every 4 weeks over 30 minutes (see section 5.1). Treatment with nivolumab is recommended until disease progression, unacceptable toxicity, or up to 24 months from first dose, whichever comes first.</p>	<p><b>DKSH MALAYSIA SDN. BHD.</b> B-11-01, The Ascent, Paradigm, No. 1, Jalan SS7/26A, Kelana Jaya, 47301 Petaling Jaya, Selangor.</p>

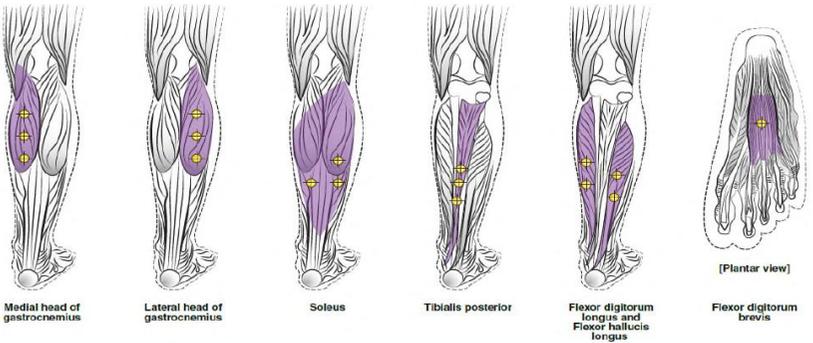
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7.	Adcetris 50mg, powder for concentrate for solution for infusion  [Brentuximab Vedotin 50mg]	<b>INDICATION :</b>  Adcetris is indicated for the treatment of adult patients with previously untreated CD30+ <b>Stage III</b> or IV Hodgkin lymphoma (HL), in combination with doxorubicin, vinblastine, and dacarbazine.	<b>TAKEDA MALAYSIA SDN BHD</b> Unit TB-L 13-1, Level 13, Tower B, Plaza 33, No.1, Jalan Kemajuan, Seksyen 13, 46200 Petaling Jaya, Selangor.

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8.	<p>BOTOX (BOTULINUM TOXIN TYPE A) IM INJECTION</p> <p>[Clostridium Botulinum Toxin Type A]</p>	<p><b>POSODOLOGY :</b></p> <p><u>BOTOX® Dosing by Muscle for Lower Limb Spasticity</u></p> <table border="1" data-bbox="510 435 1205 703"> <thead> <tr> <th>Muscle</th> <th>Recommended Dose Total Dosage (Number of Sites)</th> </tr> </thead> <tbody> <tr> <td>Gastrocnemius medial head</td> <td>75 Units divided in 3 sites</td> </tr> <tr> <td>Gastrocnemius lateral head</td> <td>75 Units divided in 3 sites</td> </tr> <tr> <td>Soleus</td> <td>75 Units divided in 3 sites</td> </tr> <tr> <td>Tibialis Posterior</td> <td>75 Units divided in 3 sites</td> </tr> <tr> <td>Flexor hallucis longus</td> <td>50 Units divided in 2 sites</td> </tr> <tr> <td>Flexor digitorum longus</td> <td>50 Units divided in 2 sites</td> </tr> <tr> <td>Flexor digitorum brevis</td> <td>25 Units in 1 site</td> </tr> </tbody> </table> <p><b>Figure</b> Injection Sites for Lower Limb Spasticity</p>  <p><u>Upper Facial Lines (Glabellar Lines, Crow's Feet and Forehead Lines):</u></p> <p>As optimum dose levels and number of injection sites per muscle may vary among patients, individual dosing regimens should be drawn up. The recommended injection volume per injection site is 0.1 mL.</p>	Muscle	Recommended Dose Total Dosage (Number of Sites)	Gastrocnemius medial head	75 Units divided in 3 sites	Gastrocnemius lateral head	75 Units divided in 3 sites	Soleus	75 Units divided in 3 sites	Tibialis Posterior	75 Units divided in 3 sites	Flexor hallucis longus	50 Units divided in 2 sites	Flexor digitorum longus	50 Units divided in 2 sites	Flexor digitorum brevis	25 Units in 1 site	<p><b>ABBVIE SDN BHD</b>            9th Floor Menara Lien Hoe,            No.8, Persiaran Tropicana,            Tropicana Golf &amp; Country Resort,            47410 Petaling Jaya,            Selangor.</p>
Muscle	Recommended Dose Total Dosage (Number of Sites)																		
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		<p><u>Glabellar Lines:</u></p> <p>BOTOX® is reconstituted with 0.9% sterile non-preserved saline (100 U in 2.5 mL or injected as 4 U/0.1 mL) and 0.1 mL is administered using a 30 gauge needle in each of 5 sites (see figure below), 2 in each corrugator muscle and 1 in the procerus muscle for a total dose of 20 U.</p> <p>Figure Injection Sites for Glabellar Lines</p>  <p>In order to reduce the complication of ptosis, avoid injection near the levator palpebrae superioris, particularly in patients with larger brow-depressor complexes. Medial corrugator injections should be placed at least 1 cm above the bony supraorbital ridge.</p> <p>In controlled clinical trials, improvement of severity of glabellar lines generally occurred within one week after treatment and the effect was demonstrated for up to 4 months. Typically the initial doses of reconstituted BOTOX® induce chemical denervation of the injected muscles one to two days after injection, increasing in intensity during the first week.</p>	

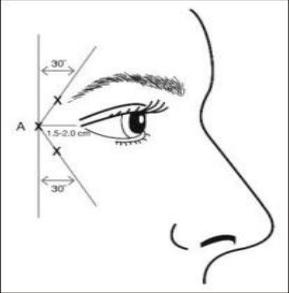
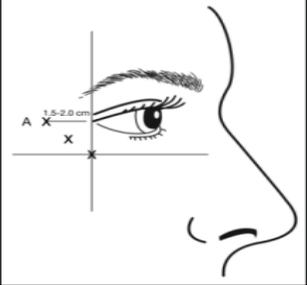
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		<p>Injection intervals should be no more frequent than every 3 months and should be performed using the lowest effective dose.</p> <p>Treatment with BOTOX® for cosmetic purposes may result in the formation of antibodies that may reduce the effectiveness of subsequent treatments with BOTOX® for glabellar lines or for other indications.</p> <p><u>Crow's Feet:</u></p> <p><b>Injections for Crow's Feet Lines should be given with the needle tip bevel up and oriented away from the eye. Using a 30-33 gauge needle, inject 4 Units/0.1 mL of reconstituted BOTOX® into 3 sites per side (6 total injection points) in the lateral orbicularis oculi muscle for a total of 24 Units/0.6 mL (12 Units per side). The first injection (A) should be made at approximately 1.5-2.0 cm temporal to the lateral canthus and just temporal to the orbital rim. If the lines in the crow's feet region are above and below the lateral canthus, inject per Figure below. Alternatively, if the lines in the crow's feet region are primarily below the lateral canthus, inject per Figure below.</b></p>	

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		<p><b>Figure Injection Sites for Crow's Feet Region Above and Below Lateral Canthus</b></p>  <p><b>Figure Injection Sites for Crow's Feet Region Primarily Below Lateral Canthus</b></p>  <p>For simultaneous treatment with glabellar lines, the dose is 24 Units for crow's feet lines and 20 Units for glabellar lines (see Glabellar Lines Administration and Figure above), with a total dose of 44 Units.</p> <p>The median time to onset of crow's feet lines treatment effect is three to four days. The duration of response with BOTOX® for crow's feet lines is up to 5 months. The safety and effectiveness of dosing with BOTOX® more frequently than every 3 months have not been evaluated.</p> <p><b><u>Forehead Lines:</u></b></p> <p>Using a 30 Gauge needle, inject 4 Units/0.1 mL of reconstituted BOTOX® into 5 sites in the frontalis muscle, for a total dose of 20 Units/0.5 mL (see Figure below).</p> <p>It is recommended to treat forehead lines in conjunction with glabellar lines (see Glabellar Lines Administration and Figure below) to minimize the potential for brow ptosis. The total dose for treatment of forehead lines (20 Units) in conjunction with glabellar lines (20 Units) is 40 Units/1.0 mL.</p>	

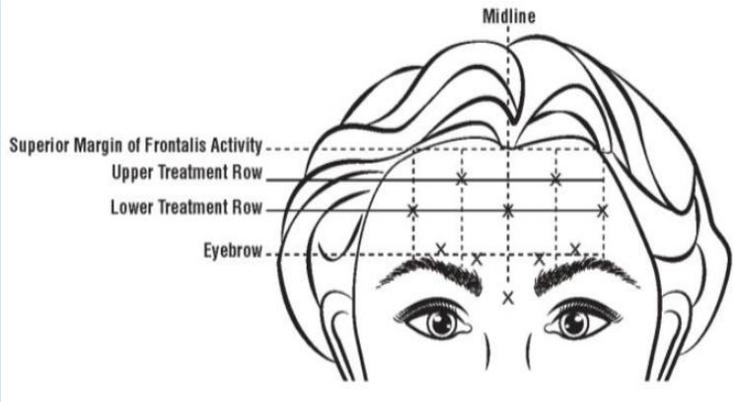
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		<p><b>When identifying the location of the appropriate injection sites in the frontalis muscle, assess the overall relationship between the size of the patient’s forehead, and the distribution of frontalis muscle activity.</b></p> <p><b>Locate the following horizontal treatment rows by light palpation of the forehead at rest and maximum eyebrow elevation:</b></p> <p><b>Superior Margin of Frontalis Activity: approximately 1 cm above the most superior forehead crease</b></p> <p><b>Lower Treatment Row: midway between the superior margin of frontalis activity and the eyebrow, at least 2 cm above the eyebrow</b></p> <p><b>Upper Treatment Row: midway between the superior margin of frontalis activity and lower treatment row</b></p> <p><b>Place the 5 injections at the intersection of the horizontal treatment rows with the following vertical landmarks:</b></p> <p><b>On the lower treatment row at the midline of the face, and 0.5 – 1.5 cm medial to the palpated temporal fusion line (temporal crest); repeat for the other side.</b></p> <p><b>On the upper treatment row, midway between the lateral and medial sites on the lower treatment row; repeat for the other side.</b></p>	

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		<p><b>Figure Injection Sites for Forehead Lines</b></p>  <p><b>Improvement in the severity of forehead lines seen at maximum eyebrow elevation occurred within one week of treatment.</b></p> <p><b>The time to retreatment of BOTOX<sup>®</sup> for forehead lines is approximately 4 months. The safety and effectiveness of dosing with BOTOX<sup>®</sup> more frequently than every 3 months have not been clinically evaluated.</b></p> <p><b>For simultaneous treatment with crow's feet lines, the total dose is 64 Units, comprising of 20 Units for forehead lines, 20 Units for glabellar lines, and 24 Units for crow's feet lines (see Crow's Feet Lines Administration).</b></p> <p><u>Hyperhidrosis Of The Axilla:</u></p> <p>The hyperhidrotic area to be injected may be defined using standard staining techniques, e.g. Minor's iodine-starch test. BOTOX<sup>®</sup> is reconstituted with 0.9% non-preserved sterile saline (100 U/4.0 mL). Using a 30 gauge needle, 50 U of BOTOX<sup>®</sup> (2.0 mL) is injected intradermally, to each axilla evenly distributed in multiple sites approximately 1-2 cm apart.</p>	

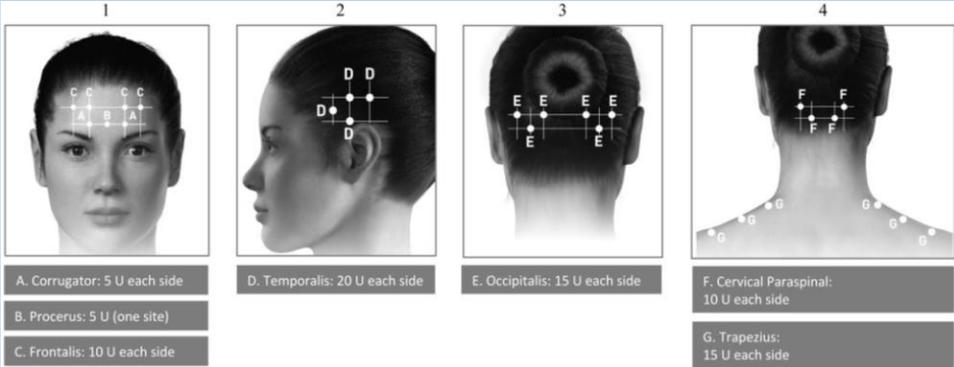
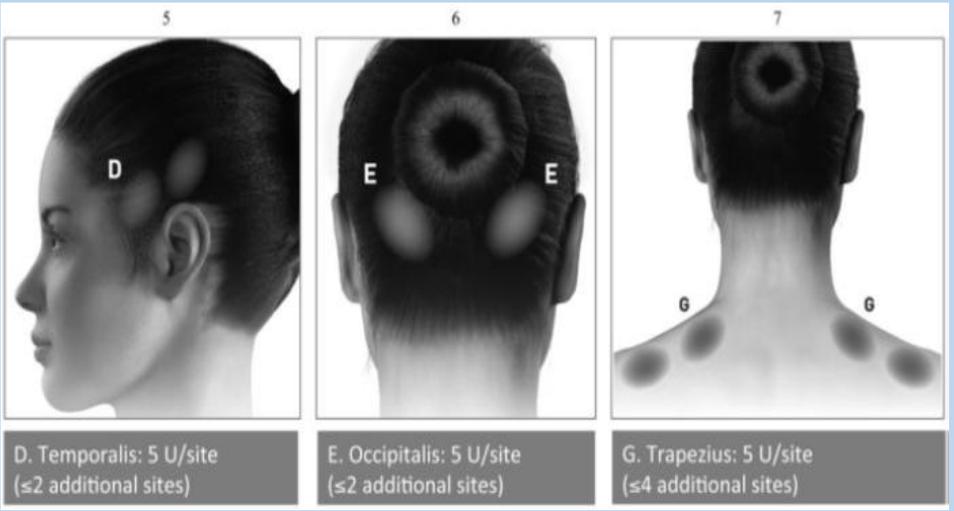
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		<p>At week 1 BOTOX<sup>®</sup> treated patients demonstrated 95% treatment responder rate based on gravimetric assessment. At 16 weeks 82% of BOTOX<sup>®</sup> treated patients were responding to treatment. Approximately 40% of patients received only 1 treatment with BOTOX<sup>®</sup> and had duration of effect for over 1 year (median time 68 weeks). When patients received at least 2 consecutive treatments with BOTOX<sup>®</sup> the mean time to re-treatment following their first treatment was 33 weeks (range 15 to 51 weeks). Repeat injections for axillary hyperhidrosis should be administered when effects from previous injections subside but usually not more frequently than every two months.</p> <p><u>Chronic Migraine:</u></p> <p>The recommended dilution is 100 U/2 mL, with a final concentration of 5 U per 0.1 mL. The recommended dose for treating chronic migraine is 155 U to 195 U administered intramuscularly (IM) using a sterile 30- gauge, 0.5 inch needle as 0.1 mL (5 U) injections per each site. Injections should be divided across 7 specific head/neck muscle areas as specified in the diagrams and table below. A 1 inch needle may be needed in the neck region for patients with thick neck muscles. With the exception of the procerus muscle, which should be injected at 1 site (midline), all muscles should be injected bilaterally with the minimum dose per muscle as indicated below, with half the number of injection sites administered to the left, and half to the right side of the head and neck. The recommended re-treatment schedule is every 12 weeks. If there is a predominant pain location(s), additional injections to one or both sides may be administered in up to 3 specific muscle groups (occipitalis, temporalis, and trapezius), up to the maximum dose per muscle as indicated in the table below.</p>	

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No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
		<p>i. Diagrams 1 – 4: Recommended injection sites for minimum 155 U dose for chronic migraine</p>  <p>ii. Diagrams 5-7: Recommended muscle groups for optional additional injections for chronic migraine</p> 	

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		<p>BOTOX<sup>®</sup> Dosing By Muscle for Chronic Migraine</p> <table border="1" data-bbox="506 371 1570 778"> <thead> <tr> <th></th> <th>Recommended Dose</th> </tr> <tr> <th>Head/Neck Area</th> <th>Total Number of Units (U) (number of IM injection sites<sup>a</sup>)</th> </tr> </thead> <tbody> <tr> <td>Frontalis<sup>b</sup></td> <td>20 U (4 sites)</td> </tr> <tr> <td>Corrugator<sup>b</sup></td> <td>10 U (2 sites)</td> </tr> <tr> <td>Procerus</td> <td>5 U (1 site)</td> </tr> <tr> <td>Occipitalis<sup>b</sup></td> <td>30 U (6 sites) up to 40 U (up to 8 sites)</td> </tr> <tr> <td>Temporalis<sup>b</sup></td> <td>40 U (8 sites) up to 50 U (up to 10 sites)</td> </tr> <tr> <td>Trapezius<sup>b</sup></td> <td>30 U (6 sites) up to 50 U (up to 10 sites)</td> </tr> <tr> <td>Cervical Paraspinal Muscle Group<sup>b</sup></td> <td>20 U (4 sites)</td> </tr> <tr> <td><b>Total Dose Range:</b></td> <td><b>155 U to 195 U (31 to 39 sites)</b></td> </tr> </tbody> </table> <p><sup>a</sup> Each IM injection site = 0.1 mL = 5 U BOTOX<sup>®</sup></p> <p><sup>b</sup> Dose distributed bilaterally for the minimum dose</p> <p><u>Bladder Dysfunction (Neurogenic Detrusor Overactivity and Overactive Bladder):</u></p> <p>Patients should not have a urinary tract infection prior to treatment. Prophylactic antibiotics should be administered 1-3 days pre-treatment, on the treatment day, and 1-3 days post-treatment.</p> <p>It is generally recommended that patients discontinue anti-platelet therapy at least three days before the injection procedure. Patients on anti-coagulant therapy need to be managed appropriately to decrease the risk of bleeding.</p> <p><u>Neurogenic Detrusor Overactivity:</u></p> <p>An intravesical instillation of diluted local anaesthetic with or without sedation, or general anaesthesia may be used prior to injection, per local site practice. If a local anaesthetic instillation is performed, the bladder should be drained and irrigated with sterile saline before injection.</p>		Recommended Dose	Head/Neck Area	Total Number of Units (U) (number of IM injection sites <sup>a</sup> )	Frontalis <sup>b</sup>	20 U (4 sites)	Corrugator <sup>b</sup>	10 U (2 sites)	Procerus	5 U (1 site)	Occipitalis <sup>b</sup>	30 U (6 sites) up to 40 U (up to 8 sites)	Temporalis <sup>b</sup>	40 U (8 sites) up to 50 U (up to 10 sites)	Trapezius <sup>b</sup>	30 U (6 sites) up to 50 U (up to 10 sites)	Cervical Paraspinal Muscle Group <sup>b</sup>	20 U (4 sites)	<b>Total Dose Range:</b>	<b>155 U to 195 U (31 to 39 sites)</b>	
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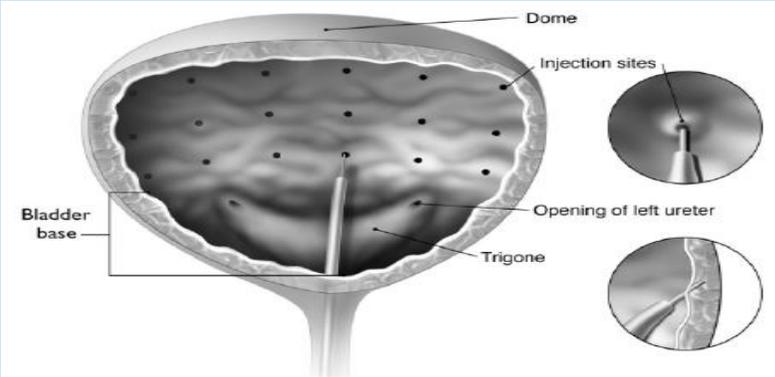
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No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
		<p>The recommended dose is 200 U of BOTOX®.</p> <p>Reconstitute two 100 Unit vials of BOTOX®, each with 6 mL of 0.9% non-preserved saline solution and mix the vials gently. Draw 4 mL from each vial into each of two 10 mL syringes. Draw the remaining 2 mL from each vial into a third 10 mL syringe. Complete the reconstitution by adding 6 mL of 0.9% non-preserved saline solution into each of the 10 mL syringes, and mix gently. This will result in three 10 mL syringes each containing 10 mL (~67 U in each), for a total of 200 U of reconstituted BOTOX®. Use immediately after reconstitution in the syringe. Dispose of any unused saline.</p> <p>Reconstitute a 200 Unit vial of BOTOX® with 6 mL of 0.9% non-preserved saline solution and mix the vial gently. Draw 2 mL from the vial into each of three 10 mL syringes. Complete the reconstitution by adding 8 mL of 0.9% non-preserved saline solution into each of the 10 mL syringes, and mix gently. This will result in three 10 mL syringes each containing 10 mL (~67 U in each), for a total of 200 U of reconstituted BOTOX®. Use immediately after reconstitution in the syringe. Dispose of any unused saline.</p> <p>Reconstituted BOTOX® (200 U/30 mL) is injected into the detrusor muscle via a flexible or rigid cystoscope, avoiding the trigone. The bladder should be instilled with enough saline to achieve adequate visualization for the injections, but over-distension should be avoided.</p> <p>The injection needle should be filled (primed) with approximately 1 mL prior to the start of injections (depending on the needle length) to remove any air.</p> <p>The needle should be inserted approximately 2 mm into the detrusor, and 30 injections of 1mL each (total volume of 30 mL) should be spaced approximately 1 cm apart (see Figure <b>below</b>). For the final injection, approximately 1 mL of sterile normal saline should be injected so the full dose is delivered. After the injections are given, the saline used for bladder wall visualization should be drained. The patient should be observed for at least 30 minutes post-injection.</p>	

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		<p>Clinical improvement may occur within 2 weeks. Patients should be considered for reinjection when the clinical effect of the previous injection diminished (median duration in phase 3 clinical studies was 256- 295 days (36-42 weeks) for BOTOX® 200 U), but no sooner than 3 months from the prior bladder injection. Based on patients who received treatments with only BOTOX® 200 Units from the pivotal studies through the open label extension study (N=174), the overall median duration of response was 253 days (~36 weeks).</p> <p>In the pivotal studies (300 Units and 200 units), none of the 475 neurogenic detrusor overactivity patients with analysed specimens developed the presence of neutralizing antibodies. In patients with analysed specimens in the drug development program (including the open-label extension study), neutralizing antibodies developed in 3 of 300 patients (1.0%) after receiving only Botox® 200 unit doses and 5 of 258 patients (1.9%) after receiving at least one 300 Unit dose. Four of these eight patients continued to experience clinical benefit.</p> <p>i. <b>Figure</b> : Injection Pattern for Intradetrusor Injections for Treatment of Neurogenic Detrusor Overactivity and Overactive Bladder</p> 	

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No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
		<p><u>Overactive Bladder:</u></p> <p>An intravesical instillation of diluted local anaesthetic with or without sedation may be used prior to injection, per local site practice. If a local anaesthetic instillation is performed, the bladder should be drained and irrigated with sterile saline before injection.</p> <p>The recommended dose is 100 U of BOTOX®. The recommended dilution is 100 U/10 mL with 0.9% nonpreserved saline solution (see dilution table). Dispose of any unused saline.</p> <p>Reconstituted BOTOX® (100 U/10 mL) is injected into the detrusor muscle via a flexible or rigid cystoscope, avoiding the trigone. The bladder should be instilled with enough saline to achieve adequate visualization for the injections, but over-distension should be avoided.</p> <p>The injection needle should be filled (primed) with approximately 1 mL of reconstituted BOTOX® prior to the start of injections (depending on the needle length) to remove any air.</p> <p>The needle should be inserted approximately 2 mm into the detrusor, and 20 injections of 0.5 mL each (total volume of 10 mL) should be spaced approximately 1 cm apart (see <b>Figure above</b>). For the final injection, approximately 1 mL of sterile normal saline should be injected so the full dose is delivered. After the injections are given, the saline used for bladder wall visualization should not be drained so that patients can demonstrate their ability to void prior to leaving the clinic. The patient should be observed for at least 30 minutes post-injection and until a spontaneous void has occurred.</p> <p>Clinical improvement may occur within 2 weeks. Patients should be considered for reinjection when the clinical effect of the previous injection has diminished (median duration in phase 3 clinical studies was 166 days [~24 weeks]), but no sooner than 3 months from the prior bladder injection. Based on patients who received treatments with only BOTOX® 100 Units from the pivotal studies through the open label extension study (N=438), the overall median duration of response was ~212 days (~30 weeks).</p> <p>In the pivotal studies, none of the 615 (0%) patients with analysed specimens developed the</p>	

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		presence of serum neutralizing antibodies to Botox <sup>®</sup> . In patients with analyzed specimens from the pivotal phase 3 and the open-label extension studies, neutralizing antibodies developed in 0 of 954 patients (0.0%) while receiving Botox <sup>®</sup> 100 Unit doses and 3 of 260 patients (1.2%) after subsequently receiving at least one 150 Unit dose. One of these three patients continued to experience clinical benefit.	